Clinical Benefits and Safety of Polynucleotides Injections for the Treatment of Painful Tendinopathies: A Multicenter, Single-Cohort, Retrospective Study

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Article

Clinical Benefits and Safety of Polynucleotides Injections for the Treatment of Painful Tendinopathies: A Multicenter, Single-Cohort, Retrospective Study

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Abstract: Background: Tendons, along with joints, are among the most affected structures in musculoskeletal disorders. This multicenter, single-cohort, retrospective clinical study evaluated the clinical benefits of Polynucleotides (PNs) injections in reducing pain and improving functionality in patients with tendinopathies. **Methods:** This retrospective study included 68 patients with different tendinopathies, all diagnosed with persistent pain lasting at least six weeks, accompanied by functional impairment and swelling. Three periarticular/peritendinous injections of a PNs-based medical device were administered at T0 (baseline), FU-1 (two weeks post-T0), and FU-2 (four weeks post-T0), with efficacy and safety assessments at FU-1, FU-2, FU-3 (eight weeks post-FU-2), and FU-4 (24 weeks post-FU-2) groups. The primary outcome measure was pain reduction, assessed using a numerical rating scale (NRS). Secondary outcomes were the Clinical Global Impression–Improvement scale (CGI-I), and patient satisfaction using a 5-point Likert scale. **Results:** Longitudinal analysis showed an average NRS score reduction of -1.76±0.08 at each follow-up, with statistically significant reductions observed between each follow-up and the final one (FU-4). Based on the CGI-I scale, 78% of the clinicians rated the clinical condition of tendinopathies at FU-4 as "very much improved" or "much improved." Additionally, 88% of patients reported being "satisfied" or "very satisfied" with treatment at the final follow-up (FU-4). No adverse events were reported. **Conclusions:** As demonstrated by the positive outcomes reported in this study, PNs injections may offer a promising therapeutic option for the treatment of tendinopathies. This study may open up new frontiers for the implementation of conservative approaches in patients affected by tendinopathies.

Keywords: tendons; tendinopathy; polynucleotides; injections; pain

1. Introduction

Tendons are vital components of the musculoskeletal system that facilitate movement and support mechanical load. Tendon disorders encompass tears and chronic diseases and represent a common musculoskeletal issue [1]. Tendon pathologies frequently affect athletes due to overuse and involve several anatomical sites such as the rotator cuff, long head of the brachial biceps, extensors and flexors of the wrist in the upper limbs, thigh adductors, patellar tendon, posterior tibial tendon, and Achilles tendon in the lower limbs [1,2]. At least 50% of tendon issues are associated with an overload. Tendon tears (partial or complete) can occur after acute traumatic stress or as a consequence of chronic degenerative condition [3]. The term "tendinopathy" refers to a clinical condition characterized by pain, swelling, and functional limitations of the tendon and nearby structures, and seems to be the effect of a chronic failure of the healing response process [4]. Both intrinsic and extrinsic factors play a key role in the pathogenesis of tendinopathy. Age and sex are the most prominent non-modifiable factors, while excessive and/or improper loading, disuse, drugs, and smoking habits are the

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most influential modifiable factors [4,5]. Tendinopathy can be viewed as the failure of the cell matrix to adapt to a variety of stresses as a result of an imbalance between matrix degeneration and synthesis [6,7].

The management of tendinopathy remains a challenge. The first-line treatment is usually conservative and includes rest, drugs, cryotherapy, physical therapy (such as eccentric training), extracorporeal shockwave treatment (ESWT), orthosis, and injections [8–13]. Surgery was indicated when conservative treatment fails [14]. Among conservative treatments, injections are a promising option [15]. Corticosteroid (CS) injections have been widely used for the treatment of tendinopathies and have reported good short-term pain relief outcomes [16]. However, the way CS injections work for the treatment of tendinopathy and their safety, particularly of repeated use, remains unclear, given the absence of substantial signs of inflammation in tendinopathies and the tenotoxicity revealed in several studies [16]. Platelet-rich plasma (PRP) injections have been shown to provide more long-term effects on pain relief and improve functionality [17]; however, their efficacy is still under debate owing to the lack of strong evidence supporting their use [17,18].

Other injectable treatments, such as sclerosing polidocanol, have been shown to be effective in managing tendinopathies [19] yielding results similar to those achieved with peritendinous hyaluronic acid injections [20]. However, high-volume injections, administered without CS and alongside standard care, were ineffective in reducing symptoms [21].

