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STUDENT JOURNAL OF THE NEW YORK COLLEGE OF PODIATRIC MEDICINE

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A Note from the Editors

The Podiatric Medical Review (PMR) is an extraordinary example of the dedication of aspiring physicians to enhance the field of Podiatry with evidence-based medicine. It is through research that we continue to improve our knowledge of the various foot and ankle pathologies that we see as podiatrists, while simultaneously educating ourselves on conservative and surgical treatment options, both new and old.

Thus, it is with great pride that we present the twenty-eighth volume of the Podiatric Medical Review. The manuscripts published in this year’s journal are of the highest quality and span a wide array of topics. We recognize and appreciate the hard work put in by all of the students who contributed to this year’s edition of PMR through their well-conducted research.

We would like to express our utmost gratitude to the senior editors, junior editors, and peer reviewers for their commitment to this volume; without their dedication, publication would have been nearly impossible. We would also like to thank our faculty advisor, Dr. Iorio, as well as the other professors who contributed to this journal via their ideas, edits, and unyielding support.

Our hope is that readers utilize this journal not only to further their knowledge of the topics presented, but also to apply what they have learned to improve the care of our patients as they progress in their career.

It is without further ado that we present to you the twenty-eighth volume of the PMR.

Jenna Friedman, BS
Farah Naz, MS, BS

Editors-in-Chief

Jenna Friedman  Farah Naz
Effects of Prolotherapy in Insertional and Noninsertional Achilles Tendinopathy: A Literature Review

By: Farah Naz, MS, BS; Jenna Friedman, BA; Nadia Hussain, BS; Ravneet Gill, BS

ABSTRACT

Introduction
Achilles tendinopathy is a chronic, non-inflammatory, degenerative condition which affects both sedentary and athletic individuals and is associated with repetitive microtrauma, aging, and chronic tendinitis. Prolotherapy has been used as a prolonged treatment regimen for chronic muscle pain, in which small amount of irritant solution (hyperosmolar dextrose) is injected at the site of the tendon, inducing intentional local cell necrosis due to osmotic shock thus initiating inflammation cascade, formation of granulation tissue, and matrix formation, causing the collagen fibers to align in the direction of the stress. The purpose of this literature review is to analyze prolotherapy as treatment for both insertional and noninsertional Achilles tendinopathy.

Study Design: Qualitative Systematic Review of Literature

Methods
Pubmed database search was conducted to include “prolotherapy AND Achilles tendinopathy” and “dextrose AND Achilles tendinopathy.” The search was further restricted to include articles which included both children and adults, consisted of “prolotherapy and Achilles tendinopathy” or “dextrose and Achilles tendinopathy” keywords in the title and/or abstract, printed in English, and articles with full text availability. After reading, evaluating, and assessing the abstracts for relevance to the topic, 10 out of 45 articles were included.

Results
Pubmed database search resulted in 45 articles. After applying the inclusion and exclusion criteria, 10 articles were ultimately used in the literature review to discuss prolotherapy as an isolated treatment for Achilles tendinopathy. There was a net decrease in tendon size, neovascularity, and pain on VAS scale that was found in the studies assessed.

Conclusion
Achilles tendinopathy is commonly associated with athletes however, it affects people who are sedentary as well. Prolotherapy is considered to be a safe and cost effective treatment that can be added adjunctively to other treatment options for Achilles tendinopathy due to minimal adverse effects indicated in research. Further research is deemed important to gain further clinical relevance of prolotherapy for Achilles tendinopathy with the addition of a longer follow up duration, increased sample size, and presence of control group.

Keywords: Prolotherapy, insertional Achilles tendinopathy, intratendinous Achilles tendinopathy, hyperosmolar dextrose, noninsertional Achilles tendinopathy

Level of evidence: 4
INTRODUCTION

Achilles tendinopathy is the sixth most common injury that occurs in athletes, especially those that place considerable load on the tendon during running and jumping. It also prevalent in the general population, which lead a more sedentary lifestyle than athletes. It is associated with decreased vascularity, repetitive microtrauma, chronic tendinitis, and aging. There are several etiologic factors that can be associated with symptomatic Achilles tendinosis including diabetes, obesity, hypertension, and steroid use. Insertional Achilles tendinopathy occurs at the point of where the Achilles tendon inserts into the posterior aspect of the calcaneus with tenderness present directly over the area. Injury to the Achilles tendon 2-6 cm proximal to its insertion (also known as intra-tendinous or midportion Achilles tendinopathy), where there is a discontinuity of muscle fibers within the tendon, is more common than insertional tendinopathy.

Most patients present with the chief complaint of generalized pain to the back of their calf, and upon physical exam will have a palpable nodular thickening within the tendon. These patients may experience painful ambulation, gait abnormalities, and decreased range of motion at their foot and ankle. Typically, athletes that present with this issue can train normally, but are unable to achieve maximal loading and report intense, sharp pain at the push off phase when running. This pain is commonly attributed to the stimulation of the nerve endings surrounding the tendon rather than inflammation associated with tendinosis.

Research has indicated that pain is one of the primary symptoms of Achilles tendinopathy and the severity of the condition can be measured with the patient’s symptoms. Achilles tendinopathy is mainly a clinical diagnosis, however radiographic findings such as the presence of traction spurs and bony prominences can support the clinical diagnosis. The mainstay radiographic testing includes ultrasound imaging and magnetic resonance imaging (MRI), which are useful in demonstrating changes in signal intensity, edema, changes to the thickness of the tendon, and the severity of the disease. Ultrasound findings show hypoechoic areas and increased neovascularization power, utilizing the doppler setting.

Imaging can be useful in directing the exact location of the injury which becomes important in treatment, as one can present with insertional versus non-insertional Achilles tendinopathy. Insertional Achilles tendinopathy is when the tendon is affected at the area of insertion into the posterior surface of the calcaneus. Non-insertional tendinopathy is generally located two to six centimeters (cm) proximal from the insertion point, where it is defined by the discontinuity of the fibers within the tendon.

Some of the initial conservative treatments for Achilles tendinopathy include activity modification, immobilization with night splints, use of ankle-foot orthoses, physical therapy with stretching exercises and eccentric loading exercises, and local use of iontophoresis and phonophoresis. Generally conservative treatments show efficacy in up to 75% of patients, however if conservative treatment fails, more invasive treatments can be performed. Operative treatments include debridement of diseases tendon and fibrous tissue, retrocalcaneal bursa, and calcific spurs.

Although corticosteroid injections are known to provide immediate relief and help reduce inflammation, they are considered
contraindicated for tendinosis due to the risk of tendon rupture.\(^5\) Hyperosmolar dextrose injections have been used for years as part of the prolotherapy treatment regimen.

Prolotherapy is a technique in which a small amount of irritant solution is injected into the tendon, initiating a local inflammatory response and localized cell necrosis at the injection site due to direct osmotic shock.\(^6\) This leads to initiation of the body’s healing cascade of inflammation, proliferation of fibroblasts, granulation tissue formation, and matrix formation, overall leading to formation of a stronger tendon.\(^2,6\) As an individual begins to perform activities of daily living, the stresses placed on the tendon will help the collagen fibers to align in the direction of the stress. Prolotherapy can also be used as a mechanism to reduce pain. Maxwell et al conducted a study which reported significant reduction in the pain score at 6 week interval, as well as decreased neovasculatry indicated by ultrasound.\(^4\) Previous studies have assessed prolotherapy in conjunction with eccentric loading exercises however, in this literature review we aim to evaluate the effectiveness of prolotherapy in isolation for insertional and noninsertional Achilles tendinopathy.

**METHODS**

All authors performed a thorough and detailed keyword literature search on PubMed database. Many key phrases were used throughout this process however, we were able to narrow our search to include the keyword search of “prolotherapy AND Achilles tendinopathy,” which yielded 12 articles and “dextrose AND Achilles tendinopathy,” which yielded 23 articles. Inclusion criteria comprised articles which included both children and adults, consisted of “prolotherapy and Achilles tendinopathy” or “dextrose and Achilles tendinopathy” keywords in the title and/or abstract, printed in English, and articles with full text availability. Exclusion criteria consisted of non-English articles, non-human subjects, duplicate articles, exercise therapy alongside prolotherapy to fully assess the effectiveness of prolotherapy as a stand alone treatment, and Achilles tendinopathy secondary to diabetes. After reading, evaluating, and assessing the abstracts for relevance to the topic, 10 out of 45 articles were included. A summary of the methods employed in this paper is depicted in figure 1.

![Figure 1: Acquisition of studies from the PubMed Database](image-url)
RESULTS

Prolotherapy treatment in isolation has been conducted and discussed in a multitude of studies up to date. The most common prolotherapy treatment contains 20% hyperosmolar dextrose injection with 1% lignocaine however, this differed in a few studies that were evaluated in other systematic reviews.

Mechanism of Action

Injecting hyperosmolar dextrose into the area of pathology leads to localized tissue damage, leading to an influx of inflammatory cells by creating cellular dysfunction and loss of membrane integrity due to the increase in osmotic pressure from the hypertonic solution.2,3 Granulocytes are attracted to the injection site, which function by debriding the injection site and secrete humoral factors attracting macrophages to infiltrate the area. Macrophages, thereby phagocytize cellular debris and secrete polypeptide growth factors that concurrently induces the activation of fibroblasts.2 Fibroblasts are essential in this process, as they are responsible for new collagen type 1 synthesis at the injection site.2,3 Newly synthesized collagen contracts due to crosslinking and dehydration of the new fibers, resulting in a stronger and tighter connective tissue in the Achilles tendon.2

Effects of Intervention

Pain. All the studies that were reviewed indicated a significant reduction of pain following prolotherapy treatment. Maxwell et al. utilized 3-mL syringe filled with 1mL of 2% lignocaine and 1 mL of 50% dextrose. Pain was analyzed on the Visual Analog scale (VAS) at 3 different time periods; pain at rest (VAS1), pain during normal daily activity (VAS2), and pain during or after sporting event (VAS3).2 Patients were instructed to refrain from heavy tendon-loading activity during the first 2 weeks after the procedure and could consume Acetaminophen based analgesia.2 There was a reduction of pain at the final follow up for VAS1 of 88.2%, for VAS2 of 84.0%, and for VAS3 of 78.1% following treatment with ultrasound guided prolotherapy treatment. Overall there was a mean change in activity VAS by 83.2% in patients with mid-portion tendinopathy and 64.7% in those with insertional.10 During their 12 month telephone follow up, they found that 20 of the 32 patients who underwent the treatment did not present with any symptoms.10

Ryan et al. conducted a similar study to Maxwell et al. later, analyzing the effects for insertional vs. non-insertional Achilles tendinopathy. In insertional tendinopathy, pain was reduced at VAS1 by 91.5%, VAS2 81.07%, and VAS3 74.6% while in non-insertional, pain was reduced at VAS1 by 90.3%, VAS2 81.07%, and VAS3 76.3%, during the final follow up.3 Ryan et al. documented a decrease in the VAS score from 70.7 prior to treatment to 36.7 post-treatment and 16.7 at follow up of 28 months for the mid-portion tendinopathy group. In patients with insertional tendinopathy, the scores decreased from 69.6 to 39.8 from pre- to post intervention, and 17.7 at the follow up.10

In the systematic review conducted by Sanderson and Bryan, the study completed by Yelland et al. in 2011 was assessed, evaluating effectiveness of prolotherapy and eccentric loading in isolation, and the combination of the two treatments in 43 subjects. The study reported prolotherapy in isolation was favored over the combination of receiving eccentric loading exercise for
short- and intermediate term pain, without statistical difference between the treatment groups over time overall. Smith et al. reviewed studies where no significant benefit of prolotherapy in isolation to eccentric loading exercises was found. Adverse Effects. Maxwell et al. did not report major adverse effects or complications following prolotherapy, profiling prolotherapy as a safe and conservative treatment. In their study, there was one reported partial Achilles tendon tear detected post intervention, although it was in existent prior to the initial prolotherapy injection. In another study, mild pain or bleeding at the site of injection was found as an adverse effect. Other studies and reviews did not report any adverse effects of prolotherapy as treatment for Achilles tendinopathy.

**DISCUSSION**

Achilles tendinopathy causes degeneration and neovascularization of the Achilles tendon due to repetitive motion in a localized area, without an inflammatory process. This degeneration causes a cascade of events, ultimately leading to disordered, haphazard fiber disorientation and thinning and collagen deposition, eventually resulting in biomechanical changes. This condition is a long-term overuse injury, seen in sedentary and active lifestyles. The main symptom of this condition is pain thus, the patient’s pain scale describes the severity of the condition. Pain for most patients is localized at either the insertion site or proximal to the insertion, which can be reproduced by palpation to the area. Most commonly, ultrasound or MRI is the choice of imaging modality to diagnose Achilles tendinopathy and evaluate post treatment effectiveness. As stated earlier, many different forms of treatment exist for Achilles tendinopathy, including conservative and non-conservative approaches. Among the conservative approaches is prolotherapy in isolation, which has been reported to induce an inflammatory reaction and reduce pain.

Prolotherapy has been widely used for over a 100 years for musculoskeletal conditions, osteoarthritis and ligamentous instability. There has been growing research of prolotherapy in treatment for tendinopathies, as the pathophysiology of the condition is becoming better understood. In the current review, the ultrasound guided dextrose injection utilized was either at the insertion site or mid portion in the Achilles tendon. The preparation for the injection varied as there is a lack of standardized injection preparation in research currently however, this did not demonstrate any correlation to the study findings. Overall, there was an improvement in pain for patients with Achilles tendinosis at the insertion site and midportion after receiving ultrasound guided hyperosmolar dextrose. A positive outcome was reported, in which there was corresponding sonographic improvement in the appearance of the Achilles tendon at the pathologic site, demonstrating reduced hypoechoic region and neovascularization. The injection is ultrasound guided and the volume of solution in the injection is dependent upon the size Maxwell et al. concluded positive results in the reduction of pain at rest and during tendon loading activities however, the cause was not attributed to reduction in neovascularity, as their study has 11 tendons with unchanged neovascularity after treatment despite changes in the tendon size. This study had 3 unsuccessful outcomes including 3 patients with insertional
tendinosis has cortical irregularity and intratendinous calcification. This led them to conclude that patients with insertional tendinopathy have an increased likelihood of less effective treatment, thus less favorable outcomes than those with intra-tendinous tendinopathy, as evaluated with decreased changes in the VAS scale. In addition, the authors indicated lack of control group as a limitation with no blinding of treatment, during the 28.6 month treatment period.

Ryan et al. reported significant short-term and long-term improvements in the pain and sonographic appearance of the tendon, specifically the reduction in size and severity of the hypoechoic regions in the Achilles tendon. Even though there was noted reduction in the hypoechoic regions within the tendon, it was concluded that hypoechogenic in the insertional remained relatively unchanged, even with the same injection therapy. The average number of injection to produce a satisfactory outcome was 5, as reported by the patient however, the authors indicated that there isn’t a standard optimum number of injections that would incite therapeutic response in the Achilles tendon. The limitation of this study was that there was no control group and no randomization protocol. They further assessed that a longer treatment duration of 28 months could improve the sonographic changes they noted.

Several studies and systematic reviews reported objective outcomes with the use of Victorian-Institute of Sports Assessment-Achilles (VISA-A), VAS for pain, and ultrasound findings pre- and post-treatment however, they reported subjective findings as well including pain, stiffness, functional limitation, and overall patient satisfaction. There were several limitations included in the studies that were reviewed. Sanderson and Bryan analyzed 5 studies that included small sample size which reduced the quality of evidence of the findings. There were discrepancy found in the concentration of dextrose, agent and concentration of additional local anesthetics, and frequency, volume and total number of injections. There was also a lack of randomized control trials available thereby, reducing the quality of evidence in literature.

In future studies, it is essential to analyze additional randomized control trials with larger sample size, and standardization of prolotherapy with a longer term follow up to receive more conclusive results for prolotherapy in isolation to evaluate its effectiveness for Achilles tendinopathy. Additional research comparing hyperosmolar dextrose therapy in comparison to other treatment options would help to further evaluate further use of prolotherapy as a treatment option.

**CONCLUSION**

This literature review contains pilot studies and systematic reviews that analyzed studies done previously to show the efficacy of prolotherapy in the treatment of Achilles tendinopathy. Further research needs to be conducted in future studies on prolotherapy due to mixed results found in prior studies. Although this is a safe, effective, and inexpensive treatment for Achilles tendinopathy with improvement in pain, reduced tendon size, decreased neovascularity and overall satisfaction, there were no clinical or statistical significance found as prolotherapy being used in isolation as treatment for insertional or midportion Achilles tendinopathy.
AUTHORS’ CONTRIBUTIONS

All three authors equally contributed to the design of the study and evaluated the available articles. All authors contributed equally in the writing of this literature review and reviewed the final version for submission.

STATEMENT OF COMPETING INTERESTS

The authors declare that they have no competing interest associated to this manuscript.

REFERENCES


Use of Properly Fitted Footwear and Orthoses to Improve the Quality of Life of Individuals with Down Syndrome

By: Jenna Friedman, BA; Farah Naz, MS, BS; Paul Marinos, BA

ABSTRACT

Introduction

Down syndrome (DS), a genetic disorder due to a trisomy of chromosome 21, presents with developmental delays, increased joint laxity, and hypotonia. These musculoskeletal abnormalities contribute to the foot pathology observed in this population, which includes but is not limited to pes planus, hallux valgus, and lesser digital contracture. These pathologies are thought to be associated with reduced physical fitness and obesity, fatigability, postural abnormalities, and an overall gait instability and imbalance. Upon observation, a substantial portion of individuals with DS have been found to not only wear improperly fitted footwear, but also lack orthotic devices, which only serves to exacerbate foot pathology. This paper aims to provide the podiatric community with information about the effect of orthoses and properly fitted footwear in the DS population and how it impacts their quality of life.

Study Design: Qualitative systematic review of literature

Methods

Three literature searches were conducted using the PubMed database. The first search was conducted using the query “down syndrome AND shoes”; a second search was conducted using the query “down syndrome AND footwear”; a third search was conducted using the query “down syndrome AND orthoses”.

Results

Application of inclusion and exclusion criteria helped to narrow down the articles that were utilized in this systematic review. Inclusion criteria encompassed articles with the key terms “down’s syndrome” or “footwear” or “orthoses” in the title. Exclusion criteria included non-English articles, articles focusing on scoliosis, head, neck, upper extremity, or hip dislocation, articles focusing on surgical technique, and response articles. After applying inclusion and exclusion criteria, and removing redundant articles, a total of 14 articles were selected for use in this literature review.

Discussion and Conclusion

A multitude of studies have been published which discuss the foot structure and pathology associated with individuals with DS. These individuals often have many foot abnormalities, including pes planus, metatarsus primus varus, lesser digital contracture, and calcaneal valgus, many of which are attributed to hypotonia and ligamentous laxity. These pathologies negatively impact their gait, resulting in discomfort, instability, and decreased ability to adapt to the environment. Utilizing properly fitted footwear and orthotic devices in the DS population is imperative to help improve foot function, stabilize gait, and subsequently more readily participate in activity and improve quality of life.

