Case Report

Umbilical Cord Tissue Allograft Defects for Ligamentous Injuries in Patients with Sinus Tarsitis: A Case Series

Robert Parker , John Shou , Crislyn Woods , Naomi Lambert * , Tyler Barrett

Posted Date: 13 February 2024

doi: 10.20944/preprints202402.0716.v1

Keywords: Sinus Tarsi syndrome; Heel pain; Extracorporeal pulse-activated therapy (EPAT); Standard-of-care treatments; Non-steroidal anti-inflammatory drugs (NSAIDs); Foot orthosis; Laser therapy

 doi:10.20944/preprints202402.0716.v1

Case Report

Umbilical Cord Tissue Allograft Defects for Ligamentous Injuries in Patients with Sinus Tarsitis: A Case Series

Robert Parker [1], John Shou [2], Crislyn Woods [3], Naomi Lambert [3,*] and Tyler Barrett [3]

[1] Parker Foot and Ankle, Houston, TX 77079, USA
[2] Baylor College of Medicine, Houston, TX 77030, USA
[3] Regenative Labs, Pensacola, FL 32501, USA
* Correspondence: naomi@regenativelabs.com; Tel.: +1 800-891-3452

Abstract: Heel pain in the "funnel-shaped" space between the calcaneus, talus, and talocalcaneonavicular and subtalar joints may be representative of Sinus Tarsi syndrome. The pain is often characterized by a burning, numbness, or tingling sensation that can stem from strains and tears on the ligaments in that area. Injury treatment typically includes balance training, muscle exercises, bracing, foot orthosis, and non-steroidal anti-inflammatory drugs (NSAIDs). This study presents Wharton Jelly (WJ) tissue allografts as an alternative intervention for patients who fail standard-care treatments. WJ targets tissue defects, unlike other therapies, which aim to reduce swelling and symptomatic pain. This study includes five female patients who have previously failed standard-of-care treatment. Each received extracorporeal pulse-activated therapy (EPAT), WJ, laser therapy, and an orthotic. After an average of 80 days, the cohort had an overall 85.29% improvement in pain. The study's limitations include a small cohort size and a non-blinded design. Given the significant improvement in pain, WJ tissue allograft, combined with other techniques, presents an optimal patient care plan for tissue defects associated with Sinus Tarsi syndrome when standard-of-care treatments fail. These results provide evidence for a more extensive, randomized study to define dosage protocols further and confirm safety and efficacy.

Keywords: sinus tarsi syndrome; heel pain; extracorporeal pulse-activated therapy (EPAT); standard-of-care treatments; non-steroidal anti-inflammatory drugs (NSAIDs); foot orthosis; Laser therapy

1. Introduction

Sinus Tarsi syndrome is a condition that presents as lateral midfoot heel pain that is located in the "funnel-shaped" space between the calcaneus, talus, and talocalcaneonavicular and subtalar joints [1]. Patients with sinus tarsi syndrome generally complain of instability with functional activities and persistent anterolateral ankle discomfort [2]. The instability occurs when the associated ligaments are damaged or ruptured; clinically, compression of the sinus tarsi area elicits acute pain. Also, patients will frequently describe aching pain while lying on their back with their foot plantar flexed and inverted. Recent literature describes the instability primarily stemming from ligamentous injuries, inflammation from damage to the synovium, and fibrotic tissue infiltration of the subtalar joint space [2]. For decades, Parker Foot and Ankle have studied the innovations of the sinus tarsi and found that not only the superficial fibular but also the deep fibular nerve innervates the sinus tarsi area in the subtalar area with multiple branches. Injury in this area creates nerve pain, frequently experienced by patients, of burning, numbness, and tingling. The incidence rate of sinus tarsi syndrome is unknown, but it is proposed that a large percentage of reported ankle sprain injuries include an injury to the subtalar joint ligaments [3]. Treatment recommendations include balance and proprioceptive training, muscle strengthening exercises, bracing, taping, and foot