To find alternative but safe and effective conservative options, several studies have recently reported that polynucleotides (PNs) have some effects on musculoskeletal pain, resulting in less difficulty in performing activities of daily living [22]. PNs are extracted from natural sources (trout gonads) by purification and high-temperature sterilization [23]. Derivatives of enzyme degradation of polynucleotide chains (simple nucleotides, nucleosides, and nitrogen bases) are physiologically present in the extracellular environment and are useful substrates for cells. Intraarticular injection progressively enriches the synovial fluid of PNs and thus of nucleotides, purine, and pyrimidine bases that cells can use to promote their vitality [24].

Furthermore, PNs administration in rat rotator cuff repair models showed satisfactory outcomes in terms of tendon healing and reduced fatty degeneration [25]. This healing process can also be reproduced in the context of tendinopathy, creating an ideal environment for the healing of damaged tendons.

Given these premises, the hypothesis of the present multicenter, single-cohort, retrospective observational clinical investigation was that periarticular injections of a medical device, PNs-based gel, would reduce pain and improve functionality in patients affected by different tendinopathies

A preliminary extract of this study was recently published by Gervaso et al. [26], demonstrating that PNs injections for hip bursitis and biceps brachii tendinopathy significantly improve pain and functional limitations.

2. Materials and Methods

For this multicenter, single-cohort, retrospective study, medical records containing clinical data of patients with chronic tendinopathies were retrieved and analyzed from the databases of the participating clinics. These included the Bioanalysis Multidisciplinary Medical Center in Codevilla, Pavia, Italy; “San Pio da Pietrelcina” Hospital in Vasto, Italy; “Celio” Military Hospital; and Policlinico Luigi Di Liegro in Rome. The data covered patient admissions from February 2023 to June 2024.

Data processing was carried out by physicians from the Italian Tendinopathies Study Group affiliated with the aforementioned Clinics. Subsequently, two authors of this study (ADI and RP) conducted further analyses to develop a customized database containing clinical information and anonymized personal data. The unique digital code assigned at the outset of this study phase ensured the maintenance of patient anonymity.

The study was performed in accordance with the standard of good clinical practice and in accordance with the Helsinki Declaration of 1975. Approval was obtained from the local IRB (CRRM2024, 06, 06, 01).

All patients included in the database provided informed consent before undergoing treatment, after which comprehensive clinical data were analyzed. The informed consent process followed these steps: (1) explanation of the treatment to the patient, (2) patient agreement, (3) completion of the consent form, (4) data verification, (5) signature, and (6) assignment of an anonymous code.

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2.1. Inclusion and Exclusion Criteria

The inclusion criteria were men and women aged 18 years or older in good general health and diagnosed with tendinopathy characterized by pain in the affected tendon elicited performing specific tests for each kind of tendinopathy (such as the Jobe's test for supraspinatus tendinopathy or the Royal London Hospital test for Achilles tendinopathy) for at least six weeks, along with impaired functionality, morning stiffness, weakness, and reduced physical and sports performance [27], and a baseline numerical rating scale (NRS) score of four or higher (on a scale of 0 to 10).

Exclusion criteria included the absence of major orthopedic and rheumatologic conditions (i.e., recent trauma or bone fractures near the affected tendon, autoimmune diseases that could affect the tendon-to-bone interface such as rheumatoid arthritis, etc.), joint infections, acute synovitis, other treatments with other injectable drugs or medical devices within six months prior to enrollment, paratendinopathy, partial or total tendon rupture, previous tendon surgery, known hypersensitivity to seafood products or any component or procedure used in data collection, and concomitant pathologies (i.e., uncontrolled diabetes mellitus, peripheral neuropathy, autoimmune or inflammatory conditions, severe metabolic and oncological diseases) that could increase general health risk. Other exclusion criteria included the use of systemic or topical steroids within the last 24 weeks and/or immunosuppressive drugs within the last three months, repeated use of nonsteroidal anti-inflammatory drugs in the past week or occasional use in the last 24 hours, recent history of medication or drug abuse within the last six months, pregnancy, and breastfeeding.