Keywords: Down syndrome, Orthoses, Footwear, Quality of Life

Level of evidence: 4
INTRODUCTION

Down syndrome (DS) is a genetic disorder affecting 1 in 1000 births worldwide, making it one of the most common causes of neurodevelopmental disability to date.\(^1,2\) Most frequently, DS is a result of a trisomy of chromosome 21 and is often attributed to increased maternal age.\(^3\) Individuals with DS present with cognitive disability, heart defects, craniofacial dysmorphia, diabetes, obesity, early-onset Alzheimer’s disease, and musculoskeletal impairments.\(^4\) Because of these cognitive and physical disorders, children with DS are often delayed in reaching critical milestones that dictate functional, motor, and social independence later in life.\(^5\) While neurotypical children tend to stand and walk independently at approximately 11-15 months of age, children with DS reach this same milestone at approximately 18 months – 3 years.

The most common podiatric problems facing individuals with DS include pes planovalgus, metatarsus primus adductus, hallux abductovalgus, hypermobile first ray, tailor’s bunion, hindfoot valgus, split toenails, fissures, and abnormal pressure sites, almost all of which are attributed to hypotonia and ligamentous laxity.\(^4,6,7\) As a result, gait abnormalities arise. Upon analysis, atypical patterns that are observed frequently include out-toeing, flat foot at initial contact, wide base of gait, and increased pronation at the subtalar and midtarsal joints.\(^5,8\) Because of these abnormal foot morphologies and gait deviations, specialized shoe gear and orthoses are often indicated; however, they are frequently not obtained due to insufficient access to proper healthcare and an overall dearth of knowledge about the importance of footwear and orthoses.\(^4\) Lack of supportive shoes and orthoses, which play a major role in stabilizing the foot and ankle during gait, have been shown to be associated with decreased physical activity and emotional status.\(^9,10,11\) This literature review serves to demonstrate that while properly fitted footwear and orthotic devices are not curative for the musculoskeletal pedal disorders associated with DS, they could greatly impact the stability and structure of the foot, thus increasing level of activity and improving the quality of life.

METHODS

Three literature searches were conducted using the PubMed database. The first search was conducted using the query “downs syndrome AND shoes”, yielding 13 articles. The second search was conducted using the query “downs syndrome AND footwear”, yielding 7 articles. The third search was conducted using the query “downs syndrome AND orthoses”, yielding 47 articles. In order to narrow down the articles used in this review, inclusion and exclusion criteria were applied. Inclusion criteria encompassed articles with the key terms “down’s syndrome” or “footwear” or “orthoses” in the title. Exclusion criteria included non-English articles, articles focusing on scoliosis, articles focusing on the head, neck, or upper extremity, articles focusing on hip dislocation, articles focusing on surgical technique, and response articles. After applying inclusion and exclusion criteria, and removing redundant articles, there was a total yield of 6 articles for the first search, 2 articles for the second search, and 6 articles for the third search. A total of 14 articles were used in this literature review.
Peoples with DS have an elevated incidence of foot deformities as compared to their typical counterparts, the most prevalent being pes planus. Without properly fitted footwear and supportive orthotic devices, the quality of life of these individuals suffers, as they are not easily able to participate in activities that their typical counterparts partake in. Educating all members of the healthcare team, as well as all caretakers of individuals with DS is paramount to enhancing their comfort, reducing their pain, and allowing them to live a more functional lifestyle. The results and findings of the literature reviewed for this article are portrayed in Table 1.
<table>
<thead>
<tr>
<th>Title</th>
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<tr>
<td>Incorrectly Fitted Footwear, Foot Pain, and Foot Disorders: A Systematic Search and Narrative Review of the Literature (2018)</td>
<td>Andrew K. Baik, Ushma Kh. Shah</td>
<td>Large percentage of population wears incorrectly fitted footwear, which is associated with foot pathology and pain. Greater emphasis should be placed upon proper footwear education.</td>
</tr>
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<td>The Relationship Between Shoe Fitting and Foot Health of Persons with Down Syndrome: A Case Control Study (2018)</td>
<td>Cesar Calvo-Lebe, Ana Ramos Garcia, Marta Elena Ledesma, Daniel Luong-Luex, David Rodriguez-Senz, Carlos Romero-Morales, Ricardo de Bouchot-Vallejo</td>
<td>12% of individuals with Down Syndrome wore poorly fitting shoes. An elevated incidence of foot disorders in individuals with Down Syndrome was found to be secondary to hypotonia and ligamentous laxity. Poorly fitted shoes are linked to increased foot pain and impairment.</td>
</tr>
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<td>Biomechanical Management of Children and Adolescents with Down Syndrome (1991)</td>
<td>Mark A. Caselli, Ellen Cohen-Sobel, Jeanette Naidoo, Joan Adler, Luz Gonzalez</td>
<td>Children with Down syndrome are delayed walkers with a predisposition to lower extremity pathology. Early orthotic and shoe therapy can help to improve the gait of these individuals and better their lifestyle.</td>
</tr>
<tr>
<td>Musculoskeletal Anomalies in Children with Down Syndrome: An Observational Study (2018)</td>
<td>Charlene Foley, Orla G. Killeen</td>
<td>Children with Down syndrome are predisposed to debilitating musculoskeletal problems, most frequently pes planus. Lifelong use of orthoses and supportive footwear is recommended. Annual musculoskeletal assessment is recommended to ensure early detection of problems.</td>
</tr>
<tr>
<td>Relationship Between the Use of Lower Extremity Orthoses and the Developmental Quotient of the Kyoto Scale of Psychological Development in Children with Down Syndrome (2018)</td>
<td>Yoshihide Kanai, Tomohide Nakamura, Ota, Nobuaki Kawasaki</td>
<td>Orthoses for individuals with Down Syndrome helped to stabilize their gait and relieve foot pain. Children with down syndrome show increased intelligence, cognition, and communication skills after their mobility improves; thus, the use of orthoses is expected to improve.</td>
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<tr>
<td>Effect of Treadmill Training and Supramalleolar Orthotic Use on Motor Skill Development in Infants with Down Syndrome: A Randomized Clinical Trial (2010)</td>
<td>Julia Loorer, Dale A. Ulrich</td>
<td>Use of supramalleolar orthoses in infants and early walkers was found to have a detrimental effect on overall motor skill development. Supramalleolar orthoses lead to a decrease in speed and time as compared to foot orthoses and barefoot walking. Supramalleolar orthoses have been suggested to limit ankle mobility, leading to limitation in functional mobility during gait. Foot orthoses provide control and do not disrupt the gait cycle.</td>
</tr>
<tr>
<td>What to Measure When Determining Orthotic Needs in Children with Down Syndrome: A Pilot Study (2012)</td>
<td>Julia Loorer, Danielle Benjamin, Mindy Nolan, Laura Schumm</td>
<td>Flexible supramalleolar orthoses on postural stability in children with Down Syndrome. Flexible supramalleolar orthoses have a positive effect on postural stability and functional mobility in children with Down Syndrome. Increased incidence of foot orthoses (including pes planus, split toenails, fissures, and abnormal pressure sites) are found in children with Down Syndrome (both with and without learning disability). Improperly fitting shoes (particularly shoe width) can result in increased pressure on the feet and may cause harm. Boys with Down Syndrome have flatter feet than typical boys their age. Exercises should be completed to strengthen the muscles in the lower extremity and provide stability. Supramalleolar orthoses are also important to provide support and improve mobility. Modifications should be made to therapeutic treatment as the foot structure changes and the boy grows.</td>
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<tr>
<td>Effects of Supramalleolar Orthoses on Postural Stability in Children with Down Syndrome (2004)</td>
<td>Kathy Martin</td>
<td>Flexible supramalleolar orthoses have a positive effect on postural stability and functional mobility in children with Down Syndrome. Flexible supramalleolar orthoses have a positive effect on postural stability and functional mobility in children with Down Syndrome. Increased incidence of foot orthoses (including pes planus, split toenails, fissures, and abnormal pressure sites) are found in children with Down Syndrome (both with and without learning disability). Improperly fitting shoes (particularly shoe width) can result in increased pressure on the feet and may cause harm. Boys with Down Syndrome have flatter feet than typical boys their age. Exercises should be completed to strengthen the muscles in the lower extremity and provide stability. Supramalleolar orthoses are also important to provide support and improve mobility. Modifications should be made to therapeutic treatment as the foot structure changes and the boy grows.</td>
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<td>Podiatric Disorders Among Children with Down Syndrome and Learning Disability (1995)</td>
<td>V. P. Posclus, Lillian Robinson, V. H. K. Kukulman, Min Cheong Chung</td>
<td>Increased incidence of pediatric pathology (including pes planus, split toenails, fissures, and abnormal pressure sites) are found in children with Down Syndrome (both with and without learning disability). Improperly fitting shoes (particularly shoe width) can result in increased pressure on the feet and may cause harm. Boys with Down Syndrome have flatter feet than typical boys their age. Exercises should be completed to strengthen the muscles in the lower extremity and provide stability. Supramalleolar orthoses are also important to provide support and improve mobility. Modifications should be made to therapeutic treatment as the foot structure changes and the boy grows.</td>
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<td>Foot Structure in Boys with Down Syndrome (2017)</td>
<td>Eva Dancerolek, Tosc, Krzysztof Nowak, Tosc, Leszek Nowak</td>
<td>Boys with Down Syndrome have flatter feet than typical boys their age. Exercises should be completed to strengthen the muscles in the lower extremity and provide stability. Supramalleolar orthoses are also important to provide support and improve mobility. Modifications should be made to therapeutic treatment as the foot structure changes and the boy grows.</td>
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<td>The Effect of Foot Orthoses on Standing Foot Posture and Gait of Young Children with Down Syndrome (2001)</td>
<td>Lisa Selby-Silverstein, Howard J. Dugan, Robert J. Diamond</td>
<td>Foot orthoses decreased pronation of children with Down Syndrome. The use of foot orthoses resulted in more internal rotation and slower gait with a prolonged stance phase. Possible reason for elongated stance phase is that the stance limb was more stable and had more ability to support the weight of the child.</td>
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<td>Single-Subject Design Study of 2 Types of Supramalleolar Orthoses for Young Children with Down Syndrome (2012)</td>
<td>Juan S. Gonzalez, Kathy S. Martin, Ellen W. Miller</td>
<td>Foot orthoses were found to be the standard of care for improving foot posture and stability in individuals with Down Syndrome. The most effective type of foot orthoses has yet to be confirmed.</td>
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</table>

Table 1: Summary of results from literature review
DISCUSSION

The leading cause of the pes planus foot type is thought to be ligamentous laxity, which is present in 88% of the DS population. Joint hypermobility results in collapse at the most movable joints of the foot, which include the talocalcaneal joint and the calcaneonavicular joint. Midfoot collapse affects foot structure both while in static position and dynamic gait; while standing, the foot appears wider with a prominent bulge at the talonavicular junction. The hindfoot assumes a valgus position, which a prominent soft tissue bulge at the lateral side of the heel. Without proper function and motion restrictive devices, a flat foot is likely to remain in a pronated position throughout the majority of the gait cycle, with the calcaneus remaining in a valgus position. In attempt to clear the foot during the swing phase, individuals with a pes planus foot type show decreased hip extension, increased hip and knee flexion, as well as exaggerated abduction of the swinging limb. A study by Foley and Killeen (2018) examined 503 children with DS and determined that 91% of those individuals were flat footed. They reported that a pes planus foot type left the children at a higher risk of callus formation and bone spurs, both of which are associated with increased ground reactive force and abnormal loading of the foot. Additionally, they found a higher incidence of repetitive ligamentous injuries, which speaks to the instability that ensues from a pronated foot type during gait. They reported that the overall decreased stability during gait results in lack of core musculature and strength that children with DS exhibit upon standing.

Another study conducted by Concolino et al. evaluated the foot structure of 50 children with DS. Physical examination showed a statistically significant higher incidence of the following deformities, as compared to typical children their age: metatarsus primus varus, hallux valgus, pes planus, and calcaneal valgus. The authors emphasized that these foot deformations result in dysfunction of the foot, thus negatively impacting gait.

Many studies have concluded that the use of properly fitted footwear and supportive, functional orthotic devices will help to improve overall foot posture, provide increased joint stability, and allow for more efficient gait. A study conducted by Calvo-Lobo et al. (2018) compared the foot types of individuals with DS and their typical counterparts, and determined whether adequate shoegear was being utilized in this population of individuals. A total of 105 individuals were included in this study, 50 of whom had DS. A physical exam was conducted to note any obvious foot abnormalities. To determine generalized ligamentous laxity, the modified Beighton 9-point scoring system was used. Finally, foot length and width were measured using a Brannock device. Physical examinations of the individuals with DS revealed that of the 50 DS participants, 46 had pes planus, 24 had metatarsus primus adductus, 26 had hypermobile first ray, 26 had nail lesions, and 40 had hyperkeratotic lesions. 73% of the DS participants were found to have ligamentous laxity. Of the 50 individuals with DS, only 24% wore correctly fitted footwear which matched their foot length and width, as compared to 83.63% of typical individuals. The shoes that the DS participants wore were found to be predominantly too narrow, which may be attributed to the wide forefoot and midfoot due to hallux valgus and pes planus, respectively. The authors recommend that proper education on shoe gear should be provided to the families of individuals with DS in order to help reduce foot pain.
improve health, and increase general mobility.

Lim et al. evaluated 50 individuals with DS, with a mean age of 10.6 years. The authors sought to find the association of foot structure and footwear fit in individuals with DS. Utilizing a PressureStat Footprint Mat, an outline was made of each participant’s foot in a relaxed position, as well as an outline of the sole of their shoes. These outlines were then retraced using a computer graphics tablet and were superimposed on one another. A comparison was made between foot shape and size with that of the shoe. 10% of participants wore shoes that were too short for their feet and 58% of the participants wore shoes that were too narrow for their feet.

Using the Oxford Ankle Foot Questionnaire for Children (OxAFQ-C), they were able to determine the impact that foot deformity and improperly fitted footwear had upon the participant’s daily life. The OxAFQ-C is a 15-item questionnaire which assesses the severity of foot and ankle problems across various domains of disability – physical, school and play, emotional – and how frequently the foot or ankle deformity affects each domain. They noted that hallux valgus deformity had a positive association with the OxAFQ-C School and Play domain. Additionally, they found a positive association between narrow shoe gear and all three OxAFQ-C domains. This suggests that foot deformity and footwear, when improperly addressed or fitted, negatively impacts the ability of these individuals with DS to participate in physical activity, school and play activity, and also hinders their emotional status. Thus, while a causative relationship cannot be drawn from this association, one can infer that wearing improperly fitted footwear is uncomfortable and does not provide adequate support, thus negatively impacting the quality of life of individuals with DS.

Early intervention is important to decrease the severity of pedal deformities later in life. Due to the ligamentous laxity often present in individuals with DS, prolonged correction is often required to maintain support and alignment. An open-toed straight last shoe offers a wide sole and rigid heel counter. It can rise to the level of the ankle, providing both foot and ankle support. The addition of an orthotic device enhances stability, which promotes independent walking. Caselli et al. found that the most beneficial orthotic devices for the DS population include leather laminates or polypropylene orthoses from the University of California Berkeley Laboratory. These authors stated that all orthoses should be modified with a deep heel cup and high medial and lateral flanges to restrict excessive pronation.

A component of DS which often negatively impacts ability to walk and function independently is poor coordination. This clumsiness is exacerbated by an unstable foot and ankle. Curious about the relationship between poor postural-motor ability, use of insoles or foot orthoses, and the effect on cognition and interpersonal skills, Kanai et al. (2018) utilized the Kyoto Scale of Psychological Development (KSPD) to analyze 78 children with DS in three vital areas of development – Postural-Motor (PM), Cognitive-Adaptive (CA), and Language-Social (LS). The PM component assesses motor function and detects motor-development status. CA assess cognition, non-verbal reasoning, and visuospatial perception. LS assess communication, interpersonal relationships, socialization, and verbal abilities. They collected data on whether the children (mean age 4.9 years) used an insole or orthosis, as well as their
responses to the KSPD. Of the 78 children, 20 used an orthotic device. The mean developmental quotient for the PM component was found to be significantly lower in those children who used an orthosis, as compared to the children who did not. This suggests that individuals with poorer coordination and motor ability need more support via an assistive orthotic device. Another important finding was that the developmental quotient for the PM component was strongly correlated with the CA component of the scale, and moderately correlated with the LS component. This suggests that individuals with lesser postural-motor ability struggle with cognition, adaptability, language, and social skills. The authors anticipated that ambulation ability would correlate with these other developmental components, as being able to move enables people to have more interpersonal and enriching experiences, which helps to improve socialization and intelligence. They concluded that prescribing foot orthoses for individuals with DS, who are classically uncoordinated, will allow them to improve not only in their motor ability, but also with their cognitive and social development, thus improving overall quality of life.

Supramalleolar orthoses (SMO) are often used to decrease pronation and provide foot and ankle support in individuals with poor muscle tone, such as individuals with DS. Martin (2004) tested 14 children with DS (mean age 5 years 10 months) for their degree of joint laxity, and their ability to function at various week intervals (1, 3, 10) on the Gross Motor Function Measure (GMFM) and the Bruininks-Oseretsky Test of Motor Performance (BOTMP). The initial scores were compiled as a baseline, without the children donning SMOs. Subsequent scores analyzed their progress after consistently wearing flexible SMOs for up to 10 weeks.

The GMFM documents change over time in gross motor function. In this particular study, Martin focused on the following dimensions – Standing and Walking, running, jumping. The standing domain monitors ability to pull-to-stand, independent standing, and picking up an object from the floor while unsupported. The walking, running, jumping domain analyzes various aspects of gait, kicking a ball, jumping, and going up and down stairs.

The BOTMP evaluates children with DS and their ability to perform in various domains, however Martin focused only on the two following domains – Running Speed and Agility, and Balance, as these are directly correlated to postural stability. These domains are measured by having the children undergo various physical tests, such as running a short distance and picking up an object, as well as various static and dynamic balance activities. All tests are timed. The authors report that while both of these domains relate to postural-motor ability, the Running Speed and Agility domain was not included in this study, as the participants were unable to run fast enough to score any points at the initial evaluation. Thus, the authors focused on the BOTMP Balance domain.

Results showed that in all 14 children, there was significantly improved performance on the GMFM Standing and walking, running, jumping domains between the shoes-only intervention and the SMO intervention. Authors postulate that this improvement is due to both the SMOs as well as postural-motor development over the course of the 10 weeks. Additionally, significant improvement was noted in the BOTMP Balance domain by the end of the study.
Tasks that were initially difficult or impossible for the children were conquered after wearing the SMOs for 10 weeks. These tasks include but are not limited to stepping over an obstacle independently, running with control, going up and down stairs in a reciprocal manner, and balancing on one leg. Martin concludes that the children’s ability to complete these tasks more easily while wearing SMOs suggests not only an improved functional ability, but also results in improved socialization with their typical counterparts.