 doi:10.20944/preprints202402.0716.v1

orthosis. These treatments aim to allow the ligament to heal naturally. NSAIDs are often used to help with pain management. They function to decrease swelling and relieve pain, but they do not address the root problem. Steroid injections function similarly to reduce pain and swelling. With a short lifespan, several injections are often required, ultimately decreasing the cost-efficiency of the treatment. For patients who fail standard-care treatments and rehabilitation, the option of arthroscopy exists for a more precise examination of the joint and to allow for surgical treatment [4]. While surgery can be effective, it is invasive, and the mean return to total activity is four months.

Given that there is no single, optimal treatment option for sinus tarsi, there is a need for alternative interventions. This retrospective study assesses the efficacy of Wharton's Jelly (WJ) application to the damaged ligaments to minimize the pain associated with sinus tarsi. WJ is a loose connective tissue found in the umbilical cord that cushions and protects the vessels within the cord from external forces and stretching. It contains collagen types I and III, hyaluronic acid, proteoglycans, growth factors, and cytokines that supplement the damaged tissue. This retrospective case series presents the application of WJ to ligament defects in the sinus tarsi of five females who have all failed previous standard-care treatments.

2. Case Presentation Section

2.1. Materials and Methods

All methods complied with the FDA and American Association of Tissue Banks (AATB) standards. This study was conducted under an Institute of Regenerative and Cellular Medicine IRB-approved protocol (RL-UCT-001), and informed consent was obtained from the study participants. Wharton's jelly tissue allograft was processed and distributed by Regenative Labs. Patient recruitment, allograft application, and patient tracking were performed at Parker Foot and Ankle.

2.2. Case Presentation

This study consists of five female patients with either left or right foot pain in the sinus tarsi aspect of the foot. All of the patients have failed previous stand-of-care treatment. Two patients presented with right-sided pain, and three with left-sided pain. The age distribution of the cohort ranged from 50 to 72 years old. Each individual received EPAT, a single application of CryoText Plus, class IV laser therapy, and a pneumatic boot. Bulleted lists look like this:

2.3. Procedure

Local anesthesia is not desirable in the immediate area of the tissue allograft. Thus, proximal blocks of the deep fibular nerve, superficial fibular nerve, and surreal nerve were performed above the ankle. Before applying the tissue allograft, patients received EPAT at approximately 11 Hrtz, 3.0 bars, and 3300 pulses to the affected tissue. While the patients received EPAT, CryoText Plus was thawed slowly in a 35-degree bath per laboratory guidelines. A single application of 1cc CryoText Plus was transplanted along the sinus tarsi and sinus canalis throughout the inflamed tissue. CryoText Plus is the WJ allograft, which contains 50mg of WJ per 1cc. During the injection of WJ, a specific needling technique was utilized to enhance neovascularization throughout Hoke's Tonsil and sinus tarsi area. After the application, two of the five patients were placed in a prefabricated Pneumatic Ankle-Foot Orthosis (Aircast foam walker) or continued with orthotics or biomechanical control. Finally, all patients were scheduled twice weekly for class IV laser therapy sessions for the two weeks following the tissue supplementation to provide photobiomodulation as a tissue healing stimulation modality. All patients were prescribed optional non-anti-inflammatory medication to help combat discomfort and instructed to avoid high-impact activities for at least eight weeks. After the initial application and two weeks of laser therapy, all individuals were assessed at a follow-up visit approximately 80 days after the WJ application to evaluate pain improvement via a visual analog scale and to ensure no adverse side effects.

 doi:10.20944/preprints202402.0716.v1

2.4. Results

The cohort's initial average visual analog scale (VAS) score was 6.8, with a final VAS average of 1. The cohort had an overall 85.29% improvement in pain after an average of 80 days from the initial application to the final follow-up date. In just 47 days, one patient had a pain improvement of 85%, and another improved 75% in the same amount of time. All patients reported an improvement in pain. The least improved patient had an improvement of 75%. One patient reported a pain improvement of 100%. No adverse reactions were reported.