2.2. Injection Protocol and Follow-Up

Patients received three periarticular or peritendinous injections of a 15 mg/2 mL viscoelastic, pyrogen-free, sterile gel containing PNs derived from a High Purification Technology (PN HPT™) (Tropho Tend©, Mastelli, Sanremo, Italy) at the following time points: T0 (baseline), T1 (two weeks after T0), and T2 (four weeks after T0). The injections were administered by physicians from the aforementioned Clinics, who are members of the Italian Tendinopathies Study Group, at the myotendinous (MTJ) or osteotendinous (OTJ) junctions, utilizing 25-30 G needles following proper skin disinfection with chlorhexidine and povidone-iodine.

The patients were monitored for seven months, with a total of five outpatient visits (T0, baseline; T1= two weeks after T0; T2= four weeks after T0; T3= eight weeks after T2; and T4, 24 weeks after T2). The results were compared with those at baseline (T0).

2.3. Score Evaluations

Improvement or worsening of pain intensity was assessed using the NRS. We also assessed, as a secondary outcome, the pain-related functional joint limitation addressed to patients (i.e., how much their movement was limited by pain), and we then referred to it as "VAS-function" scale ranging from 0 to 10, where 0 means no limitations. The Clinical Global Impression–Improvement scale (CGI-I), a 7-point scale (1=very much improved; 2=much improved; 3=minimally improved; 4=no improvement; 5=minimally worse; 6=much worse; 7=very much worse), was used by clinicians to rate disease progression at follow-ups. Patient satisfaction was evaluated using a 5-point Likert scale (1=very dissatisfied, 2=dissatisfied, 3=indifferent, 4=satisfied, and 5=very satisfied). An average reduction of 40% in the VAS scores from baseline (T0) to the final appointment (T4) was considered indicative of significant clinical improvement. Other expected outcomes included overall improvement and patient satisfaction at the end of the study.

The patients were advised to avoid strenuous physical activities at home. Additionally, they were asked to document any potential adverse events (such as pain, swelling, heat, or functional limitations), particularly following injections, and report them to their physician for further evaluation. If needed, ice packs and acetaminophen were permitted.

2.4. Statistical Analysis

Descriptive data were presented as absolute numbers and percentages for categorical variables. Linear mixed models with random intercepts and slopes were applied using time since enrollment as the time scale. Three models were used to sequentially analyze changes in the NRS score and VAS function: the first, an Unconditional Means Model (Model A), considering the population averages for both variables under study. Second, an Unconditional Growth Model (Model B) was used to

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assess the effects of time within the study. Third, a Saturated Model (Model C) examined the effects of age, sex, BMI, and second-order interaction between time in the study and age. All data processing and statistical analyses were conducted using SAS version 9.4 for Windows (SAS Institute, Inc., Cary, NC), with statistical significance set at P <0.05 (two-sided).

3. Results

A total of 68 patients were recruited (69 tendinopathies, including one patient with bilateral tendinopathy) of whom 34 were male (49.28%). There were no significant age differences between males and females (64.00±14.26 vs. 65.26±12.12, p=0.70). The most reported conditions among the participants were gluteal tendinopathy (34 patients, 49.28%), biceps tendinopathy (10 patients, 14.49%), and Achilles tendinopathy (seven patients, 10.14%) (Table 1). On average, men had a higher BMI than women, although the difference was not statistically significant (26.07±3.48 vs. 24.38±4.28, age-adjusted p=0.08).

Table 1. Frequency distribution of the treated tendons.

Tendons	Number	Frequency
Achilles tendinopathy	7	10.14
Biceps tendinopathy	10	14.49
Epicondylitis	3	4.35
Epitrocleitis	2	2.90
Gluteal tendinopathy	34	49.28
Latissimus Dorsi	1	1.45
Patellar tendinopathy	2	2.90
Plantar fasciitis	2	2.90
Rotator cuff	3	4.35
Supraspinatus tendinopathy	3	4.35
Triceps tendinopathy	1	1.45
Trochanteritis	1	1.45

3.1. NRS-Score for Pain

In the Unconditional Means Model, the population had an average NRS score for pain of 7.74±0.19, with a within-person variance of 1.92±0.19, and a between-person variance of 1.51±0.46 (Table 2).

Table 2. Mixed Model: Analysis of variation of NRS-score for pain during follow-ups according to age, times of the study, sex, and BMI.