Other research, however, implies that SMOs may actually hinder individuals with DS and their ability to adapt their gait to the environment. Looper and Ulrich (2010) utilized the GMFM to compare two groups of pre-walking infants with DS and their performance in the Standing, Crawling and Kneeling, and Walking, Running, and Jumping domains. Each of these infants were undergoing treadmill training, which involves parent-assisted walking on a treadmill and continued until the child was able to take 3 independent steps without support. The experimental group donned SMOs after their initial evaluation and proceeded to wear them until the end of the study. The control group, however, received their SMOs later on in the study, after they were able to take a few steps independently. Data collection was completed once per month until independent ambulation was achieved, and then once more after the child could ambulate unsupported.

Up until 1 month of independent ambulation, scores on the GMFM in all domains were comparable between groups; however, upon final examination after 1 month of unsupported walking, results show that the children in the control group scored higher in each domain of the GMFM than the experimental group. Looper and Ulrich concluded that the use of SMOs during this developmental period may limit the ability of the foot and ankle to move freely, and thus hinders overall motor-skill development. The results suggest that healthcare providers should delay the use of SMOs until after independent ambulation is achieved.

CONCLUSION

Compared to their typical counterparts, individuals with DS show higher incidence of pes planus, hallux valgus, metatarsus primus varus, calcanea valgus, and lesser digital contracture, all of which contribute to abnormal loading of the foot. Many of these deformities are greatly attributed to ligamentous laxity. Abnormal foot structure has a largely negative impact on the gait cycle, often resulting in unstable and inefficient gait. Improperly fitted footwear is not only uncomfortable, but also lacks the support and motion control necessary to help improve foot function. The use of properly fitted footwear, foot orthoses, and SMOs only serves to benefit individuals with DS by providing excess support and stability, allowing them to walk more efficiently, participate in physical activity, and socialize with their peers, all of which positively impacts their quality of life.

AUTHORS’ CONTRIBUTIONS

All three authors equally contributed to the design of the study and evaluated the available articles. All authors contributed equally in the writing of this literature review and reviewed the final version for submission.

STATEMENT OF COMPETING INTERESTS

The authors declare that they have no competing interest associated to this manuscript.
REFERENCES


ABSTRACT

Introduction
A diabetic foot is often associated with a loss of protective sensation. The lack of sensation of the extremities can cause a diabetic ulcer that is difficult to treat due to the lack of blood flow to that area. Prompt and proper treatment of an open ulcer may alleviate infections, and eventually amputation. In urban areas a patient can easily seek treatment; however, in rural or lower income communities, obtaining treatment is a greater obstacle. Telemedicine may be able to remove this obstacle. This paper presents a review of multiple studies that assessed the efficacy of telemedicine compared to standard clinical visits.

Study Design: Qualitative Systematic Review of Literature

Methods
The PubMed search was done using the query “Mhealth AND foot AND ulcer AND diabetes”. Inclusion criteria included articles with human subjects, peer-reviewed articles, articles printed in English and articles with full text availability through New York College of Podiatry Medicine library or interlibrary loan. Exclusion criteria included feasibility articles, articles only discussing protocol, articles not discussing ulcer management, articles that discussed technology rather than telemonitoring and articles not printed in English.

Results
The PubMed search resulted in 55 articles. After applying the inclusion and exclusion criteria, 11 articles from the PubMed database were selected to be included in the literature review to discuss the role telemedicine has in diabetic ulcer treatment. Studies included the use of mobile phone cameras and integrated healthcare communications.

Conclusion
Telemedicine consults may eventually be a common treatment alternative for diabetic foot ulcers. However, there are too many constraints nowadays to incorporate this care.

Keywords: Mhealth, diabetes, ulcer, foot

Level of evidence: 4
INTRODUCTION

There are currently over 350 million people worldwide diagnosed with diabetes, 18 million of whom are in the United States.\(^1\)\(^2\) Diabetes is classified as a disease resulting in high blood sugar levels. There are two types of diabetes known as Type I and Type II diabetes. Sugar is designed to enter cells through a peptide hormone known as insulin, which ensures the body’s use of sugar for energy. Type I diabetes, also known as juvenile diabetes, is when a patient has had an autoimmune response that has attacked their pancreatic beta cells that produce insulin. Type II diabetes, also known as adult onset diabetes, occurs when the body loses its capability to produce adequate amounts of insulin due to resistance. With a partial or complete lack of insulin functionality, the body lacks its necessary nutritional needs and as a result, a patient develops hyperglycemia.\(^3\)

Hyperglycemia in long-term diabetes mellitus is associated with many morbidities including, but not limited to kidney disease, cardiovascular disease, blindness and neuropathy.\(^4\) A diabetic foot, or neuropathic foot, is caused by a reduction in blood supply to the lower extremity, resulting in the peripheral nerves receiving inadequate nutrition, leading to death of the nerves and loss of sensation.\(^3\)

The lack of sensation of the extremities can cause a diabetic ulcer that is difficult to treat due to the lack of blood flow to that area. Blood supply is essential in wound healing process because of the nutrients and oxygen needed for successful treatment.\(^3\) Approximately 25% of diabetics will have an ulcer at one point in their life.\(^5\) Prompt and proper treatment of an open ulcer is important as it may alleviate long term damage because an open wound can be a portal for bacteria, infections, and eventually amputation. Estimates have shown that 3.4% of all inpatients worldwide have a diabetic foot ulcer, with 1.5% of amputations coming from the same disease population.\(^6\) If an ulcer is found, the patient should seek medical care to monitor and treat the wound to prevent infection. In urban areas where hospitals and medical professionals are more accessible, a patient can easily seek treatment; however, in rural or lower income communities, obtaining treatment is a greater obstacle. By eliminating barriers, telemedicine, a sight into the future of new innovations, has allowed patients to communicate with medical professionals over long distances.\(^7\) In addition to the increased accessibility that telemedicine may bring, there is an additional cost benefit. Chronic wound costs in the United States costs an estimated 6-15 billion dollars annually. Reducing travel time for the patients and reducing hospital and clinic volume can lower this cost significantly.\(^8\)

While telemedicine is currently used for multiple medical disciplines such as radiology and dermatology, diabetic ulcers present a unique dilemma. Diabetic ulcers need to be carefully measured and evaluated for depth and signs of infection. Modern camera technology has allowed patients to capture the required picture for clinicians to help gather information for the physical exam.\(^8\) One important obstacle to the use of technology for healthcare is the assumption that all patients are technologically literate. While the use of camera phones and video conferencing may be second nature to many, the growing elderly population may have difficulties; however, there are methods which could help to resolve these problems. For example, for patients who are not able to properly capture their wound independently, a visiting nurse or mobile screening center may be better suited.\(^9,10\) This paper presents
a review of multiple studies that assessed the efficacy of telemedicine compared to standard clinical visits. Studies took place in multiple countries, each with their own healthcare systems and clinical guidelines.

**METHODS**

Literature search was performed on PubMed. The PubMed search was done using the query “Mhealth AND foot AND ulcer AND diabetes”, yielding 55 articles. Inclusion criteria included articles with human subjects, peer-reviewed articles, articles printed in English and articles with full text availability through New York College of Podiatry Medicine library or interlibrary loan. Exclusion criteria included feasibility articles, articles only discussing protocol, articles not discussing ulcer management, articles that discussed technology rather than telemonitoring and articles not printed in English. After applying the inclusion and exclusion criteria, 11 articles from the PubMed database were selected to be included in the literature review.

![Figure 1: Article acquisition with inclusion and exclusion criteria](image)

**RESULTS**

The PubMed search resulted in 55 articles. After applying the inclusion and exclusion criteria, 11 articles from the PubMed database were selected to be included in the literature review to discuss the role telemedicine has in diabetic ulcer treatment. Studies included the use of mobile phone cameras and integrated healthcare communications. The treatment modalities and significant results are summarized in Table 1.

With respect to mobile phones, there were several significant results to note. Three groups examined mobile technologies and patient outcomes. Van Netten et al. studied the reliability and validity of mobile phone images in remotely assessing diabetic foot ulcers. 50 diabetic patients with ulcers were recruited. The average age of the participants was 61 and the mean duration of diabetes was 20 years. All patients were seen in a regular clinic setting in Australia. Wounds were assessed for 7 clinical characteristics and 3 treatment decision
factors. Images were taken by research assistants who have had no prior podiatric training. The assistants went through a training module similar to what patients or their family members would use to take their own photographs. 4 pictures were taken of different angles and distances from the ulcer. The images were sent to 5 remote clinical podiatrists who had access to the photos and relevant lab values to the case. The remote physicians were asked to complete the same wound assessment previously completed in the clinic. They reported minimal validity and reliability.

Pak et al. examined the accuracy of pressure ulcers evaluation comparing telemedicine with manual in-person evaluations in Korea. They followed 60 patients over the course of four weeks. Photographs and videographs of the ulcers were taken and evaluated off site. The method to determine depth of ulcers included use of cotton swabs and sizes were used using digital measurements. The study found there was agreement for ulcer size with 87.9% accuracy, distance of depth with 94.6% accuracy, and edges of wound with 90% accuracy using telemedicine. Out of 60 patient participants, 8 patients’ wounds worsened during the study.

Kim et al. studied patients with various stages of ulcers at two Veteran Affairs (VA) Hospitals in the United States. They evaluated level of agreement between telemedicine and in-person of wound conditions. They had data from 70 patients with a sum of 430 visits, which is up to 6 visits per wound. Nurses were used to upload photos, wound dimensions, and other wound specific information. The data was reviewed by a clinician and compared to the results for the same patient’s in-patient visit. They examined the accuracy measures of sensitivity and specificity of several diagnostics. They found that sensitivity ranged from 0.32 for cellulitis to 0.63 for necrosis and specificity ranged from 0.80 for necrosis to 0.91 for cellulitis (p-values <0.01).

Integrated health care, was the second measure analyzed in eight studies and two literature reviews. Integrated health care studies had interdisciplinary health teams to provide care and the studies used telemedicine either to track ulcer healing or to identify patients at risk. Several studies also compared telemedicine with in person care. Clemensen found that it can be possible to provide expert coordinated treatments to the patient in their homes. Wilbright reported 75% ulcer healing for the test subjects and 81% for the control group (P=.55). While both groups evaluated in Wilbright’s research had similar healing time (P=.83), healing time ratio adjusted for age (P=.1), and unhealed ulcers or loss to follow-up (P=.13), the results were at high risk for bias due to lack of randomization. Thus, a systematic review concluded that there is not enough evidence from this study to determine if telemedicine consultations are as effective.

With respect to diabetic foot or lower limb health, Turnin et al. noted that there was insufficiency of screening during general practice for lower limb vascular disease. They also noted those who are at risk for ulceration (405 out of 1436 patients) structural abnormalities (54.2%) calluses (71.8%). Sood et al. found that 75% of wounds improved or healed, and there was a 72% reduction in the number of hospitalizations. After following their patients for a year, they found that the 72% ulcer healing for the test subjects and 73% healing for the control subjects were similar (P=.42). Both groups had similar rates of amputations (P = .59). Without successful understanding, the telemedicine group of
patients had a higher rate of mortality (P= .0001).

Smith-Strøm et al. found that telemedicine was non-inferior to in person care. They also found that healing times and mortality rates were not significantly different between the two groups and found lower amputations in the TM medicine group compared to the in-person group. A second systematic review, found that there is substantial lack of published data to use meta-analyses data to reach a conclusion.

<table>
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<th>Article</th>
<th>Study Design</th>
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<td>Smith-Strøm 2018</td>
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<td>Tchero 2017</td>
<td>Systemic literature review</td>
<td>N/A</td>
<td>Not enough data</td>
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Table 1: Summary of Articles Reviewed
DISCUSSION

Mobile phones

The study by van Netten concluded that only one of their 10 studied characteristics were statistically valid and reliable. Therefore, mobile phone images should not be the sole diagnostic instrumentation for remote ulcer assessment. However, they do note a limitation to this study of the absence of some ulcer descriptions. The study did not address the size, depth, or duration of an ulcer. Further studies would need to validate mobile phone assessment of these values.

Pak et al. used mobile images and videos to remotely assess pressure ulcers. The video captured a patient using a cotton probe to assess the depth of the wound, solving a limitation stated by Van Netten. However, a major limitation to this study is the absence of any treatment plan. The study showed that an ulcer can be monitored from a distance using technology, but it did not state any method of curing the ulcer. A third study that controls for the limitations by van Netten (the lack of video), and Kim (no curative suggestions) was conducted by Kim et al. They used nurses to upload photos, wound dimensions, and other wound specific information. The data was reviewed by a clinician and was compared to the same patient’s in-patient visit. The addition of nurses allowed new treatment plans to be created for the patients. While the specificity is helpful for advancing the prevalence of telemedicine, the low specificity gives reason for pause. Low sensitivity means the physicians misdiagnosed many images. They recommend only using telemedicine for people who are unable to go to a clinic.

Integrated care

Clemensen et al. evaluated the use of a visiting nurse to communicate and coordinate treatment with experts at a hospital utilizing a videophone and an internet-based patient record. The videophone was convenient to use and allowed the visiting nurse to describe the location and the ulcer itself to those back at the hospital. The patients and their family also felt like they were a part of the treatment plan, because they were able to communicate to the experts in the hospitals and were able to listen in on the treatment plan. For the online medical record, the nurses were able to upload images of the ulcer from their visits and it made it easier to compare ulcer from one visit to another visit. It was found that it can be possible to provide expert coordinated treatments to the patient in their homes. Some of the limitations included scheduling an online consultation as everybody’s schedules had to match, clinical manifestations had to be clearly described, and the nurses needed to be trained in the technical jargon of ulcer care. While there was no data described in this study, the physician’s involved felt that there was adequate information for medical treatment.

In 2017, a study was published that helped solve some of Clemensen’s limitations. Wilbright et al. ran a clinical trial to compare treatment of telemedicine and in-clinic care for diabetic ulcers. A real-time interactive video program was utilized to connect a DFP (diabetic foot program) clinician and physical therapist with a patient and a nurse specialist. The nurse specialist provided majority of the ulcer care including fabricating simple off-loading devices with the support of the DFP team. The use of skilled nurses helped mitigate the need of extra training for the nurses in Clemensen.
Wilbright recruited 140 subjects between 2 hospitals. 20 patients were treated by telemedicine treatment and the remaining 120 received traditional care. Although the p-values were not significant, they showed that telemedical care with a nurse was not inferior to in-clinic visits with a clinician.

Some of the stated limitations of this study included small sample size of the telemedicine group (20) and some of the telemedicine patients had to be seen one time at the DFP clinic for off-loading devices. It is believed that the similarity can also be due to trained practitioners. However, the authors believe that telemedicine does provide timely access to physicians and foot specialist which will allow for timely delivery of care. The lower costs should also allow the expansion of telemedical care in rural populations.

A similar approach was also conducted in 2017 by Turnin. Mobile screening was used to collect and transmit data out of rural or suburban areas to different health specialists (ophthalmologist, diabetologist, podiatrist). Those same health specialists then provided a summary of the screening results and reminder of recommendations to assist the general practitioners (GP) in the care of their patients. The study screened patients who have not had similar testing in the past year for 5 tests (retinal photography, microalbuminuria, ankle-brachial pressure index, monofilament test, plantar pressure distribution).

This screening program did not treat any health problems. However, it successfully identified diabetic patients who are at risk for developing foot ulcers. This is important for the future of telemedicine as a patient can be screened and identified without going to see a podiatric specialist.

Sood et al. analyzed 10 years of the CICAT system in France. CICAT, or Centre D'information et de Conseil Sur Les Aides Techniques, is an integrated wound-care system where trained nurses are dispatched to remote areas to assess and treat a patient. Like the previous studies, the collaboration involved phone calls and imaging transfers to physicians. They found that 75% of wounds improved or healed, and there was a 72% reduction in the number of hospitalizations. In communities where there are few podiatrists, a mobile screening with collaboration from a doctor can lead to less frequent ulcers and its associated morbidities.

In 2015, the first randomized clinical trial to compare telemedicine care to standard care was published. One hundred and ninety-three patients were randomized into telemedicine or standard care. The telemedicine group consultations were conducted with phone calls between nurses and physicians, with an image taken of the ulcer. Each patient was seen twice via phone call and once in clinic, while the in-patient population was treated three times in a clinic.

Their studies perpetuated a moderate risk for bias due to lack of blinding; however, the possibility to blind the patient and clinician from obvious ailments is nearly impossible. This led to their conclusion that further studies need to assess comorbidities in diabetic patients before deciding on treatment through telemedicine.

Another randomized trial was conducted a few years later. Smith-Strom et al. randomized one hundred and eighty-two people to study whether telemedicine is inferior to standard care. Like Rasmussen, there were local nurses in contact with physicians during the trial. However,
Smith-Strøm et al. treated the clinic patients every 6 weeks and distance patients every second week.

CONCLUSION

Telemedicine consults may eventually be a common treatment alternative for diabetic foot ulcers. However, there are too many constraints nowadays to incorporate this care. Based on data from Van Netten and Pak, mobile phones are unable to assess depth of an ulcer. Even including videos with a swab to measure depth is currently inadequate for assessing tunneling and exudate from a wound. The many European studies as well as Wilbright showed that integrating skilled nurses with teleconference to physicians is non-inferior to standard care. The model would allow for greater access to care for remote populations, but the cost of traveling nurses would need to be considered. Further studies would be needed to evaluate the potential healthcare dollars saved by patients being seen via telemedicine, compared to the cost of sending trained wound-care nurses to the patients’ homes.

AUTHORS’ CONTRIBUTIONS

All authors contributed equally to this literature review. All authors agreed upon the final submission of this draft.

STATEMENT OF COMPETING INTERESTS

All authors declare they have no competing interests.

REFERENCES


Utilizing Computerized Gait Analysis to Achieve Symmetrical Gait in a Pediatric Patient: A Case Report

By: Maham Subhani, MPH, BS

ABSTRACT

Introduction

Limb length discrepancies are common in the pediatric population and can result in asymmetrical function in gait. Orthotic devices have many applications, such as providing support to assist the feet in reaching their optimal abilities. Once orthoses are dispensed, it is important to use a tool to objectively assess how the feet are functioning. The F-scan computer analysis software is an in-shoe system which provides dynamic pressure, force, and timing information for foot function and gait analysis. When using the F-scan in practice, the information obtained can immediately be used to adjust orthotic devices in order to provide support and balanced gait. The purpose of this case report is to investigate the findings that can be analyzed from the F-scan system and how the results can be utilized to provide symmetrical support and gait. Asymmetry in function will be assessed via F-scan and adjustments to orthotic devices will be made based on the data.