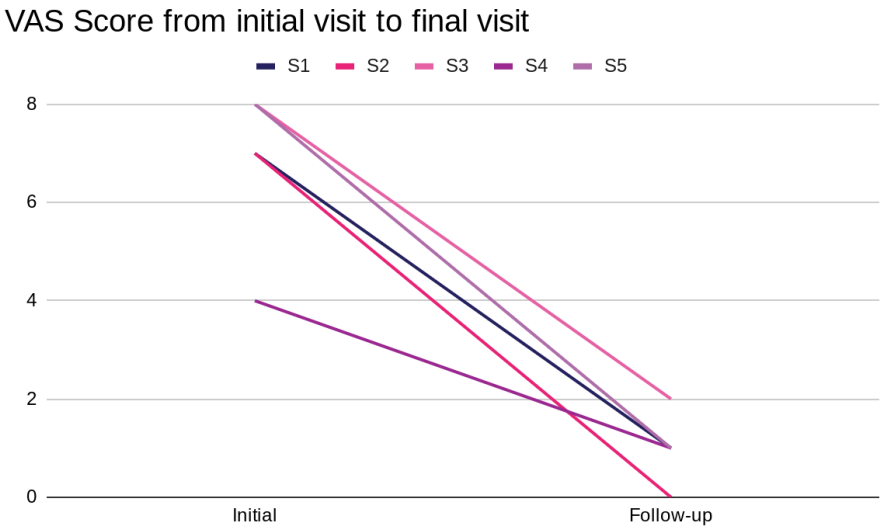

Figure 1. Patient reported VAS scores, a scale from 0-10, lower scores mean less pain.

3. Discussion

This study has shown significant pain improvement within a small cohort of females presenting with tissue defects to the sinus tarsi, causing pain and aching in the foot. Limitations of the study include a small cohort size along with following a non-blinded design. A small cohort size impacts the diversity of the patients, may present more variability in results, and cannot show statistical significance. The effect of a non-blinded study design may lead to the placebo effect. By not including a placebo, some patients may report an imagined improvement. The patients rated their pain on the NPRS scale to combat this effect. The results of this study warrant continued research on more extensive and more diverse cohorts to evaluate further the safety and efficacy of WJ in combination with EPAT, laser therapy, and a pneumatic boot to treat tissue defects associated with sinus tarsi. Each modality used in this study has an independent function and has been tested independently to show improvement in a patient's path to recovery.

EPAT has been reported to show successful outcomes in treating Achilles tendinopathy in a study completed by Saxena, which included 60 patients who received EPAT treatment for three weeks [5]. This study discovered that 78.38% of tendons showed clinically significant improvement by at least one-year post-treatment. Another study by Furia, with 35 patients, produced similar results, stating that 83% of the cohort had shown successful results [6]. This study also identified that local field anesthesia may decrease the effectiveness of the EPAT procedure. Current literature agrees that EPAT is an effective technique in relieving pain and has the potential to promote exponential pain improvement associated with sinus tarsi defects when used in conjunction with WJ.

After EPAT and WJ Application, each patient received class IV laser therapy. Class IV laser therapy has been shown to reduce pain and inflammation and improve tissue quality. It also can decrease erythrocyte deformability and platelet coagulation, resulting in membrane revitalization, viscosity reduction, and erythrocyte stress adaptation [7]. Brandl found that blood flow increased

 doi:10.20944/preprints202402.0716.v1

significantly by 86.38 arbitrary units [7]. Decreasing erythrocyte deformability and platelet coagulation allows for more effective blood flow, which allows the body's natural healing factors to be administered at a quicker rate, ultimately improving patient recovery.