		Model A Unconditional Means Model	Model B Unconditional Growth Model	Model C Saturate model
Intercept	γ_{00}	7.74±0.19 ***	7.94±0.20 ***	3.32±1.65 *
Age	γ_{01}			0.06±0.01 ***
Sex	γ_{02}			0.25±0.31
BMI	γ_{03}			0.02±0.04
Intercept (time)	γ_{10}		-1.76±0.08 ***	-1.01±0.38 **
Interacion age*time	γ_{10}*γ_{01}			-0.02±0.01 *
Within person	δ^2_e	1.92±0.19 ***	1.89±0.19 ***	1.88±0.19 ***
In initial status	δ^2_0	1.51±0.46 ***	1.62±0.48 ***	1.06±0.40 **
In rate of change	δ^2_1		0.22±0.07 **	0.20±0.07 **
Covariance	δ_{01}		-0.23±0.15	-0.12±0.14
Intraclass correlation	ϱ	0.44		
	AIC	1538.3	1369.8	1342.1

Note: $\gamma 00$ = intercept of the average trajectory; $\gamma 01$ = intercept of the age trajectory; $\gamma 02$ = intercept of the sex trajectory; $\gamma 03$ = intercept of the BMI trajectory; $\gamma 10$ = intercept time effect; $\gamma 10$* $\gamma 01$ = intercept for the interaction at the time of the study effect for age; δ 2 e = within-person variance components; δ 2 0 = initial status variance

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components; δ 2 1 = rate of change variance components; δ01 = covariance estimate; ϱ = intraclass correlation; AIC = Akaike information criterion. * p-value<0.05; ** p-value<0.01; *** p-value<0.001.

Approximately 44% of the total variation was attributed to differences between the subjects (Table 2, Model A). In the Unconditional Growth Model, which examined the effects of different time points in the study, there was an average reduction of -1.76±0.08 per time point (p<0.001) (Table 2, Model B). Figure A1 (Appendix A) presents age-related trends in residuals stratified by study time. At each time point, a decrease in NRS scores for pain was observed with age, and the differences between each follow-up and the final one (FU-4) were statistically significant (Baseline vs. FU-4:7.07±0.30, p<0.001; FU-1 vs. FU-4:3.84±0.24, p<0.001; FU-2 vs. FU-4:1.83±0.17, p<0.001; FU-3 vs. FU-4:0.35±0.08, p<0.001). Additionally, older subjects had higher baseline pain scores but showed greater improvement during follow-ups compared to younger patients.

Finally, in Model C, the fully saturated model, it was found that there was a second-order effect for the interaction between study time and age. This means that older patients reported higher NRS pain scores, and the reduction in pain during the study was less pronounced compared to younger patients (-0.02±0.01; interaction p-value = 0.04).

3.2. VAS-Function

In the Unconditional Means Model, the population had an average VAS-function score of 4.26±0.18 with a within-person variance of 10.23±0.88 and a between-person variance of 0.14±0.41.

Approximately 2% of the total variation was attributable to the differences between individuals (Table 3, Model A). In the Unconditional Growth Model, which accounted for the effect of various study time points, there was an average reduction of -1.74±0.07 per time point (p<0.001) (Table 3, Model B).

Table 3. Mixed Model: Analysis of variation of VAS-Function during the follow-up according to age, times of the study, sex, and BMI.

		Model A Unconditional Means Model	**Model B Unconditional Growth Model**	**Model C Saturate model**
Intercept	γ_{00}	4.26±0.18 ***	7.75±0.23 ***	1.71±1.78
Age	γ_{01}			-0.07±0.01 ***
Sex	γ_{02}			0.36±0.33
BMI	γ_{03}			-0.02±0.04
Intercept (time)	γ_{10}		-1.74±0.07 ***	-0.60±0.37
Interacion age*time	γ_{10}*γ_{01}			-0.02±0.001 **
Within person	δ^2_e	10.23±0.88 ***	1.97±0.20 ***	1.96±0.20 ***
In initial status	δ^2_0	0.14±0.41	2.28±0.60 ***	1.29±0.45
In rate of change	δ^2_1		0.22±0.07 **	0.17±0.06 **
Covariance	δ_{01}		-0.35±0.17 *	-0.12±0.14
Intraclass correlation	ϱ	0.02		
	AIC	1750.4	1363.5	1329.2

Note: γ00 = intercept of the average trajectory; γ01 = intercept of the age trajectory; γ02 = intercept of the sex trajectory; γ03 = intercept of the BMI trajectory; γ10 = intercept time effect; γ10* γ01 = intercept for the interaction at the time of the study effect for age; δ 2 e = within-person variance components; δ 2 0 = initial status variance components; δ 2 1 = rate of change variance components; δ01 = covariance estimate; ϱ = intraclass correlation; AIC = Akaike information criterion. * p-value<0.05; ** p-value<0.01; *** p-value<0.001.