Study Design: Case Report

Methods

A 10-year-old female accompanied by her mother presented to the practice with chief complaint of feet appearing flat. Prior to this visit, the patient was not evaluated by any other podiatrist or physician for this concern. The first step in analysis included performing a biomechanical exam to assess the lower extremity. Next, F-scan computerized gait analysis was performed and asymmetrical functioning in gait was noted. The patient was casted for orthoses using plaster splints with the subtalar joint in neutral position to create an ideal model of how the foot should be functioning. Then, based on measurements from the biomechanical exam and observational gait analysis, the appropriate orthoses prescription was written. Once the orthoses were dispensed to the patient, it was important to analyze how well they were supporting gait. After two weeks of the patient wearing the orthoses, the F-scan system was used again to capture data to determine if any adjustments needed to be made.

Results

Biomechanical exam was performed and provided detailed information regarding the functioning of both feet. The results from this exam indicated the patient had a cavus foot off-weightbearing, which pronated on-weightbearing. Limb length was not measured as a part of the exam. A forefoot varus along with everted rearfoot was also noted. The F-scan system was utilized to obtain information about the patient’s walking pattern. First the F-scan was performed barefoot and indicated the time spent in various phases of gait. The midstance values were 25 on the left and 27 on the right, propulsion 26/21 (left/right), and heel 49/61. This indicated that the patient spent less time on the heel of the left foot and more time on the heel of the right foot as well as more time in propulsion on the left foot. This suggested the left limb may be shorter than the right. Orthoses were prescribed using calculations from the biomechanical exam. There was a forefoot and rearfoot varus post along with a ¾” deep heel cup bilaterally. Once the orthoses were fabricated and dispensed to the patient, she wore them for two weeks before returning back to the clinic for a follow-up. With the patient’s new orthoses, the F-scan again showed asymmetry in gait between the left and right limb. With orthoses, the F-scan data showed midstance 22/28, propulsion 28/21, and heel 49/61. First, a heel lift was added to the left side using ¼” felt. The F-scan was repeated and the values were midstance 25/29, propulsion 25/19, and heel 54/64. Given that symmetry was still not present, ¼” rubber heel lift was used and F-scan was repeated with data showing midstance 29/23, propulsion 22/26, and heel 61/53. These values indicated that there was still a discrepancy between both limbs. A ⅜” rubber
heel lift was then placed on the left. F-scan was repeated and the values showed midstance 26/26, propulsion 24/23, and heel 56/57. With the assistance of the F-scan, it was noted that a ⅛” rubber heel lift provided symmetrical gait for this patient.

**Conclusion**
Orthoses are a crucial tool in order to help achieve proper support and function in the pediatric population. With the assistance of a gait analysis software such as F-scan, podiatrists can visually show patients the difference an orthotic device can immediately make. The F-scan provides the podiatrist with information to make alterations that will provide the most beneficial care to the patient. This case shows that without the use of a system to analyze how a patient is walking when wearing orthoses, the appropriate adjustments could not have been made. Computerized analysis is an indispensable tool to ensure symmetrical gait and support. Therefore, it should be a mandatory component of each biomechanical exam and orthotic device prescription.

**Keywords:** gait analysis, pediatric, orthoses, F-scan, biomechanical exam

**Level of evidence:** 5
INTRODUCTION

The human gait requires symmetrical functioning for efficient locomotion. However, most individuals are neither structurally nor functionally symmetrical. Limb length discrepancy (LLD) is a common occurrence in the pediatric population that continues on to adulthood. Most individuals have a certain degree of limb inequality in either structure or function. A study conducted at the Growth Study Center of Children’s Hospital in Boston found a limb length discrepancy to be present in 95.5% of patients evaluated. Given the high prevalence of limb length discrepancies, it is important for the practitioner to assess limb asymmetry in their biomechanical evaluation in order to provide the most appropriate treatment. Clinically, identifying limb length asymmetry is important, but it is more crucial to assess the lower limb in action.

Dynamic gait assessment using computer-assisted gait analysis can identify torque and stress as well as determine asymmetry that may be a result of a limb length discrepancy. This method is not only non-invasive and reliable, but it provides information that cannot be observed by the naked eye. The F-scan computer gait software is an in-shoe system which provides dynamic pressure, force, and timing information for foot function and gait analysis. When using the F-scan in practice, the information obtained can be used to make real-time adjustments to orthotic devices, provide optimal support, and ensure symmetrical gait in the individual.

After dispensing orthoses and allowing an individual time to acclimate, computer-assisted gait analysis can reveal functional asymmetry in those that have a limb length discrepancy. It is also useful in identifying asymmetry in individuals who did not initially present with any measurable lower extremity asymmetry. Equal limb length or a level pelvis also does not ensure functional symmetry whereas those with LLD may have symmetrical functioning.

When a limb length discrepancy is present, the foot on the longer limb side is relatively pronated to decrease the length of the limb. This is also evident as increased time in midstance. The shorter side is relatively supinated in an attempt to extend its length and spends less time in midstance while more time in propulsion. The F-scan system is useful for determining the time an individual spends in these different phases of the gait cycle.

When asymmetry is noted, heel lifts are used standardly to achieve symmetry in function. It is suggested to begin with a 1/8th-inch heel lift and increase in height if necessary. With the use of computer-assisted gait analysis, the practitioner can immediately determine in-office if symmetry is obtained after adding a heel lift. Often, heel lifts are not a permanent treatment and need to be monitored for continued effectiveness. The aim of this study was to evaluate how a computer-assisted gait analysis program such as F-scan is a useful clinical and objective method to identify, quantify, and manage asymmetry.

CASE PRESENTATION

A 10-year-old female presented to the private practice of a podiatric physician with her mother with the primary complaint of feet appearing very flat when walking. Prior to this visit, the patient was not evaluated by any other podiatrist or physician for this concern. Past medical history consisted of
the patient having rolled her ankle on multiple occasions, but no serious injuries or fractures occurred.

The first step in analysis included performing a biomechanical exam. The data from the full biomechanical exam is shown in Table 1. The exam showed there was a high arch morphology off-weightbearing, but a flattening foot was present on-weightbearing. There was also forefoot deviation in the frontal plane of 22° on the left and 15° on the right, indicating a forefoot varus was present. The total varus of the foot was calculated by first measuring the angle of the forefoot in the patient’s relaxed standing position. Then the patient is placed in neutral position and subtracting gives the total varus. These measurements were 46° on the left and 47° on the right. Relaxed calcaneal stance position was not measured, but was noted to show significant eversion, greater on the left than the right. Limb length was also not measured. With the knee extended, the ankle range of motion was 12° on the left and 22° on the right. When the patient stood, genu recurvatum was also noted, suggesting equinus may be present. The collapsible cavus foot type resulted in flattening and pronated feet.

Table 1: Biomechanical exam

<table>
<thead>
<tr>
<th>Arch morphology</th>
<th>Left foot</th>
<th>Right foot</th>
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<td>H+5</td>
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<tr>
<td>On-weight</td>
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<tr>
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<td>Ankle position</td>
<td>Knee extended</td>
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<th>Forefoot deviation</th>
<th>Frontal</th>
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| Total varus           | 46        | 47        |

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<th>Relaxed calcaneal stance position</th>
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A barefoot walking exam was performed using the computerized gait analysis system in order to obtain baseline information of functioning without orthoses. This is shown in Figure 1. Data correlating to barefoot walking is shown in Table 2. The values for midstance and propulsion in the tables represent the percent of gait cycle spent in that specified parameter. The value for heel represents the percentage of duration in
stance. The midstance values were 25 on the left and 27 on the right, propulsion 26/21 (left/right), and heel 49/59.

Figure 1: Barefoot F-scan.

The findings of all exams were thoroughly discussed with the mother and patient. The different components of the patient’s foot were causing her foot to function less than optimal. The recommended treatment of choice was custom foot orthoses to correct for the various deviations. The patient was casted using plaster splints with the subtalar joint in neutral position to create an ideal model of how the foot should be functioning.

Based on measurements from the biomechanical exam and observational gait analysis, an orthoses prescription for a Healthflex type orthotic was written. The prescription included a deep heel seat along with a rearfoot 3° varus post on the right and 4° varus post on the left as well as a forefoot 8° varus post on the right and 7° varus post on the left. The prescription also indicated to reduce the undercuts and to use vinyl top covers. Once the orthoses were dispensed to the patient, she was advised to start wearing them 2 hours the first day, 4 hours the next day, and to progressively increase use over the week until she is able to tolerate them full-time. The patient was then seen two weeks later to further analyze her gait. At this point, it was important to dynamically assess gait to determine if any changes needed to be made. To do this, the F-scan system was used. F-scan was performed with the orthotic device in the patient’s Saucony sneakers. This test was repeated to ensure that the results were accurate and reproducible. The results from this test are shown in Figure 2 and Table 3.

Table 2: Data from barefoot test.
An immediate discrepancy was shown suggesting an LLD. Data showed midstance was 22/28, propulsion 28/21, and heel 49/61. This shows that the left limb spent more time in propulsion and less time in midstance as well as less time on the heel. In an attempt to provide symmetry, a ¼” felt heel lift was added to the left and the test was repeated. The results using a ¼” felt heel lift on the left are shown in Figure 3 and Table 4. This changed the values to midstance 25/29, propulsion 25/19, and heel 54/64, indicating that the values were still not symmetrical. Given the ability of felt to easily flatten, the felt was removed and a ¼” black rubber heel lift was inserted on the left. The results from this test are shown in Figure 4 and Table 5 but again symmetry was not present. Midstance values were 29/23, propulsion 22/26, and heel 61/53. Next, a ⅜” black rubber heel lift was placed on the left. Results from this test are shown in Figure 5 and Table 6. The results show symmetry in different parameters of the gait cycle including midstance 26/26, propulsion 24/23, and heel 56/57. This test was repeated to ensure accuracy. It was determined that this patient needed a ⅜” heel lift on the left in order to obtain symmetrical gait. The patient was sent home with the heel lift and advised to keep the heel lift on the left side under the orthotic device. The patient will be reevaluated at 6 months to determine if gait symmetry is still present and if any other modifications need to be made.
Figure 3: F-scan of Healthflex with ¼” felt heel lift on the left.

Table 4: Data after addition of ¼” felt heel lift.

Figure 4: F-scan of Healthflex with ¼” black rubber heel lift on the left.

Table 5: Data after addition of ¼” rubber heel lift.
DISCUSSION

The most obvious effects of limb length discrepancy are on posture and gait. LLD makes the gait of an individual less efficient, requiring greater energy expenditure, increased activity of postural muscles, and more fatigue. When an LLD is present, the foot accommodates, in an effort to find symmetry.

The foot on the longer limb side is relatively pronated to decrease the length of the limb. This is also evident as increased time in midstance as well as decreased time in propulsion. The shorter side is relatively supinated in an attempt to extend its length and spends less time in midstance and on the heel while more time in propulsion. Figure 2 and Table 3 show the F-scan results when the patient returned to the office after wearing the Healthflex orthoses for 2 weeks. This scan shows that the left limb spent less time and pressure in midstance and more time in propulsion, whereas the right limb showed greater values for midstance and less for propulsion. This suggests that the left limb is the shorter limb and the right is longer. When ¼” felt heel lift was added to the left, the results in Table 4 show that the values were coming closer together; however, the left limb was still being identified as the shorter limb and asymmetry was present. Ultimately when a ⅜” rubber heel lift was used, Table 6 shows almost perfectly symmetrical gait. The midstance, propulsion, and heel values are all within one point between both limbs.

Alterations in the biomechanics of the foot can result in significant changes in the functioning of the foot. Asymmetry in
function may be present even if legs are equal in length which is why dynamic assessment is beneficial.\textsuperscript{1,2} Interventions for this include orthotic devices, which is what was used in this patient to improve malignation.\textsuperscript{1,8} Once orthoses are dispensed to patients, dynamic gait assessment can be performed using computer assisted gait analysis.\textsuperscript{1,4} The goal of this dynamic gait assessment is to determine if both limbs spend the same amount of time on the ground and produce the same amount of normal pressure.\textsuperscript{1,4}

In the case of the patient presented in this case report, using computerized gait analysis software showed to be indispensable in identifying asymmetrical gait. The dynamic analysis provided data that could not have been gathered by observational methods of gait analysis. This method of data collection provides podiatrists with information to make modifications to their treatment plan that will best suit the needs of the patient.\textsuperscript{7} By using tools such as F-scan, podiatrists can identify pathologies and objectively evaluate the effectiveness of orthotic devices.

Limitations

A limitation of this study is not assessing limb length discrepancy clinically from methods such as measuring actual or apparent limb length. Limb length can also be measured radiographically, which was not done. If limb length was measured at the patient’s initial visit, this may have also given a hint towards a possible asymmetry in length. As discussed, asymmetry in function may still be present with equal limb lengths. Therefore, using dynamic gait assessment can still be beneficial by providing data that may be otherwise unobtainable.

The results from Table 5 show that the left limb spends more time and pressure in midstance and less in propulsion, whereas the other limb is the opposite. This would suggest that the left limb is pronating and acting as the longer limb and the right limb is supinating to act as the shorter limb. The values for this data could have been repeated for accuracy. However, the final results in Table 6 using the \( \frac{3}{8} \)” heel lift show symmetry and therefore it was thought that the values from Table 5 may have been a result of other factors such as the patient adjusting to the heel lift or walking differently.

Lastly, since this is a case report, further studies including larger sample sizes would be beneficial to show either replication of the results or to show any discrepancies and differences in results.

CONCLUSION

In this case report, the utilization of computer gait analysis software F-scan provides invaluable data regarding gait and symmetry. The F-scan provided information that could not have been gathered using standard methods of observational gait analysis. For this patient, F-scan provided the ability to make appropriate modifications such as adding a heel lift. This treatment resulted in symmetrical gait for the patient. The clinical relevance of this case report identifies that computerized gait analysis is an essential tool to ensure symmetrical gait and support. The data provided through this tool can help physicians better treat patients and make appropriate alterations to individuals using orthotic devices.
STATEMENT OF COMPETING INTERESTS

The author of this case report has no competing interests.

REFERENCES

Oral Antibiotics and Shorter Duration IV Antibiotic Therapy in the Treatment of Osteomyelitis

By: Spencer Stringham, BA; Ridvan Husic, BS

ABSTRACT

Introduction
Osteomyelitis is a disease that requires prompt and swift treatment to avoid serious complications and morbidity. The historical approach to treatment has been through debridement and intravenous antibiotics. However, the use of intravenous antibiotics can pose consequences such as thrombosis, embolization, infection, and significant expenses. Recent studies have shown alternatives to circumvent these complications. One of the most debated topics in current years is whether the efficacy of oral antibiotics is comparable with intravenous administration. The purpose of this paper is to perform a literature review of direct comparisons between oral versus intravenous antibiotics including short duration of IV antibiotics followed by oral regimens.

Study Design: Systematic Review of Literature

Methods
Two searches were conducted on PubMed. The first search used the phrase “osteomyelitis oral antimicrobial.” After applying exclusion criteria, 6 articles were used from the search. The second search used the phrase “bone infection AND oral antibiotics versus intravenous antibiotics.” After applying exclusion criteria, 1 article was used for the literature review. A total of 7 articles were used for analysis.

Results
Three articles were analyzed to determine the efficacy of a short duration IV antibiotic regimen followed by oral antibiotics to a long duration of IV antibiotics in the treatment of osteomyelitis. 4 articles were analyzed to determine the efficacy of exclusive intravenous antibiotics versus exclusive oral antibiotics in the treatment of osteomyelitis. There was sufficient evidence indicating that stepdown oral therapy and oral therapy in isolation is comparable to intravenous therapy specifically in cases of uncomplicated osteomyelitis. Furthermore, studies provided evidence that certain oral drugs such as rifampin, amoxicillin/clavulanic acid, cephalosporins, clindamycin, and quinolones were effective in treating osteomyelitis. It was also noted that intravenous catheters were associated with higher rates of complications.

Discussion
The overall trend of the reviewed articles highlights the possibility that oral antibiotics may be comparable to intravenous antibiotics in certain cases of osteomyelitis. However, there was limited evidence supporting the notion of oral antibiotics in complicated cases such as MRSA infection and immunodeficient patients. Furthermore, a significant limitation was that many studies were not matched based on sample size and study design. Although the results are promising, serious infections like osteomyelitis must be extensively documented in strong randomized control trials in order to consider a drastic change in current treatment protocols.
**Conclusion**
Oral stepdown and oral antibiotic therapy may be a viable option in treating uncomplicated cases of osteomyelitis. More research and randomized control trials are needed to determine efficacy in certain populations such as those with complicated infections and co-morbidities.

**Level of evidence:** 4
INTRODUCTION

Background and Epidemiology

Osteomyelitis is a potentially devastating condition characterized by a bone infection.\(^1\) Osteomyelitis can be subdivided into two major categories depending on the manner of pathogenesis.\(^1\) Hematogenous osteomyelitis, more often presenting in children, occurs when pathogens reach distant sites via the bloodstream.\(^1\) The other form is described as non-hematogenous, more commonly seen in adults.\(^2\) However, these forms are not mutually exclusive, as adults can present with cases of hematogenous pelvic, sacral, and sternal osteomyelitis.\(^2\) This condition can also be classified based on the duration of infection as acute, subacute, or chronic.\(^2\) While all forms are dangerous, chronic infections are the most detrimental. If acute infections are not resolved in a timely manner, significant consequences can occur such as the need for multiple surgeries, avascular necrosis, sepsis, and severe disease.\(^3\) The incidence of osteomyelitis has been increasing in recent years. In one study that examined incidence rates in Olmstead County, Minnesota, investigators found an increase of 11.4 cases per 100,000 to 21.8 cases per 100,000 when comparing the periods of 1969-1979 to 2000-2009 respectively.\(^4\) The investigators also noted an increased incidence in older individuals due to the increasing rates of diabetes and peripheral vascular disease.\(^4\) This rationale is not alarming, as diabetic patients with poor circulation often present with ulcerations on the lower extremity.\(^5\) In addition, these patients also have poor wound healing potential, exacerbated by poor blood supply, increasing the likelihood of exposed areas of tissue at risk of infection.\(^5\) If the wounds penetrate deeper, they can expose bone tissue or create a point of entry for pathogens to infect the bone.\(^5\) One of the most serious risks in this population is amputation, which can occur as high as 66% of diabetic wound cases.\(^6\) Evidence has shown that mortality following amputation can range from 30% to 69%, depending on whether the patient can ambulate.\(^7\) Complications from osteomyelitis places a significant toll on health care costs associated with treatment, surgery, and inpatient hospitalizations.\(^6\) Therefore, it is in the best interest of the patient, health care provider, and institution to treat this condition in an efficient manner while minimizing complications.