The final aspect of the multi-modality patient care protocol is the pneumatic boot application and orthotics. The boot and orthotics function to stabilize and limit the range of motion to allow for safe and effective recovery while preventing further injury. While all care methods used have evidence of success when used independently, the protocol presented in this study was designed to maximize patient recovery by combining the benefits of each therapy for a higher success rate of patients who perceived pain improvements.

4. Conclusions

This study exemplifies significant pain improvement of the sinus tarsi ligaments after applying WJ in combination with EPAT, laser therapy, orthotics, and a pneumatic boot. The results align with other literature's positive outcomes regarding each element used in the care procedure as stand-alone applications. Further research regarding the use of WJ for sinus tarsi ligament defects could be completed to compare the efficacy of WJ to standard-care treatments and surgery. Limitations to the study include a small cohort and a non-blinded design. A more extensive, more diverse, and randomized study would be beneficial in future studies to define dosage protocols further and confirm safety and efficacy.

Author Contributions: Conceptualization, R.P., J.S. and T.B.; methodology, R.P.; software, T.Y.; validation, N.L., C.W. and T.Y.; formal analysis, N.L., C.W.; investigation, R.P.; resources, N.L., C.W.; data curation, R.P.; writing—original draft preparation, R.P., N.L., C.W.; writing—review and editing, R.P., N.L., C.W.; visualization, R.P., N.L., C.W.; supervision, J.S., T.B.; project administration, T.B.; funding acquisition, R.P., T.B. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board of the Institute of Regenerative and Cellular Medicine (protocol code IRCM-2022-311 and approved on 12 January 2022).

Informed Consent Statement: Any research article describing a study involving humans should contain this statement. Please Written informed consent has been obtained from the patient to publish this paper.

Data Availability Statement: Raw data is available upon request.

Acknowledgments: The authors would like to thank Desiree Hornung, administrator, and the staff Stacy, Laura and Greta, at Parker Foot and Ankle for their contribution to data collection and filing.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Tu, P., & Bytomski, J. R. (2011). Diagnosis of heel pain. *American family physician*, *84*(8), 909–916.
2. Helgeson K. (2009). Examination and intervention for sinus tarsi syndrome. North American journal of sports physical therapy : NAJSPT, 4(1), 29–37.
3. Hubbard, T. J., & Hertel, J. (2006). Mechanical contributions to chronic lateral ankle instability. *Sports medicine (Auckland, N.Z.)*, *36*(3), 263–277. https://doi.org/10.2165/00007256-200636030-00006
4. Oloff, L. M., Schulhofer, S. D., & Bocko, A. P. (2001). Subtalar joint arthroscopy for sinus tarsi syndrome: a review of 29 cases. *The Journal of foot and ankle surgery : official publication of the American College of Foot and Ankle Surgeons*, *40*(3), 152–157. https://doi.org/10.1016/s1067-2516(01)80081-8.
5. Saxena, A., Ramdath, S., Jr, O'Halloran, P., Gerdesmeyer, L., & Gollwitzer, H. (2011). Extra-corporeal pulsed-activated therapy ("EPAT" sound wave) for Achilles tendinopathy: a prospective study. *The Journal of foot and ankle surgery : official publication of the American College of Foot and Ankle Surgeons*, *50*(3), 315–319. https://doi.org/10.1053/j.jfas.2011.01.003
6. Furia J. P. (2006). High-energy extracorporeal shock wave therapy as a treatment for insertional Achilles tendinopathy. *The American journal of sports medicine*, *34*(5), 733–740. https://doi.org/10.1177/0363546505281810

 doi:10.20944/preprints202402.0716.v1

7. Brandl, A., Egner, C., Reisser, U., Lingenfelder, C., & Schleip, R. (2023). Influence of high-energy laser therapy to the patellar tendon on its ligamentous microcirculation: An experimental intervention study. *PloS one*, *18*(3), e0275883. https://doi.org/10.1371/journal.pone.0275883