It is interesting to note in Figure A2 (Appendix A) that with increasing age, the pain from tendinopathy was perceived as more disabling (the slope of the lines is very steep at baseline and tends to flatten during the FU).

Stratifying by study time, a decrease in VAS function scores was observed at each time point, with statistically significant differences between the time points, using FU-4 as the reference (baseline vs. FU-4:6.92±0.32, p<0.001; FU-1 vs. FU-4:3.72±0.23, p<0.001; FU-2 vs. FU-4:1.73±0.16, p<0.001; FU-3 vs. FU-4:0.27±0.08, p<0.001). In Model C, the fully saturated model, the effect of follow-up time was no longer significant (p=0.11) because the variance was explained by the second-order interaction

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between study time and age. Older patients reported higher VAS disability scores, and the decrease in disability during the study was less noticeable compared to younger patients (-0.02±0.01; interaction p-value = 0.002).

3.3. Satisfaction

Patient satisfaction with treatment (scored 0-4, with 0 being very dissatisfied) improved throughout the follow-up period. Using FU-4 as the reference point, FU-1 showed an improvement of -0.46±0.10 ($p<0.001$), FU-2 showed -0.26±0.08 ($p<0.001$), and FU-3 showed -0.07±0.03 ($p=0.02$) compared to FU-4. For the CGI (0-7), a high level of satisfaction was already seen at FU-1 (0.49±0.09, $p<0.001$), which decreased at FU-2 (0.20±0.08, $p=0.02$) and was no longer statistically significant by FU-3 (0.03±0.04, $p=0.48$) compared to FU-4. Three patients left the study: one due to a superficial allergic skin reaction that resolved spontaneously, another due to a lack of perceived benefit after the second injection, and the third because of significant improvement after the first injection, making further treatment unnecessary. Finally, physicians were asked to assess the device used for infiltration and evaluate its handling, ease of performing the procedure, and ease of extraction. The device consistently received high ratings for manageability and ease of use across all components.

4. Discussion

Managing tendinopathies remains a significant challenge; however, recent advancements in conservative treatments, particularly injectable drugs, show promise. In this multicenter, single-cohort, retrospective observational clinical study, three injections of PNs administered biweekly for three times demonstrated a statistically significant improvement in both NRS-score for pain and VAS-function scores at each FU. Clinicians' satisfaction, measured using the CGI-I, also showed significant improvements at FU-1 and FU-2, with a slight decrease at FU-2 compared to FU-1, but no significant changes were noted at FU-3 and FU-4. Additionally, the Likert scale revealed significant patient satisfaction at all four follow-ups.

PNs, a medical device gel comprising salified chains of deoxyribonucleic acids [23], function through both non-pharmacological and pharmacological mechanisms [28]. These mechanisms include cell differentiation, fibroblast maturation, collagen production, tissue regeneration [23], and inflammation reduction, partially inhibiting the NF-κB pathway and increasing the Smad2/3 pathway, and via adenosine A2A receptor stimulation [29,30].

PNs significantly increased, in vitro, protein synthesis and collagen I and collagen III production [23]. In an experimental mouse model comparing four superficial intradermal injections of PNs, hyaluronic acid, and NaCI 0.9% saline solution as the control group, all the animals were observed for 24, 48, and 72 h, one and two weeks, and then the injected tissues were obtained from the sacrificed animals and analysed to assess tissue composition. The authors demonstrated that PNs injections enhance fibroblast growth and viability; moreover, they observed a significant increase in cellularity in the treated cultures [23].

PNs have been demonstrated to be effective for OA and cute repair with anti-aging effects [28,31]. PNs are polymers that form a three-dimensional gel that can embed water, and when intraarticular injection could hydrate cartilage, restoring a more favorable environment for chondrocytes [28]. Although PNs injections have been studied for treating knee osteoarthritis [32–35], their effectiveness in managing tendinopathies remains underexplored, as no studies have been conducted so far.