Traditional Approaches to Treatment and Drawbacks

Traditional approaches to treating osteomyelitis have been through surgical management and 4-6 weeks of IV antibiotics.\(^8\) IV drugs have been long preferred because of their ability to access bone tissue.\(^8\) Although it is difficult for antibiotics to reach bone, IV drugs can be monitored and delivered systemically in order to achieve high concentrations in the blood and therefore diffusion into bone.\(^9\) Additionally, drugs such as Beta lactams, glycopeptides, and lipopetides, which have little to no absorption, can better access bone tissue when administered through an IV line.\(^9\) Furthermore, IV lines have been preferred in pediatric populations because of suspected malabsorption of the drugs in the GI tract.\(^10\) However, IV lines present with complications and significant drawbacks. Venous thrombosis resulting from catheterization has been observed in numerous hospitalized populations irrespective of the underlying condition.\(^11,12\) Other complications of this treatment modality include venous stenosis, additional infections, bleeding, pulmonary complications, and embolism.\(^13\) From a
financial perspective, IV antibiotics are more expensive than their oral counterparts. Some patients, especially in the pediatric population, must also be sedated before line insertion which increases the financial burden.\textsuperscript{10}

Evidence for Oral Antibiotic Usage and Predictions

As a result of these drawbacks, newer research has investigated whether there are alternatives to using an IV line, such as using oral antibiotics. While some oral drugs have low bioavailability and are inferior to their intravenous counterparts, there are others that can achieve sufficiently high concentrations in bone tissue such as fluoroquinolones, cyclines, macrolides, sulfamides, rifamycins, and oxazolidinones.\textsuperscript{9} If it is possible to treat osteomyelitis with oral drugs, patients would be able to avoid the complications often associated with venous catheters. The purpose of this paper is to perform a literature review of studies comparing the efficacy of oral vs IV antibiotics in the treatment of osteomyelitis. We also examine studies investigating the efficacy of a shorter duration IV antibiotics followed by oral administration.

METHODS

This study was conducted by means of a systematic review of the literature on PubMed. Two searches were conducted using the advanced search toolbar. The first search was performed using the phrase “osteomyelitis oral antimicrobial” yielding 857 articles. The filters “From 2009/01/01 to 2019/12/31” and “humans” were then used to exclude non-human subject research and articles published before 2009. This narrowed the search to 293 articles. 287 were then excluded for reasons including irrelevance to the topic, infections related exclusively to joints, oral versus IV antibiotics in diseases other than osteomyelitis/bone infection (such as endocarditis, septic arthritis), protocol studies, and recommendations for research. The technical form of this search was as follows (before individually selecting which articles were used): osteomyelitis oral antimicrobial AND ( "2009/01/01"[PDat] : "2019/12/31"[PDat] ) AND Humans[Mesh]. The second search that was conducted was also through PubMed. This search used the phrase “Bone infection AND oral antibiotics versus intravenous antibiotics” in the advanced toolbar yielding 29 articles. The same filters “From 2009/01/01 to 2019/12/31” and “humans” were used as in the previous search narrowing it down to 10. 9 were excluded for the same reasons as in the previous entry. The technical form of this search was as follows: (bone infection) AND oral antibiotics versus intravenous antibiotics AND ( "2009/01/01"[PDat] : "2019/12/31"[PDat] ) AND Humans[Mesh]. In total, 7 articles were used for the literature review.
**RESULTS**

*Step-Down Approach: Short Duration of IV Antibiotics Followed by Oral Antibiotics Versus Prolonged IV Antibiotics*

The step-down approach will be defined in this review as a short duration of IV antibiotics followed by oral antibiotics. In a study by Zaoutis et al., investigators examined the step-down approach to therapy in pediatric patients diagnosed with acute osteomyelitis, excluding those with complications and co-morbidities. 13 1969 children were selected across 29 children’s hospitals, 1021 of whom had received prolonged IV antibiotics and 948 who were started on an IV line but switched early to oral antibiotics. Both groups were compared for treatment failure, defined by re-hospitalization 6 months post diagnosis.

Rates of treatment failure were almost identical, 5% in the intravenous group and 4% in the step-down group. They also found that children treated with long term IV antibiotics had a higher incidence of complications related to the catheters.

In a retrospective study by Flury et al., investigators examined 61 adult patients at the University Hospital of Basel, Switzerland who were diagnosed with vertebral osteomyelitis. 14 The primary purpose of the study was to assess the safety of switching from IV to oral antibiotics 2-3 weeks after the initial diagnosis. 72% of patients were switched to oral antibiotics by 2.7 weeks (median) and 34% were switched to oral antibiotics by 2 weeks. At one year follow up, there were no recurrences of osteomyelitis, with 2 deaths unrelated to the diagnosis of vertebral osteomyelitis. The
investigators found that the independent predictor for switching to oral drugs was a decreased blood level of C reactive protein (CRP). They concluded the switch to oral drugs was safe as long as CRP levels decreased and abscesses were drained. They also found that drugs considered bactericidal such as first-generation fluoroquinolones (ciprofloxacin) and rifampin, were effective and most chosen for oral regiments.\textsuperscript{14}

McNeil et al. examined the route of antibiotic treatment in children with acute hematogenous osteomyelitis and/or septic arthritis caused by \textit{Staphylococcus aureus}.\textsuperscript{15} The investigators examined data for 192 children, 102 of which had bacteremic osteoarticular infections. In cases of bacteremia, patients were either discharged on outpatient parenteral therapy (68 patients), oral therapy (most commonly cephalaxin, clindamycin, and linezolid after a 7 day period of intravenous antibiotics- 26 patients) and those that remained in the hospital for complete hospital IV therapy (7 patients). Patients with a short duration of IV antibiotics followed by outpatient oral therapy were compared with parenterally treated patients for CRP, fever duration, and long-term orthopedic complications. The investigators found no significant difference in complications. However, it was noted that the patients chosen for oral therapy was likely due to a shorter duration of fever, lower CRP levels, and no presence of MRSA.\textsuperscript{15}

\textbf{Oral Vs Intravenous Antibiotics}

Roul-Levy et al. examined treatment outcomes in children diagnosed with acute osteomyelitis without co-morbidities.\textsuperscript{16} The investigators included the medical charts of 45 children, treated with either oral amoxicillin/clavulanic acid exclusively or a step-down approach with initial IV cefamandole followed by oral amoxicillin/clavulanic acid. The majority of cases were caused by \textit{Staphylococcus aureus}, most of which were sensitive to Methicillin. The investigators concluded that there was no significant difference in healing between the two groups assessed at 6 months. Furthermore, treatment failure was found in only 3 patients treated with step down therapy and 1 patient treated exclusively with oral antibiotics. Lastly, the investigators noted that there was an insignificant difference between duration of hospitalization and treatment time between the two groups (42.5 day IV, 43 day oral).\textsuperscript{16}

Keren et al., investigated the treatment outcomes of post discharge oral vs intravenous antibiotics in children diagnosed with acute uncomplicated osteomyelitis.\textsuperscript{17} In this retrospective cohort study, investigators selected records from 36 hospitals, 1055 children were discharged with oral antibiotics and 1055 children were discharged on an intravenous catheter. Children discharged with oral antibiotics were often given clindamycin and cephalaxin. Children discharged with a catheter were most often given cefazolin, ceftriaxone, and vancomycin. When comparing treatment failures, the investigators found a failure rate of 5% in the oral group versus 6% in the intravenous group. Adverse events related to drug reactions were low in both groups, although slightly higher in the intravenous group. There was a statistical significance associated with the findings in children under 5 years old with a positive culture of MRSA. In this subset of patients, there was no substantial difference in outcome between the oral versus intravenous group.\textsuperscript{17}

Euba et al. conducted a randomized clinical trial of patients diagnosed with chronic staphylococcal osteomyelitis in which oral
antibiotics were compared to a step-down approach.\textsuperscript{18} 50 patients were included in the study, who were acquired through teaching hospital in Barcelona, Spain. The median patient age was 44 years with a standard deviation of 20 years, 14 of which had other co morbidities/ immunodeficiencies. MRSA isolates were not found in any patients, as all Staphylococcus identified were susceptible to oxacillin, rifampin, and cotrimoxazole. Patients were randomly placed into one of two groups, the first group receiving 6 weeks of intravenous cloxacillin followed by 2 weeks of oral cloxacillin, and the second receiving oral rifampin-cotrimoxazole for 8 weeks. Patients were followed up at 10 years, during which time the investigators reported 2 relapses in the intravenous group and 3 relapses in the oral group. In terms of cure rates, were no significant differences, with an overall rate of 89.6%. The investigators concluded that oral rifampin-cotrimoxazole treatment for chronic staphylococcal osteomyelitis was comparable to those treated with IV cloxacillin.

Li et al. conducted a randomized trial of patients diagnosed with bone and joint infections in order to compare the efficacy of oral versus intravenous antibiotics.\textsuperscript{2} 1015 patients over the age of 18 were assessed in the final study and were selected from 26 sites in the U.K. All participants were randomly placed into either oral or intravenous groups and treated no longer than 7 days of initial surgical or antibiotic treatment. There was no exclusion criteria used for patients based on drug of choice or the infecting pathogen. Endpoints were assessed based on definitive treatment failure or probable/possible treatment failure. In the oral treatment group, definitive treatment failure occurred in 67 of 509 participants (13.2%) and probable treatment failure in 10 of 509 participants (1.2%). In the intravenous group, definitive treatment failure occurred in 74 of 506 participants (14.6%) and probable treatment failure in 6 of 506 participants (1.2%). The investigators concluded that both methods of treatment were comparable and that oral regiments are non-inferior to the traditional IV approach. In addition, the investigators found a greater duration of hospital stay and complications of catheterization in the intravenous versus oral group.

**DISCUSSION**

**Step Down vs Intravenous Antibiotics**

The 3 studies comparing the step-down approach to intravenous antibiotics were conducted using a retrospective analysis of records and provided similar findings. McNeil et al. examined cases of acute pediatric osteoarticular infections, found no significant difference in the long-term complications between the intravenous group and step-down group.\textsuperscript{15} There were many specific factors which determined whether patients were placed on the step-down method or kept on intravenous antibiotics, including rate of decline of CRP, presence of MRSA, and duration of fever.\textsuperscript{15} While the researchers found limited evidence that the step-down approach may be noninferior in cases of MRSA, it was not statistically significant.\textsuperscript{15} Zaoutis et al., who also examined acute cases of osteomyelitis in children published similar results.\textsuperscript{13} The researchers in the study concluded that treatment failure is comparable between the oral step-down approach versus intravenous antibiotics.\textsuperscript{13} Furthermore, this study provides additional evidence to the fact that long term intravenous regimens increases the risk of complications and re-admittance to the hospital.\textsuperscript{13} Flury et. al, while examining vertebral osteomyelitis primarily in adults, confirmed the findings of the prior
two studies.\textsuperscript{14} They concluded that the stepdown approach likely could be a viable option if certain criteria is met, such as a decrease of CRP.\textsuperscript{14}

From the aforementioned articles, two studies examined pediatric cases and another evaluated adult populations, a common theme surrounded complications, comorbidities, and severity of infections.\textsuperscript{13,14,15} Patients were not placed into either group systematically by the researcher, as the study designs were not RCT. Therefore, investigators evaluated the decision making of physicians selecting certain therapies for different patients. McNeil et al. found that patients were placed on step down therapy when there was a quicker resolution of symptoms and not compromised with MRSA, an infection notorious for drug resistance.\textsuperscript{15} Similarly, Zaoutis et al. and Flury et al. only recruited cases of immunocompetent patients.\textsuperscript{13,14} Like McNeil et al., Flury et al. also found specific criteria that would predict whether patients were placed on the step-down method.\textsuperscript{14,15} Certain studies were also specific as to the oral regimens that could compare to intravenous drugs, most frequently being fluoroquinolones, clindamycin, linezolid, and rifampin.\textsuperscript{14,15}

It is also important to mention the limitations to these studies, the first being the sample selection. In two of the studies analyzed, only pediatric cases were examined, whereas the third study primarily examined adults.\textsuperscript{13-15} While the study conducted by Zaoutis et. al can be considered a strong representative sample, the other two had far smaller sample sizes making it more difficult to generalize the results.\textsuperscript{13-15} Additionally, while two studies did not exclude cases based on the infecting pathogen, Mcneil et al. exclusively examined infections by \textit{Staphylococcus aureus}.\textsuperscript{13-15} Perhaps the most noteworthy limitation was in the study design itself, as no study examined in this category was a randomized control trial.\textsuperscript{13-15}

\textbf{Oral Versus Intravenous Antibiotics}

The following group of studies examined a direct comparison between oral versus intravenous antibiotics in the treatment of osteomyelitis. Keren et al. and Roul-Levy et al. compared the two treatment options in uncomplicated, acute pediatric cases of osteomyelitis.\textsuperscript{16,17} Both studies published similar findings in regard to treatment failure, as there was no significant difference between groups.\textsuperscript{16,17} While evidence thus far has not fully supported this method of treatment in cases of MRSA, Keren et al provided support for the efficacy of oral drugs in the treatment of this organism, specifically in cases under 5 years of age.\textsuperscript{17} Keren et al. also provided more support for the notion that intravenous catheters are associated with an increased risk of complications.\textsuperscript{17} The oral drugs used in these studies were amoxicillin/clavulanic acid, clindamycin, and cephalosporins.\textsuperscript{16,17}

The last two studies examined were randomized clinical trials examining an older group of participants. However, the results provided evidence that oral drugs may be noninferior to intravenous routes of administration. Euba et al. found that a regimen of oral rifampin-cotrimoxazole provided no significant difference in relapses and cure rates when compared to intravenous cloxacillin in healthy patients diagnosed with staphylococcal chronic osteomyelitis.\textsuperscript{18} Li et al. also published similar results in a randomized control trial of an adult population diagnosed with orthopedic infections.\textsuperscript{2} The researchers concluded that there was no significant difference in treatment failure between oral
and intravenous groups. Furthermore, they found that there was an increased risk of hospitalizations and complications in the groups placed on IV antibiotics. In this study, the commonly prescribed drugs were rifampin and quinolones. However, in contrast to the previous study, no exclusionary criteria was given based on the infecting pathogen. It is also important to note that Li et al. reasserted the notion that or al drugs may still not be the first line for drug resistant pathogens and complications such as poor GI absorption.

There were some notable limitations in these studies. Two studies exclusively examined acute pediatric cases of osteomyelitis and were not conducted using randomized control trial study designs. While the study conducted by Keren et al. can generally be considered a strong study design and sample selection, Roul-Levy et al. used a significantly smaller sample size acquired from a single hospital. While the two randomized control trials provided definitive evidence, they differed than the prior two in terms of sample selection. Both RCTs studied an older population, Euba et al. exclusively examining staphylococcal cases of chronic osteomyelitis, and Li et al. with a more nonspecific group of subjects. Despite providing a large sample size in the Li et al. study, it contrasted with the study conducted by Euba et al., which used a very small sample from one hospital. Another important limitation to consider is how some studies were operationally defining variables. In this group of studies, the researchers were exclusively comparing oral versus intravenous antibiotics. However, two studies were not clear on how they were defining the oral groups. For example, Keren et al. examined post discharge antibiotic regimens in patients (oral versus intravenous), without mentioning which method of therapy was used when the patients were hospitalized. It is unclear whether these patients had already been paced on an IV line during the hospital stay yet were still considered part of the “oral” group post discharge. Furthermore, Li et al. defined groups based on the regimen patients were placed on within 7 days of initial treatment. This study considered patients to be a part of the oral group even if the patient had been on an IV line for the past 7 days, as long as it did not extend beyond that period.

**CONCLUSION**

Based on the review of literature, an oral antibiotic step down approach to treating osteomyelitis may be comparable to the traditional intravenous regimen of 4-6 weeks in cases of healthy, immunocompetent patients. An exclusively oral regiment may also be plausible in this same group of patients. Results from the studies also confirm the risks associated with intravenous catheters and provide evidence that oral drugs can be efficacious such as rifampin, amoxicillin/clavulanic acid, cephalosporins, clindamycin, and quinolones. While these results are promising, it must be noted that any suggested change in current treatment protocols must be viewed with an eye of caution. More research must be done in randomized control trials to provide more support for the proposed changes in treatment. Furthermore, due to the limitations associated with differences in selected samples and study designs, more research must be conducted to specifically define efficacy in different subpopulations. From these studies, it is also inconclusive whether this method should be the choice regiment in severe infections such as in MRSA or in cases of debilitating co-morbidities. While these conclusions are
promising in certain subsets of patients, future research should focus exclusively on specific pathogens, acute versus non-acute cases, and the differences in age groups. Additionally, as only one study compared the step-down method to oral drugs only, it would be more useful to continue more trials on this particular subject. Lastly, future research should examine whether certain oral regimens are comparable in cases of MRSA and those who are pre-disposed to immunodeficiencies.

AUTHORS’ CONTRIBUTIONS

Both authors equally contributed to the design of the study and evaluated the available articles. All authors contributed equally in the writing of this literature review and reviewed the final version for submission.

STATEMENT OF COMPETING INTERESTS

The authors declare that they have no competing interest associated to this manuscript.

REFERENCES


A Systematic Review of Gait Analysis and Intervention in Individuals with Cerebral Palsy

By: Amira AbiHaidar, MS, BS

ABSTRACT

Introduction
Cerebral palsy (CP) is a neuromotor disorder caused by an early injury to brain regions or pathways that control movement. CP patients present with a limited range of motion that inhibits their functional motor disabilities, and thus impedes their gait patterns. Standard gait deviations can be grouped into the gait patterns of spastic hemiplegia and spastic diplegia. Gait analysis is crucial for treatment and assessment of outcome when evaluating the change in motor status over time for CP. The purpose of this review is to assess the effectiveness of gathering early gait analysis in cerebral palsy to designate appropriate treatment, which will help improve spasticity, range of motion, and, ultimately, the quality of life.

Study Design: Systematic Review of the Literature

Methods
A literature search was conducted using PubMed. The search used the term "cerebral palsy AND gait analysis" yielded 1403 articles. The inclusion criteria included articles that assessed motor intervention treatments and articles published between 11/01/2009 and 11/01/2019. Exclusion criteria included articles that were written in a language other than English, non-human participants, and articles that did not focus on specific treatment plans. Therefore, my search was written as follows: “Cerebral palsy and gait analysis and early intervention and treatment.” This yielded seven total articles. After the inclusion and exclusion criteria were applied, four papers specifically included treatment intervention and were included in this review.

Results
After appraising several parameters, it can be deduced that patient-specific treatment for CP patients is the most beneficial approach to improving spasticity, increasing range of motion, and decreasing gait abnormalities. Conservative treatments such as treadmill training lead to earlier onset of independent walking. In addition, Botulism Botulinum toxin injection increased dorsiflexion angle of the ankle during gait after long-term intervention. More aggressively, surgical treatments such as selective dorsal rhizotomy and bilateral multilevel soft-tissue release of hamstrings have also shown to provide improved ROM and decrease spasticity.

Conclusion
Improving motor function, ROM, comfort, and mobility are important goals for therapy in children with CP. It has shown across many trials that early non-surgical intervention and surgical intervention can significantly improve quality of life in CP individuals. Based on the compilation of these reviews, whether surgical or non-surgical procedures are considered, it is crucial to create a goal-oriented treatment that is patient and situation-specific.

Keywords: Cerebral palsy, spasticity, gait analysis, range of motion

Level of evidence: 4
INTRODUCTION

Cerebral Palsy (CP) is a non-progressive (static) insult to the developing brain with a prevalence of approximately 2/1000 live births. Children with CP suffer from multiple cognitive and physical disabilities, such as developmental delays, weakness, fatigue, incoordination, rigidity, spasms, and clonus. Symptoms of CP vary with each individual and should be approached clinically on a case by case basis in order for optimal treatment to be delivered.

One of the main clinical findings that impair movement in CP patients is spasticity. Spasticity is a velocity-dependent increase in muscle tone with hyperreflexia resulting in hyperexcitability of the stretch reflex. Objective spasticity measures help in documenting baseline and responses to various therapeutic modalities. Due to abnormal muscle, coordination, and increased spasticity, abnormal gait deviations are clinically seen. Although gait deviations are patient-specific, standard deviations in CP can be grouped into the gait patterns of spastic hemiplegia (drop foot, equinus with different knee positions) and spastic diplegia (true equinus, jump, apparent equinus with crouch). While it is essential to notice and label these gait patterns, an examiner must try to distinguish primary gait deviations from compensatory strategies.

Patients with spastic CP typically present with various physical deficits, including an impaired degree of range of motion (ROM) that affects the positioning of the lower and upper extremity. Appropriate muscle and joint movement is an essential determinant to completing everyday activities. Impairment in range of motion often develops into contractures that further limit normal function. CP patients are more likely to have a decreased ROM because of reduced mobility, and the presence of spasticity and dystonia. ROM assessment is one of the central musculoskeletal evaluations carried out during physical exams with CP patients. Measurements are taken on consecutive occasions and are used by clinical experts to monitor change over time. During the ROM examination, the most commonly used measurements of movement are the ankles, knees, hips, shoulders, elbows, wrists, and fingers.

CP patients are best cared for with an individualized treatment plan that provides a combination of interventions. The interventions should begin as early as possible, preferably during early childhood, to target mobility, prevent contractures, and improve quality of life. These interventions can be complicated and often tricky. It ultimately requires a multidisciplinary team, serial evaluations, and individualized treatment planning.

Successful treatment of gait deviations involves a multidisciplinary approach, which includes interventions such as physical therapy, podiatry, and/or orthopedic surgery management. Treating spasticity and improving CP symptoms can be accomplished through different methods which include both surgical and non-surgical treatments. This can lead to the appropriate intervention of lower extremity strength, tone, ROM, and motor coordination in order to influence ambulatory progress. The purpose of this review is to evaluate the effectiveness of gathering early gait analysis in CP in order to designate appropriate treatment, which will help improve spasticity, range of motion, and, ultimately, the quality of life.
METHODS

A literature search was conducted using PubMed. The search used the term "cerebral palsy AND gait analysis" yielded 1403 articles. The inclusion criteria included articles that assessed motor intervention treatments and articles published between 11/01/2009 and 11/01/2019. Exclusion criteria included articles that were written in a language other than English, non-human participants, and articles that did not focus on specific treatment plans. Therefore, my search was written as follows: “Cerebral palsy and gait analysis and early intervention and treatment.” This yielded seven total articles. After the inclusion and exclusion criteria were applied, four papers specifically included treatment intervention and were included in this review.

RESULTS

The goal of this literature review is to examine different intervention modalities that can ultimately improve gait patterns and quality of life in CP patients. Studies were selected based on their approaches on whether to treat CP abnormalities with conservative intervention, surgical intervention, or a mixture of both. All articles selected for review agree that obtaining a comprehensive understanding of evaluating gait, spasticity, and range of motion. Refer to Table 1 for a listing of the analyzed studies, methods, and outcomes.

A study performed by Matsuda et al. observed the effects of botulinum toxin type A treatment in children with CP. The collection of data consisted of video recording around the knee and ankle joints. Step length, gait speed, and observation gait using foot contact scale (FCS), physicians rating scale (PRS), and range of motion (ROM) were used via video-recorded gait in...
the sagittal plane\textsuperscript{4}. The subjects included nine children with CP and FCS, PRS, and ROM were measured before the injection, then 4, 8, 12 weeks after the botulinum toxin type A injection\textsuperscript{4}. The results presented that the maximum dorsiflexion angle of the ankle during gait was significantly increased at eight weeks after treatment, and knee joint extension was significantly increased at 12 weeks after surgery\textsuperscript{4}. In conclusion, the maximum effect of botulinum toxin type A becomes more clinically noticeable during long term intervention vs. after early stage of treatment\textsuperscript{4}.

A retrospective matched cohort study by Mungar et al. observed long term outcomes after selective dorsal rhizotomy (SDR). SDR is a spinal surgery that is usually performed on children with spastic CP in hopes of improving mobility, reducing pain, and relieving lower limb spasticity\textsuperscript{5}. The study consisted of 35 participants total with 24 participants who underwent SDR and 11 who did not undergo SDR surgery\textsuperscript{5}. All of the participants that were included in the study were measured for a baseline standard-of-care gait analysis\textsuperscript{5}. When comparing the two groups, spasticity significantly decreased in those with SDR\textsuperscript{5}. In the non-SDR group, gait deviation index improved\textsuperscript{5}. Overall, SDR and non-SDR groups had improvement in gait pathology over time. When comparing SDR and non-SDR intervention therapy, these results suggest SDR intervention improved mobility, reduced pain, and relieved lower limb spasticity\textsuperscript{5}.

Improving motor function, ROM, comfort, and mobility are essential goals for therapy in children with CP\textsuperscript{6}. Chang et al. prospectively studied 25 children with CP who were gross motor function classification system (GMFCS) level II to IV and underwent bilateral multilevel soft-tissue release for knee flexion gait. GMFCS is a classification of motor function in daily life with an emphasis on sitting, transfer, and mobility\textsuperscript{6}. Based on this classification, the higher the GMFCS level, the more immobile and physically dependent the patient is\textsuperscript{6}.

Knee flexion gait is a common energy-consumption gait disorder in children with CP\textsuperscript{6}. In Chang et al., this specific gait disorder was used as a model to evaluate how surgery intervention, which involved bilateral multiple soft-tissue release of the hamstring, affects the range of motion, spasticity, and selective motor control (SMC). Patients were evaluated preoperatively, and postoperatively at 6 weeks, 3 months, and 6 months for a GMFCS score, range of motion, spasticity, and selective motor control\textsuperscript{6}.

In Chang et al., the study showed that the soft tissue release of the hamstrings improved ROM, spasticity, and SMC. Postoperative GMFCS scores decreased six weeks postoperatively but then increased 3 months later. However, more considerable improvement at six months after surgery was noted in the younger subjects who underwent the bilateral multilevel soft-tissue release\textsuperscript{6}. This postoperative decrease followed by an increase was most apparent in older children (10-11 years old) with GMFCS level II. Therefore, GMFCS level and age were the main predictors for postoperative changes and overall motor function improvement\textsuperscript{6}.

Children diagnosed with CP are usually delayed in their motor development, which limits children's ability to move and achieve motor milestones such as walking, running, and jumping\textsuperscript{7}. Valentin-Gudio et al. studied how partial weight support with treadmill
training in neuromotor delayed children under the age of six provides an opportunity to walk for long enough periods of time. This study suggested that treadmill intervention could eventually lead to earlier onset of independent walking when compared to no treadmill intervention. The neuromotor delayed participants under the age of six included down syndrome, CP, and children born pre-term. Although a general conclusion was made regarding early treadmill intervention benefiting neuromotor delayed children under the age of six, no specific findings about CP participants were determined.

<table>
<thead>
<tr>
<th>ARTICLE</th>
<th>PARTICIPANTS</th>
<th>TREATMENT MODALITY</th>
<th>CONCLUSION</th>
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<tr>
<td>Matsuda et al.</td>
<td>N = 9 children with CP</td>
<td>Botulinum toxin Injection</td>
<td>- Maximum dorsiflexion angle of the ankle during gait was significantly increased at eight weeks after treatment, and knee joint extension was significantly increased at 12 weeks after treatment. - In conclusion, the maximum effect of botulinum toxin type A becomes more clinically noticeable during long term intervention vs. after early stage of treatment.</td>
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<td>Mungar et al.</td>
<td>N = 35 total participants with spastic CP. N = 24 who underwent SDR N = 11 non-SDR (control)</td>
<td>Spinal Surgery: Selective dorsal rhizotomy</td>
<td>- Spasticity significantly decreased in those with SDR - Gait deviation index improved more in participants without SDR than those with SDR - Compared with the SDR group, participants without SDR underwent significantly more subsequent interventions.</td>
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<tr>
<td>Chang et al.</td>
<td>N = 25 children with CP who were GMFCS level II to IV</td>
<td>Orthopedic Surgery: Bilateral multilevel soft-tissue release of hamstring for knee flexion gait</td>
<td>- The direct surgical effects with improved ROM, spasticity, and SMC - GMFM scores decreased 6 weeks postoperatively, then increased at 6 months postoperatively. - More significant improvement at 6 months after surgery was noted in younger children.</td>
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<tr>
<td>Valentin-Gudio, et al.</td>
<td>N = 139 children with neuromotor disability (total) N = 73 in the treadmill (intervention group) N = 66 (control group)</td>
<td>Treadmill training (in which the child is supported by a harness)</td>
<td>- Evidence suggested that treadmill intervention could lead to an earlier onset of independent walking when compared to no treadmill intervention in patients with neuromotor disability.</td>
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Table 1: Summaries of Articles Reviewed

**DISCUSSION**

Improving motor function, ROM, comfort, and mobility are important goals for therapy in children with CP. The best type of treatment plan for children with CP includes integrative yet individualized treatment plans. It is essential to take a comprehensive history and genetic background in addition to a complete physical and neurological examination in order for a correct diagnosis and specialized treatment to be appropriately made.

Treatment of CP must be goal-oriented, with the aim of assisting with mobility, reducing contraction, preventing contracture, and improving positioning and comfort.
Multiple developmental and physical evaluations are necessary for children for proper diagnosis and follow up treatment. Specific treatment options for children with CP can include anything from drug treatments for spasticity (local, intrathecal, systemic) to aggressive orthopedic and neurosurgical interventions. Most patients require combinations of these therapies in order to improve gait function and case-specific developmental progress.

Two main approaches to CP intervention were studied in this review, which included surgical vs. non-surgical treatments.

**Non-surgical Treatments:**

One of the most common motor disturbances in CP is muscle spasticity. Botulinum toxin type A is considered the first-line treatment for focal spasticity in people with CP. Matsuda et al. found that the maximum effect of botulinum toxin type A becomes more clinically noticeable during long term intervention vs. after early stage of treatment. This study goes to show that conservative treatment can be considered and thoroughly monitored in CP patients prior to committing to orthopedic surgical intervention.

Although Valentin-Gudio et al. had promising data in regards to children with neuromotor disability, inadequate data could be applied to the CP population correctly.

**Surgical Treatments:**

Although surgery is not the first line of treatment for patients with CP, it is an aggressive option that can be considered on a case by case basis. Lower-risk options are typically first attempted, such as medications and various types of physical therapy. If these options don’t seem to be helping the patient’s quality of life, then surgery can be considered as an option for treatment. Surgery can help relieve multiple symptoms due to the side-effects of CP. Various orthopedic procedures are aimed to address muscle stiffness and spasticity. For a child with CP, surgery aims to reduce muscle spasms, muscle stiffness, relieve pain, improve posture and balance, and correct damaged joints. Easing spasticity with surgery enhances the range of motion and motor control. This can ultimately increase quality of life by assisting patients walk with or without assistive devices, and grasp small items.

**CONCLUSION**

This literature review collectively contains a retrospective study, Cochrane systematic review, a randomized control trial, and cohort studies that show various surgical and non-surgical treatment modalities and interventions for CP patients. Due to several of the studies not having a control group, the main limitation revolved around preoperative vs. postoperative outcomes. Therefore, it is objectively difficult to compare the effectiveness of these treatments.
Based on the compilation of these reviews, it is crucial to create a goal-oriented treatment that is patient and situation-specific to determine the best outcome for each CP patient. This will ultimately help you create the best treatment plan to help decrease spasticity, increase ROM, and decrease gait abnormalities. With this vision and patient-specific approach, improved quality of life for CP patients can hopefully be obtained.

**STATEMENT OF COMPETING INTERESTS**

The author declares that they have no competing interest associated to this manuscript.

**REFERENCES**

Evaluating Factors that Increase Patient Compliance in the Podiatric Clinical Setting: A Literature Review for Podiatrists Working in the 21st Century Healthcare System

By: Ivan Cruz, BA; Yasamin Daneshvar, BA; Jaffer Shah, BS

ABSTRACT
Introduction
Patient compliance has not been extensively studied for working Podiatrists. The aim of this study is to research current main factors that increase patient compliance in the podiatric clinical setting, compared to factors that increase patient compliance in clinical settings outside of podiatric medicine. Due to the rapidly changing nature of podiatric medical and surgical practices, we hypothesize that these factors may be different for podiatric medicine compared to other medical specialties.

Study Design: Systematic Review of Literature

Methods
Using PubMed, a search with “Podiatry” [MESH] AND “Compliance” [MESH] AND “Surgery” [MESH] resulted in eleven articles. The authors used inclusion criteria such as studies restricted to human beings, articles written in English, and publishing dates restricted by parameters (1999/01/01 [PDAT]: 2019/12/31 [PDAT]). Of these eleven articles, six were excluded because they were either not related to our research study, not accessible or complete for analysis, or involved pediatric studies. We excluded pediatric studies due to the fact that children can only give assent, and patient compliance cannot be studied in this manner. Using Cochrane Library, a search with “Patient Compliance with Foot and Ankle Surgeries” resulted with twenty-three articles. The authors used inclusion criteria such as studies restricted to human beings, articles written in English, and publishing dates restricted by parameters (1999/01/01 [PDAT]: 2019/12/31 [PDAT]). Of these twenty-three articles, thirteen were excluded because they were either duplicated in the literature search, not related to our research study, not accessible/complete for analysis, or involved pediatric studies. We excluded pediatric studies due to the fact that children can only give assent, and patient compliance cannot be studied in this manner.

Results
34 articles total were found with the initial search query when the inclusion criteria were applied. The application of exclusion criteria narrowed the results to the 15 articles reviewed in this paper.

Discussions and Conclusions
Health literacy still remains an important factor for increasing patient compliance and maintaining a positive podiatric physician-patient relationship. Therefore, the factors for increasing patient compliance are the same for podiatric, osteopathic, and allopathic medicine. In addition, factors that decreased patient compliance were unexpectedly encountered during the literature review, such as cultural beliefs and psychiatric disease. The current literature suggests that all factors leading to increased and decreased patient compliance in the podiatric clinical setting need further investigation because of our evolving healthcare system; and these factors are only correlated to changes in patient compliance.

Keywords: Patient Compliance, Factors, Podiatric Clinical Setting, 21st Century Healthcare System

Level of Evidence: 4
INTRODUCTION

Currently, in the United States healthcare system, podiatric physicians and surgeons are rapidly advancing in their field by expanding their medical education, training, and scope of practice.\textsuperscript{1} Podiatric Medicine, as a medical specialty, has been and continues to be well established and respected in mainstream healthcare as well as society.\textsuperscript{1} As a result, podiatrists are recognized as highly competent physicians and surgeons, just like their allopathic and osteopathic physician colleagues. However, as the patient population continues to increase in the United States, desired podiatrists need to be cognizant about increasing patient compliance.\textsuperscript{2} Morris et. al, defines patient compliance as "the extent to which a person’s behavior in terms of; taking medications, following diets, or executing lifestyle changes, coincides with medical or health advice."\textsuperscript{3} Unfortunately, there are limited studies in podiatric medicine pertaining to factors that increase patient compliance. In studies involving podiatric procedures, there is not marked research in regards to increasing patient compliance. Therefore, podiatrists need to look further into patient compliance in order to maintain their excellent rapport with various healthcare systems.

Noncompliance in general is a major public health problem that always needs to be addressed.\textsuperscript{3} In addition, Podiatrists are viewed as equals with allopathic and osteopathic doctors. Consequently, it is a podiatrist’s responsibility to help the healthcare system increase patient compliance and prevent this type of public health issue.

For historical purposes, compliance has always been measured by analyzing therapeutic outcomes, conducting interviews, and by providing patients with self-report surveys, or questionnaires, depending on ease and convenience.\textsuperscript{3} One predominant factor that increases patient compliance includes health literacy, which is a method of increasing patient education in the form of providing written documents, or oral instructions.\textsuperscript{4} In addition, a respectful physician-patient relationship seems to also increase patient compliance.\textsuperscript{6}

In the early 1990s, non-compliance was a significant factor which increased cost of treatments in the general healthcare settings.\textsuperscript{3} For example, the treatment of moderate to severe hypertension at the time costed about 5,000 dollars per patient for a fully compliant patient. The average cost rose to approximately 10,500 dollars per patient if the patient was noncompliant with taking their hypertension medication. The source of noncompliance was the lack of health literacy and behavioral instability of patients.\textsuperscript{3} Increased costs from lack of patient compliance are never wanted in healthcare. In general, compliance can vary based on other factors such as the patient’s level of comfort with treatment, physician-patient relationship as previously stated, and the physical and emotional impact of the disease on the patient.\textsuperscript{5,6,7}

It is essential to increase compliance, as it will allow the U.S. healthcare system to benefit both podiatric physicians by decreasing burnout, as well as patients, in terms of faster treatment outcomes and patient satisfaction. The outcome of maintaining financial cost, or stability, is also a benefit for the podiatric physician, patient, and for their designated healthcare institution. Curiously, rapid evolution of the U.S. healthcare industry leads to our hypothesis that factors for increasing patient compliance may be different for podiatric medicine compared to other medical specialties. The main goal of this study is to assess factors that are pertinent for
increasing patient compliance which can be translated into podiatric practice. Podiatrists can currently start applying this knowledge towards their various clinical practices.

**METHODS**

Using PubMed, a search with “Podiatry” [MESH] AND “Compliance” [MESH] AND “Surgery” [MESH] resulted in eleven articles. The authors used inclusion criteria such as studies restricted to human beings, articles written in English, and publishing dates restricted by parameters (1999/01/01 [PDAT]: 2019/12/31 [PDAT]). Of these eleven articles, six were excluded because they were either not related to our research study, not accessible or complete for analysis, or involved pediatric studies. We excluded pediatric studies due to the fact that children can only give assent, and patient compliance cannot be studied in this manner. As seen in Figure 1, including the exclusion criteria left five articles included for this literature review.