The progressive spread of PNs in clinical practice might reduce the use of CS in the treatment of tendinopathies, thus also improving the treatment of these tendon ailments in diabetic patients who could not receive local CS injections because of their underlying pathology [24,36]. Furthermore, CS injections do not completely alleviate pain, and medium- and long-term responses are much lower than the initial effects [37]. Additionally, concerns about the tenotoxic effects of CS injections [38], including increased risk of tendon rupture through increasing necrosis and decreasing cell viability [16,38], may further encourage the use of alternative treatments such as PN-based injectable compounds [39].

Interestingly, our findings revealed notable differences in how patients and clinicians perceived pain control and the success of PN therapy. The patients consistently reported gradual and steady improvements throughout the study phases. However, clinicians observed symptomatic improvement primarily during the first two follow-ups, with little to no further progress. While patients

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subjectively felt improvements in pain control and functional recovery, which enhanced their quality of life and autonomy, clinicians noted a more rapid initial improvement. Moreover, outcomes in elderly patients warrant attention, as pain sensitivity increases with age, and symptom improvement over time is noticeably less. Based on the VAS function scale, older patients reported lower performance and less functional recovery during follow-up, which was expected [40].

Although cytokine-driven inflammation may be involved in the healing process, its exact role in the development, resolution, and recovery from tendinopathy in elderly patients remain debatable. Prolonged low-grade inflammation in elderly individuals with tendinopathy may contribute to tendon injury and chronicity, potentially leading to a persistent failed healing response and resulting in chronic pain and dysfunction [41–43].

There are various hypotheses regarding how low-grade inflammation can alter or contribute to chronic pain. While peripheral nerve endings (nociceptors) and the DRG (the somata of nociceptors) are directly exposed to circulating products and other danger signals, it is unclear whether repeated, chronic stimulation by low-grade inflammation is sufficient to excite nerve endings or prime sensory neurons. Neuroinflammation during ageing contributes to the initiation and maintenance of chronic pain. During chronic low-grade age-related inflammation, activation of spinal microglia and astrocytes may increase central sensitization through the release of various inflammatory mediators [44].

Strengths and Limitations

The main strength of our study is the extended follow-up period of 24 weeks from baseline, providing sufficient time for PNs to exert their healing properties, as tendons typically require at least 12 weeks to restore their physiological properties after regenerative treatment [45,46]. Furthermore, the published preliminary extract of this study by Gervaso et al. [26] has already shown that the significant statistical values obtained for both pain and functional impairment indicated a promising role of PNs in treating the investigated tendinopathies. In particular, the results obtained in the earlier phases of treatment (i.e., at FU-1 and FU-2) indicate that this treatment both had positive outcomes and showed short-term efficacy.

However, our study had several limitations. The patient sample size was relatively small, although this is a multicenter study on a new injectable treatment, suggesting the need for future studies with larger sample sizes. As a single-cohort retrospective study, we lacked a control group for comparison; however, the positive outcomes can serve as a basis for future randomized clinical trials. Moreover, we could not provide complete data reporting of the outcome measures, as suggested by the International Scientific Tendinopathy Symposium Consensus [27] because, given the multicenter nature of the present study, data were retrospectively collected in different ways (i.e., using different software) but using similar diagnostic tools and treatment approaches.

In conclusion, direct comparison with other studies was not feasible due to the absence of clinical research on the use of PNs for tendinopathies, as well as the fact that the medical device employed in this study is a novel PN-based gel with distinctive properties. However, the positive results observed may encourage the use of PNs injections for tendinopathies in clinical practice, especially in combination with other treatments, such as physical therapy and therapeutic exercise.

5. Conclusions

The findings from this retrospective analysis support the efficacy and safety of PNs treatment in patients with tendinopathies, as it led to significant improvements in pain and function.

PNs injections represent a promising therapeutic approach for tendinopathy management, given the encouraging outcomes observed.

Further high-quality clinical studies, including control groups (e.g., receiving placebo or alternative injectable treatments), are needed to validate these findings. Such research would also enhance the molecular understanding of PNs, helping to better define their therapeutic role—either as a standalone treatment or in combination with other therapeutic protocols—for managing tendinopathies.

Patents: Tropho Tend©: Mastelli, Sanremo, Italy.

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Informed Consent Statement: Informed consent was obtained from all the subjects involved in the study.

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