![PubMed Article Search and Exclusion Criteria](image)

**Figure 1: PubMed Article Search and Exclusion Criteria**

For Cochrane Library, a search with “Patient Compliance with Foot and Ankle Surgeries” resulted with twenty-three articles. The authors used inclusion criteria such as studies restricted to human beings, articles written in English, and publishing dates restricted by parameters (1999/01/01 [PDAT]: 2019/12/31 [PDAT]). Of these twenty-three articles, thirteen were excluded because they were either duplicated in the literature search, not related to our research study, not accessible/complete for analysis, or involved pediatric studies. We excluded pediatric studies due to the fact that children can only give assent, and patient compliance cannot be studied in this manner. As seen in Figure 2, including the exclusion criteria left ten articles included for this literature review.
**Figure 2: Cochrane Article Search and Exclusion Criteria**

### RESULTS

<table>
<thead>
<tr>
<th>Author</th>
<th>Nature of Study</th>
<th>Population</th>
<th>Time Period</th>
<th>Parameters Increase Compliance</th>
<th>Parameters Decrease Compliance</th>
<th>Study Aim</th>
</tr>
</thead>
<tbody>
<tr>
<td>Netten et. Al</td>
<td>Systematic Review</td>
<td>30 controlled studies 44 non-controlled studies</td>
<td>N/A</td>
<td>Health Literacy</td>
<td>N/A</td>
<td>Investigate the effectiveness of interventions to prevent first and recurrent foot ulcers in persons with diabetes who are at risk for ulceration.</td>
</tr>
<tr>
<td>Grubhofer et. Al</td>
<td>Prospective RCT</td>
<td>N=76 adults (41 female and 35 male) patients</td>
<td>July 2016 to January 2017</td>
<td>N/A</td>
<td>Uncomfortable constricting effect of CS</td>
<td>To evaluate the CS wearing time and patients’ compliance by the use of a sensor device implanted covertly into the CS.</td>
</tr>
<tr>
<td>Garcia-Paris et. Al</td>
<td>Retrospective Longitudinal</td>
<td>N=134</td>
<td>10 months period</td>
<td>Use of the SSC Positive physician patient relationship</td>
<td>N/A</td>
<td>To adapt and implement SSC within the field of podiatric surgery and to evaluate its impact upon safety standards and post-surgical complications.</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Patients</td>
<td>Procedure</td>
<td>Outcomes</td>
<td>Purpose</td>
<td></td>
</tr>
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<tr>
<td>Armstrong et. Al</td>
<td>Double blind RCT</td>
<td>N=115 patients with diabetes who had foot infections</td>
<td>12 week period</td>
<td>Use of the foot-level mechanical compression and an increased trend toward wound healing. Patient Education</td>
<td>To evaluate the proportion of healing of foot infections in subjects with diabetes undergoing aggressive edema reduction with the use of intermittent pneumatic foot compression after foot-level debridement.</td>
<td></td>
</tr>
<tr>
<td>Chiodo et. Al</td>
<td>Single blind</td>
<td>N=51 consecutive adult orthopaedic patients with unilateral lower-extremity abnormality</td>
<td>N/A</td>
<td>Health literacy in the form of instruction Cultural beliefs Diminished comprehension Low motivation Psychiatric diseases</td>
<td>To measure patient compliance with a period of prescribed non-weight-bearing.</td>
<td></td>
</tr>
<tr>
<td>Cooke et. Al</td>
<td>RCT</td>
<td>N=584 Aged 16 or over with acute severe ankle sprain</td>
<td>N/A</td>
<td>Health literacy in the form of written documents about procedures to the patients</td>
<td>To estimate the clinical effectiveness and cost-effectiveness of three methods of ankle support compared with double layer tubular compression bandage.</td>
<td></td>
</tr>
<tr>
<td>Frykberg et. Al</td>
<td>Prospective clinical trial</td>
<td>N=31</td>
<td>December 2014 to February 2016</td>
<td>Higher safety of treatment Co-morbidities</td>
<td>To observe the effects of viable cryopreserved human placental membrane (vCHPM) treatment for chronic complex diabetic foot wounds with exposed tendon and/or bone</td>
<td></td>
</tr>
</tbody>
</table>
| Griffin et. Al | RCT | N=151 patients with acute displaced intra-articular calcaneal fractures randomly allocated | 2007-2009 | Complication s and reoperations | To investigate whether surgery by open reduction and internal fixation provides benefit compared with non-operative treatment for displaced, intra-
to operative (n=73) or non-operative (n=78) treatment.

<table>
<thead>
<tr>
<th>Study Source</th>
<th>Study Design/Design Characteristics</th>
<th>Study Duration</th>
<th>Outcome Measures</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hashmi et. Al</td>
<td>Randomized Comparable Trial</td>
<td>N=46 with plantar calluses</td>
<td>Health literacy</td>
<td>Supporting a self-management plan for the patient</td>
</tr>
<tr>
<td></td>
<td></td>
<td>August 2012-October 2013</td>
<td>N/A</td>
<td>to test the efficacy of two home treatments for plantar callus using novel, objective outcome measures</td>
</tr>
<tr>
<td>Hinman et. Al</td>
<td>RCT</td>
<td>N=164 patients with medical knee osteoarthritis</td>
<td>6 months</td>
<td>Treatment that do not accommodate patient’s life style</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>N/A</td>
<td>To evaluate the efficacy of unloading shoes in alleviating knee osteoarthritis symptoms</td>
</tr>
<tr>
<td>Martin et. Al</td>
<td>Prospective Randomized Crossover</td>
<td>N=44 preoperative orthopedic foot and ankle patients</td>
<td>N/A</td>
<td>Discomfort with types of treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Patient specific assistive device</td>
<td>To compare physiologic demand, perceived exertion, and patient preference between a hands-free single crutch (HFSC) and standard axillary crutches (SACs) in foot and ankle patients</td>
</tr>
<tr>
<td>Mittal et. Al</td>
<td>CROSSBAT Combined Randomized &amp; Observational</td>
<td>N=160 Randomized cohort N=276 Observational cohort</td>
<td>August 2010 to October 2013</td>
<td>Personalized medicine Negative emotional impact of surgical treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>To determine if surgery is superior to non-surgical management for the treatment of these fractures</td>
</tr>
<tr>
<td>Spaulding et. Al</td>
<td>Pilot</td>
<td>N=6 participants with TMA N=6 control</td>
<td>N/A</td>
<td>Increased comfort level of treatment Discomfort with treatment Lack of ankle mobility</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>To provide evidence for selection of orthotic designs in clinical practice. To justify the use of BA versus AABA devices</td>
</tr>
<tr>
<td>Suchak et. Al</td>
<td>RCT</td>
<td>N=110 patients with a surgically repaired Achilles</td>
<td>October 2003 to May 2006</td>
<td>Health literacy Treatment that do not accommodate patient’s life style</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>To compare the effect of early weight-bearing with that of non-weight-bearing on early postoperative</td>
</tr>
</tbody>
</table>
Netten et al. conducted a systematic review in regards to preventing foot ulcers of high risk diabetic patients. For this study, they identified 30 controlled studies as well as 44 non-controlled studies from various databases such as PubMed, EMBASE, CINAHL and the Cochrane. The results indicated the need for patient education, therapeutic footwear, as well as professional foot treatment. Their conclusion, of supporting a self-management plan for the patient, mentioned one factor that increased patient compliance. Particularly, that one factor was health literacy in the form of a written self-management plan for the patient to follow; which increases patient compliance. However, the study suggested that more should be done to scientifically prove the connection over time.

Grubhofer et al. conducted a randomized control trial in regards to analyzing the effects of using compressive stockings after hind foot and ankle surgery. For this study, 76 consecutive patients were involved during the final analysis, and a sensor was placed in the compressive stocking for collecting data. The rate of cast adjustment from the low compliance group was 71% compared to the rate from the compliance group which was 63%. High compliance group rate was not statistically different from the low compliance group rate. Their conclusion, that there were no significant beneficial effects of postoperative compressive stocking therapy, mentioned one factor that decreased patient compliance. Particularly, that one factor was increased feeling of discomfort; which decreases patient compliance.

Garcia-Paris et al. conducted a retrospective longitudinal study in regards to analyzing the effects of implementing a World Health Organization Checklist in a podiatric surgery unit in Spain. For this study, a sample size of 134 medical histories were used in the University of Seville’s podiatry clinic. The sample size was divided into three groups for collecting data, one group

<table>
<thead>
<tr>
<th>Study</th>
<th>Type</th>
<th>N</th>
<th>Description</th>
<th>Positive Patient Relationship</th>
<th>N/A</th>
<th>To Achieve a Better Understanding of the Perspectives and Needs of Indigenous People with Diabetes in the Torres Strait and to Identify Ways to Promote Successful Self-Management of Diabetes.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wong et. Al</td>
<td>Descriptive</td>
<td>N=67</td>
<td>Positive Patient Relationship and Health Literacy</td>
<td>N/A</td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>(26 men and 41 women) with diabetes</td>
<td></td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
prior to the implementation process (65), one group with the checklist (34), and one group without the checklist (35). An improvement of compliance was observed with the Prophylaxis Protocol and signed consent form (p=0.00). There was also a statistically significant relationship between the correct antibiotic prophylaxis and using the checklist (p=0.049). Their conclusion, that there were increases in patient compliance, reduced complications, and improved safety, mentioned factors that increased patient compliance. Particularly, the two factors were a positive physician-patient relationship from signing the consent forms, and health literacy in the form of using the written checklist; which increase patient compliance.

Armstrong et al. conducted a 12-week double blind study in regards to observing the effects of foot compression device wound healing from a debrided diabetic foot infection. For this study, a sample size of 115 diabetic patients was used. The sample size was 74% male, and all had foot infections that required incision and debridement. Eighteen patients total did not complete the study and were not assessed in the final analysis. Of the 18, eleven Patients did not comply because the procedure negatively affected them physically. Five Patients did not comply for unknown reasons. Also, two patients did not comply since they associated negative outcomes with the specific type of procedure conducted on them. Overall data showed a significant trend towards increased proportion of healing from placebo noncompliant to placebo-compliant, to active non-compliant to active compliant groups ($X^2$ trend=8.3, p<0.05). Their conclusion, that there were increases in wound healing from increased patient compliance and from using the pump and wrap system of the compression device, mentioned factors that increased as well as decreased patient compliance. Particularly, one factor was health literacy, or patient education, in the form of instructing the patient; which increases patient compliance. The two factors that decreased patient compliance include physical discomfort that the patient experiences with the treatment, as well as emotional impact of the procedure on the patient.

Chiodo et al. conducted a single blind study in regards to patient compliance with postoperative Lower extremity non-weight-bearing restrictions. For this study, a pressure-sensitive film was embedded into short leg casts of 51 consecutive adult orthopedic patients with unilateral lower-extremity abnormality who had been instructed to be strictly non-weight-bearing. Noncompliance was defined as maximum detectable pressure exerted on greater than or equal to 50% of the film. Fourteen (27.5%) of 51 patients were noncompliant with the non-weight-bearing restriction. Six (42.9%) of the 14 noncompliant patients compared with 11 (29.7%) of the 37 compliant patients experienced an adverse event (p =0.51). Sex, age, language spoken, body mass index, time in the cast, and the treating surgeon did not have a significant influence on weight-bearing performance (p > 0.05). Their conclusion, that weight bearing compliance is impacted by the time of year, mentioned one factor that increased patient compliance. Particularly, that one factor was health literacy in the form of instruction or direction; which increases patient compliance. The four factors that decreased patient compliance include cultural beliefs that differ from patient to patient, diminished comprehension (or lack of health literacy), low motivation that may include
lack of support system, and presence of psychiatric disease.

Cooke et al. conducted a randomized control trial in regards to analyzing the clinical effectiveness and cost-effectiveness of three types of mechanical ankle support with tubular bandage. For this study, a double layer of tubular bandage was applied from the level of the tibial tuberosity to the base of the toes. Sizing of the tubular bandage was undertaken as per the manufacturer’s instructions. Patients were instructed to remove the tubular bandage at night. The results indicated half of the participants (49%) had experienced an ankle injury previously and 9% of the sample reported recurrent sprain. Their conclusion, that ankle sprains with an inability to weight bear have a prolonged recovery, mentioned one factor that increased patient compliance. Particularly, that one factor was health literacy in the form of presenting written documents about procedures to the patients; which increases patient compliance.

Frykberg et al. conducted a prospective single-arm clinical trial in regards to observing the effects of viable cryopreserved human placental membrane (vCHPM) treatment for chronic complex diabetic foot wounds with exposed tendon and/or bone. For this study, between December 2014 and February 2016, a total of 31 patients were prospectively treated with weekly applications of a cryopreserved human placental membrane graft. Four patients terminated early from the study, and two of these were lost to follow-up. Two patients terminated their participation early because of lingering infection that subsequently necessitated transmetatarsal amputation (TMA). Therefore, 27 patients completed the entire study protocol and were available for the final outcome assessment at week 16. Patients with chronic DFUs who achieved complete wound closure by 12 weeks was significantly higher in patients who received weekly applications of vCHPM compared with standard of care ($P=0.0001$). Their conclusion, that the vCHPM protocol shows promising clinical outcomes, mentioned factors that increased as well as decreased patient compliance. Particularly, one factor that increased compliance was comfort level with the type of treatment. In other words, higher safety of treatment increases the compliance. The one factor that decreased patient compliance was co-morbidities. Patients with co-morbidities are less likely to be compliant with particular podiatric procedures, due to the decreased improvement outcomes and increased complications that are commonly associated with co-morbidities.

Griffin et al. conducted a randomized control trial in regards to analyzing operative versus non-operative treatment for closed, displaced, intra-articular fractures of the calcaneus. For this study, 151 patients with acute displaced intra-articular calcaneal fractures were randomly allocated to operative (n=73) or non-operative (n=78) treatment. Their conclusion, that complications and reoperations were much more common in the operatively treated group, mentioned one factor that decreased patient compliance. Particularly, that one factor was comfort level with the type of treatment; which decreases patient compliance. In this case, patients were uncomfortable with the idea of receiving surgical interventions or treatments, and patients opted for non-operative procedures.

Hashmi et al. conducted a three-armed randomized comparable trial in regards to analyzing three treatments for plantar callus. For this study, Participants were randomly allocated to one of three groups:
potassium hydroxide (KOH, 40 %); trichloroacetic acid (TCA); and podiatry treatment. Participants were followed for 3 weeks after their initial intervention appointment (days 7, 14 and 21). Forty-six participants (61 ft.) with plantar calluses were recruited. The podiatry treatment showed immediate and significant changes in all objective outcomes, associated foot pain and function (p <0.01). Their conclusion, that the podiatry treatment showed immediate and significant changes in skin and associated foot pain and function, mentioned two factors that increased patient compliance. Particularly, the two factors were health literacy in the form of receiving an informed consent for a podiatric procedure and implementing a self-management plan for the patient in the form of a long-term treatment regimen similar to the TCA treatment; which increase patient compliance. Interestingly, the article emphasized that podiatric noncompliance was unknown.

Hinman et al. conducted a randomized control trial in regards to analyzing the effects of Unloading Shoes for self-management of Knee Osteoarthritis. For this study, 164 persons with medial knee osteoarthritis participated. Participants were provided a pair of appropriately sized shoes on the basis of their random assignment and were asked to wear them as much as possible every day (≥4 hours/day) for 6 months and to avoid changing shoes. Participants were provided the shoes at no cost and were permitted to keep the shoes regardless of whether they completed the trial. Although ankle and foot pain was more common with unloading shoes (n = 16 [20%]) than conventional shoes (n = 7 [9%]), the proportion of persons discontinuing treatment for this reason did not differ between groups (n = 3 [4%] and 2 [2%], respectively). Their conclusion, that walking shoes with modified midsoles to unload the knee conferred no benefit over conventional walking shoes for persons with symptomatic medial knee osteoarthritis, mentioned one factor that decreased patient compliance. Particularly, that one factor was treatments that do not accommodate patient’s lifestyle; which decreases patient compliance. The factor was seen in both unloading and conventional shoe groups.

Martin et al. conducted a prospective, randomized, crossover study in regards to observing Patient Preference and Physical Demand for Hands-Free Single Crutch (HFSC) vs Standard Axillary Crutches (SAC) in Foot and Ankle Patients. For this study, the sample consisted of 35 males and 9 females. The mean body mass index (BMI) was 26 (19-36), the mean height was 1.7 m, and the mean weight was 82 kg. Patient data and pre-activity heart rate were recorded for all patients, who were then randomized to either an HFSC or SACs. Therefore, The HFSC was preferred by 86% of patients. Significantly lower dyspnea scores (2.8 vs 5.3; P < .001), fatigue scores (2.4 vs 5.5; P < .001), pre-activity and post-activity change in heart rate (28 vs 46 bpm; P < .001), and mean post-activity heart rate (107 vs 122 bpm; P < .001) were found using the HFSC compared with the SACs. Their conclusion, that HFSC demonstrated superior patient preference, perceived exertion, and physiological demand compared with SACs, mentioned factors that increased as well as decreased patient compliance. Particularly, two factors that increased compliance were increased comfort level with the type of treatment, and personalized medicine; which is patient-specific treatment. The one factor that decreased patient compliance was discomfort with types of treatment.
Mittal et al. conducted a Combined Randomized and Observational Study (CROSSBAT) to determine if surgery is superior to non-surgical management for the treatment of isolated Type B Fractures. For this study, eligible participants willing to be randomized were randomly allocated in a 1:1 ratio to either the surgical or non-surgical intervention. Eligible participants who declined randomization were invited to enter the observational cohort. Treatment for the observational cohort was determined by participant and surgeon preference. In the randomized cohort, 80 participants were randomized to non-surgical management and 80 were randomized to surgical management. At 12 months, 68 (85%) and 71 (89%) participants were followed up in the nonsurgical and surgical groups, respectively. In the observational cohort, 257 participants were treated non-surgically and 19 were treated surgically as most patients declined surgery when informed of equipoise regarding the two treatment arms. At 12 months, 202 (79%) participants were followed up in the nonsurgical group, and 18 (95%) participants were followed up in the surgical group. Their conclusion, that that surgical management is not superior to non-surgical management in type B ankle (fibula) fractures with minimal talar shift in the short term and is associated with increased adverse events, mentioned factors that increased as well as decreased patient compliance. Particularly, one factor that increased compliance was personalized medicine; which is patient-specific treatment, and the patient has control over their care. The one factor that decreased patient compliance was the negative emotional impact of surgical treatment for the patient, especially for the observational cohort. Even in the randomized control trial, with respect to the Foot and Ankle Outcomes Questionnaire, there was a statistically significant difference favoring the non-surgical group (mean difference 3.2; 95% CI 0.4 to 5.9; p=0.028), but this difference was not clinically meaningful.

Spaulding et al. conducted a Pilot Study, or a “within-group repeated measures crossover design,” to analyze the selection of an above or below-ankle orthosis for individuals with neuropathic partial foot amputation. For this study, three independent tests were performed to assess the biomechanical gait parameters, plantar pressure distribution and satisfaction of the two orthotic designs, the Below Ankle (BA) condition and the Above-And-Below Ankle (AABA) condition. In the sagittal plane, the AABA device reduced motion between the participant’s shank and shoe (‘dorsiflexion angle’) approximately 10 degrees, with about 4.5 fewer degrees of plantar flexion at foot strike, and 5.2 fewer degrees of dorsiflexion at terminal stance. All subjects felt improved balance with the use of the BA orthosis as compared to nothing; while one individual felt more balanced with the use of the AABA, as compared to the BA orthosis while standing and walking. Their conclusion, that different effects on balance while walking with the BA and AABA devices are individually specific, mentioned factors that increased as well as decreased patient compliance. Particularly, one factor that increased compliance was increased comfort level of treatment. The two factors that decreased patient compliance were the amount of discomfort with the treatment, and lack of ankle mobility as stated in the literature.
Suchak et al. conducted a Randomized Control Trial to analyze the influence of early weight bearing compared with non-weight-bearing after surgical repair of the Achilles tendon. For this study, 110 patients with a surgically repaired Achilles tendon rupture were enrolled from one of two major trauma-care tertiary hospitals. At the two-week postoperative visit, patients were randomized to either weight-bearing or non-weight-bearing for an additional four weeks. Compliance was measured with a pressure sensor in the fixed-hinge ankle-foot orthosis given to each patient. Ninety-eight patients (89%) completed the six-month follow-up. Patients in the weight-bearing group also reported fewer limitations of daily activities at six weeks postoperatively (p < 0.001). Their conclusion, that the randomized controlled trial demonstrated a clear patient benefit for weight-bearing as tolerated compared with non-weight-bearing, mentioned factors that increased as well as decreased patient compliance. Particularly, one factor that increased compliance was health literacy in the form of receiving an informed consent for a podiatric procedure; which increases patient compliance. The one factor that decreased patient compliance was treatments that do not accommodate the patient’s lifestyle; which decreases patient compliance. The non-weight bearing versus weight bearing study was an excellent example for showing decreased patient compliance.

Wong et al. conducted a descriptive study in regards to gaining perspectives on clinic attendance, medication and foot-care among people with diabetes in the Torres Strait Islands and Northern Peninsula Area. For this study, Sixty-seven Torres Strait Islanders (26 men and 41 women) with diabetes from eight Torres Strait and Northern Peninsula Area communities participated. Participants who expressed satisfaction with clinical-initiated sessions when called highlighted positive relationships and encouraging feedback from doctors. Their conclusion, that service providers in health and other sectors need to place more emphasis on supporting self-management of diabetes, mentioned factors that increased patient compliance. Particularly, the two factors were a positive physician-patient relationship, and health literacy in the form of educating the patient; which increase patient compliance.

**DISCUSSION**

Collectively, studies found that there were a balanced amount of factors present throughout the 15 articles. The prevalent factors that increased patient compliance throughout the literature review were positive physician-patient relationships, devices that promote increased patient specific wound healing, and treatments that were deemed safe in the literature. Moreover, other prevalent factors that increased patient compliance include personalized medicine treatments, increased comfort levels with the type of treatment involved, as well as health literacy in the forms of written and oral patient education. In addition, the main factors that decreased patient compliance were physical and/or emotional discomfort with treatment, cultural beliefs, as well as decreased health literacy via low comprehension and motivation. Furthermore, other main factors that decreased patient compliance include psychiatric diseases, co-morbidities, lack of ankle motility from the article as written by Spaulding et al, and treatments that do not accommodate a patient’s lifestyle. Another factor that specifically decreased patient compliance was complications and/or reoperations as indicated by Griffin et al. These were all of the factors that were emphasized in this literature review.
Factors that deceased patient compliance were not expected to appear in the literature review, yet they equivalently appeared as much as factors that increased patient compliance. Therefore, presence of factors that decreased patient compliance is a strong indicator that knowing what makes a patient noncompliant is equally as important as knowing what typically makes a patient compliant with podiatric healthcare procedures. Netten et al. suggested that more should be done to scientifically prove the connection over time, and that all factors are only correlated to changes in patient compliance. Interestingly, Grubhofer et al. indicated that questionnaires do not help measure compliance as previously thought before the year 2000. The article supports the notion that current measures of compliance have inherent errors, and there needs to be more research done in our rapidly evolving healthcare system that more accurately measures patient compliance. Financially, Griffen and Frykberg et al. emphasized that healthcare costs are high due to extended hospital stay, delayed or no return to work, as well as unresolved complex diabetic foot ulcers. The literature states that unresolved complex diabetic foot ulcers contribute around 25-50% of the estimated total cost of diabetes in the United States; which is 245 billion dollars. By understanding these factors, the cost of healthcare can be reduced for the podiatric physician, U.S. healthcare institutions, as well as for the patient. Ultimately, podiatric physicians can benefit from increased patient compliance, since increased compliance can decrease physician burnout. Patients also benefit when they comply with certain podiatric procedures, and the benefits include faster treatment outcomes as well as patient satisfaction. Overall, all patient compliance factors that were hypothesized to be different for podiatric medicine were not unique, and the factors were indeed the same as osteopathic and allopathic medicine factors.

**CONCLUSION**

In conclusion, there are limited studies in podiatric medicine pertaining to factors that increase patient compliance. Knowing these factors allows podiatrists to maintain their excellent rapport with various healthcare systems. When a podiatrist applies any of these factors towards their own practices, there are many enhanced benefits for the podiatric physician, the patient, and the healthcare setting. Since there are inherent errors with measuring compliance, more research needs to be done in order to accurately measure patient compliance for our rapidly evolving healthcare system. Evaluating factors that decrease patient compliance are equally as important for any type of physician and/or surgeon.

**AUTHORS’ CONTRIBUTIONS**

Three authors contributed equally to the production of this article. All considered the topic, initial reviews, and contributed substantially to its revision. All authors read and approved the final submission of this draft.

**STATEMENT OF COMPETING INTERESTS**

None of the authors have any competing interests.
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17. Suchak AA, Bostick GP, Beaupré LA, Durand DC, Jomha NM. The Influence of Early Weight-Bearing Compared with Non-Weight-Bearing After Surgical Repair of the Achilles Tendon. The Journal

A Systematic Review of Subungual Exostosis: The Most Effective Diagnoses and Treatment Outcomes for an Uncommon Podiatric Pathology

By: Yasamin Daneshvar, BA, Ivan H. Cruz, BA

ABSTRACT

Introduction
A subungual exostosis is a benign, slow growing, permanent bony overgrowth that arises from the distal phalanx of the toe. It usually occurs in children and young adults. Its pathology mainly involves the overgrowth of normal bone, which may present beneath the toenail or adjacent to the nail, and can be a source of pain and nail deformity. The purpose of this systematic review is to analyze different methods available for the diagnosis and treatment of Subungual Exostosis, and determine which method is the most preferred in terms of enhanced treatment outcomes for this particular podiatric pathology.

Study Design: Systematic Review of the Literature

Methods
A PubMed search was conducted with the following phrases: (Subungual exostosis[MeSH Terms]) AND toes[MeSH Terms]. Inclusion criteria required articles to be published in the English language, published after the year 2000, and considered Subungual exostosis of toes. Exclusion criteria eliminated articles describing subungual exostosis of the upper extremity, toenail tumors other than subungual exostosis, and non-English written articles. The primary search yielded 65 articles. By evaluating and screening articles based on inclusion and exclusion criteria seven articles were carefully analyzed and included in this systematic review.

Results
7 articles were analyzed in this systematic review. Our study demonstrated the importance of radiographic findings as the best method for differential diagnosis. Demographic findings associated with SE are presented to introduce guidelines for better management planning.

Discussion
Subungual Exostosis is an adult as well as a pediatric boney deformity that mostly affects children. Radiological findings are the best differential diagnosis method to minimize misdiagnosis of Subungual Exostosis and histopathologic examination can be used to confirm the diagnosis. Complete excision of Subungual Exostosis is the best treatment method with a low recurrence rate. Wound management post excision may lead to satisfactory clinical results while avoiding onychodystrophy, a common complication after excision.

Conclusion
Radiological examination is essential for the diagnosis of SE. Complete excision of Subungual Exostosis is the best treatment method with a low recurrence rate.

Keywords: Subungual Exostosis, Nail Toe Disorder, Foot, Hallux, Dupuytren’s Exostosis

Level of Evidence: 4
INTRODUCTION

Nail disorders are one of the most common podiatric complaints amongst patients. Subungual exostosis (SE), also known as Dupuytren’s exostosis, is an uncommon benign bony overgrowth of the toes and fingers. Most often, SE appears as a bony attachment to the distal surface of the hallux, less frequently appearing on the lesser digits. This lesion is typically diagnosed in children and adolescents.

SE develops slowly over months and causes detachment of the nail plate from the nail bed, leading to nail deformity and digit pain. This may result in possible ulceration and infection. Some studies suggest that microtrauma, chronic infection, or hereditary abnormalities could be a possible etiology of SE. Molecular studies reported a translocation t(X;6)(q22;q13-14) to be linked to subungual exostosis. Having a unique chromosomal rearrangement suggests that SE is a real neoplastic lesion and not a reactive process in response to previous trauma. Despite these theories, there is currently no significant evidence to support single pathogenesis as the causative agent.

The most common complications that bring the patient with SE to the podiatric office are pain, erythema, and deformity of the nail bed. The tumor itself is not painful, however, pain may develop due to mechanical irritation or secondary infection. Clinical presentation is not the best differential diagnostic evidence for the diagnosis of subungual exostosis. The clinical findings of SE are broad and similar to other nail disorders. That can be the reason why SE is often misdiagnosed. The differential diagnoses for SE include, but are not limited to, subungual verruca, pyogenic granuloma, osteochondroma, amelanotic subungual melanoma, and glomus tumor. Its similarity to other disorders and frequency of misdiagnosis often leads to inadequate or unsatisfactory treatments.

The main purpose of this systematic review of the literature is to evaluate the differential diagnosis and treatment plans for subungual exostosis. In order to help podiatrists with the best decision plan and increasing satisfaction of patients with SE, it is important to diagnose it correctly and treat it appropriately.

METHODS

The authors performed a systematic search utilizing PubMed. “Subungual exostosis and toes” was used as a search term. Entering (Subungual exostosis[MeSH Terms]) AND toes[MeSH Terms] on PubMed yielded 65 potential articles. Of these 65 articles, 15 articles were excluded because they were written in languages other than English. 22 articles were excluded as they were published prior to 2000 and 21 articles were excluded due to be non-relevant studies or full text not available from PubMed.
Inclusion criteria required articles written in the English language, subungual exostosis of the toes, and articles written after the year 2000. Exclusion criteria eliminated articles describing subungual exostosis in the upper extremity, other tumors of the toenail, and non-English written. By evaluating and screening articles based on inclusion and exclusion criteria seven articles were selected to be analyzed for the purpose of this article (Figure 1) followed by the presence of a mass/swelling and nail deformity. The percentages associated with the most common complaints are shown in Figure 2. Subungual Exostosis was seen the most on hallux (80.33%), followed by the 3rd digit (7.1%), 2nd digit (6%), 4th digit (5%), and 5th digit (2%). The proceeding time was varied between patients from 2 weeks to 2 years. Having a previous trauma at the location of the exostosis was seen in 29% of patients and the previous infection was seen in 14%. Excision was the treatment method for almost all these patients except 6 who underwent amputation. The reoccurrence chance was 4% (Table 2). 9, 13-18

![PubMed Article Search and Exclusion Criteria](image)

**RESULTS**

Throughout the 7 articles used in this systematic review, a total number of 299 cases of individuals with SE were reviewed. The mean age of 16.6 was calculated using the weighted means formula. The female to male ratio was 149: 150 (Table 1). The most common symptoms associated with SE were pain followed by the presence of a mass/swelling and nail deformity. The percentages associated with the most common complaints are shown in Figure 2. Subungual Exostosis was seen the most on hallux (80.33%), followed by the 3rd digit (7.1%), 2nd digit (6%), 4th digit (5%), and 5th digit (2%). The proceeding time was varied between patients from 2 weeks to 2 years. Having a previous trauma at the location of the exostosis was seen in 29% of patients and the previous infection was seen in 14%. Excision was the treatment method for almost all these patients except 6 who underwent amputation. The reoccurrence chance was 4% (Table 2). 9, 13-18

**Most Common Complaints**

![Most common complaints associated with Subungual Exostosis](image)
<table>
<thead>
<tr>
<th>Study</th>
<th>Journal type</th>
<th>Study design</th>
<th># Cases</th>
<th>F</th>
<th>M</th>
<th>Mean Age (yrs)</th>
<th>Study Aim</th>
</tr>
</thead>
<tbody>
<tr>
<td>DaCambra et al.</td>
<td>Orthopedic</td>
<td>SR</td>
<td>N= 289</td>
<td>146</td>
<td>143</td>
<td>25.7</td>
<td>To address the best surgical approach, demographic distribution, and complications after treatment</td>
</tr>
<tr>
<td>Ghosh et al.</td>
<td>Pediatric</td>
<td>Case Report</td>
<td>N=1</td>
<td>0</td>
<td>1</td>
<td>13</td>
<td>Present a Subungual Exostosis case</td>
</tr>
<tr>
<td>DaCambra et al.</td>
<td>Orthopedic</td>
<td>Case Report</td>
<td>N=1</td>
<td>1</td>
<td>0</td>
<td>13</td>
<td>Management of the postsurgical wound in a case of hallucal subungual exostosis</td>
</tr>
<tr>
<td>Morais et al.</td>
<td>Family physician</td>
<td>Case Report</td>
<td>N=1</td>
<td>0</td>
<td>1</td>
<td>17</td>
<td>Present a Subungual Exostosis case</td>
</tr>
<tr>
<td>Stănescu et al.</td>
<td>Embryology</td>
<td>Case Report</td>
<td>N=1</td>
<td>0</td>
<td>1</td>
<td>14</td>
<td>Present a Subungual Exostosis case</td>
</tr>
<tr>
<td>Campanelli et al.</td>
<td>Medicine</td>
<td>Case Report</td>
<td>N=1</td>
<td>1</td>
<td>0</td>
<td>12</td>
<td>Present a Subungual Exostosis case</td>
</tr>
<tr>
<td>Storlazzi et al.</td>
<td>Cancer</td>
<td>Case Series</td>
<td>N=5</td>
<td>1</td>
<td>4</td>
<td>18.4</td>
<td>To identify the genes that are critical for neoplastic transformation</td>
</tr>
</tbody>
</table>

SR=Systematic Review, F=Female, M=Male, yrs=Years

Table 1: Summaries of articles reviewed

DaCambra et al. conducted a systematic review, which emphasized previously published demographic and symptomatology associated with SE. In their search for literature, they found 124 related articles and summarized 13 articles, which met their inclusion criteria. Total number of 287 patients were reported in the 13 included articles. Based on the DaCambra et al. literature review, the hallux was the dominant location of SE, a finding supported by Davis and Cohen. However, they found that the rate of SE in pediatric population (55%) is higher than adults and there is a 1:1 ratio of female to male. These findings were in contrast with the previously published article by Davis and Cohen. Davis and Cohen reported 16% pediatric and a 2 to 1 ratio of female to male patients.

Based on DaCambra et al. review, radiographs of the exostoses were an important method for differential diagnosis. Complete excision of the
Lesion by curetting or burning down to the normal trabecular bone was suggested as the best treatment plan with the lowest incidence of recurrence. The authors also suggested that adequate wound management postexcision can help to minimize the chance of onychodystrophy, a common complication post treatment.13

<table>
<thead>
<tr>
<th>Study</th>
<th>Altered digit</th>
<th>Dominant complaint</th>
<th>Etiology</th>
<th>Diagnostic method</th>
<th>Preceding time</th>
<th>Treatment</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>DaCambra et al.13</td>
<td>Hallux</td>
<td>Pain (77%)</td>
<td>Trauma 29%</td>
<td>NR</td>
<td>2 weeks to 10 years</td>
<td>Mostly Excision</td>
<td>4%</td>
</tr>
<tr>
<td></td>
<td>Dig 2</td>
<td>Swelling (31%)</td>
<td>Infection 14%</td>
<td></td>
<td></td>
<td>Amputation in 6 patients</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dig 3</td>
<td>Nail change (15%)</td>
<td>Family history 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dig 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Dig 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ghosh et al.14</td>
<td>Hallux</td>
<td>Pain small, pink</td>
<td>NR</td>
<td>Clinical presentations Radiological features</td>
<td>6 months</td>
<td>Excision</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td></td>
<td>colored, hard, exophytic growth projects</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DaCambra et al.15</td>
<td>Hallux</td>
<td>Pain</td>
<td>No</td>
<td>Radiological findings Histological analysis</td>
<td>1 month</td>
<td>Excision Portable VAC</td>
<td>No</td>
</tr>
<tr>
<td>Morais et al.16</td>
<td>Hallux</td>
<td>exophytic, non-tender, fixed, firm flesh-colored subungual nodule</td>
<td>No</td>
<td>Clinical appearance and radiographic findings</td>
<td>2 years</td>
<td>Excision</td>
<td>No</td>
</tr>
<tr>
<td>Name</td>
<td>Location</td>
<td>Clinical Findings</td>
<td>Histological Findings</td>
<td>Duration</td>
<td>Treatment</td>
<td>Outcome</td>
<td></td>
</tr>
<tr>
<td>-----------------------</td>
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<td></td>
</tr>
<tr>
<td>Stănescu et al.</td>
<td>Hallux</td>
<td>Pain, Bleeding</td>
<td>Trauma</td>
<td>Clinical, histopathological and radiographic data</td>
<td>2 years</td>
<td>Excision</td>
<td>No</td>
</tr>
<tr>
<td>Campanelli et al.</td>
<td>Hallux</td>
<td>Mass, Onycholysis</td>
<td>NR</td>
<td>Clinical and radiographic findings</td>
<td>3 months</td>
<td>Excision</td>
<td>No</td>
</tr>
<tr>
<td>Storlazzi et al.</td>
<td>Hallux</td>
<td>NR</td>
<td>NR</td>
<td>FISH</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
</tbody>
</table>

N/A=Not applicable, NR=Not Reported, Dig= digit, VAC= Vacuum Assisted Closure, FISH= fluorescence in situ hybridization

Table 2: *Summaries of clinical findings*

Ghosh et. al presented a case of subungual exostosis in a 13 year old boy with a growth beneath the nail of the right hallux (Figure 3). The patient complained about pain for 6 months at the lesion site. A bony hard nodule 20x15 mm diameter was presented. The authors confirmed the diagnosis of SE with radiograph findings and clinical presentations. Radiographic imaging showed a calcified projection on the dorsolateral part of the distal phalanx, continuous with underlying bone (Figure 4). The authors mentioned that the bony consistency of the nodule could also help to differentiate the diagnosis of SE. Regarding treatment, complete excision or curettage was recommended by these authors.14
DaCambra et al. presented a case report to introduce a novel strategy for the management of postsurgical wound in the case of hallucal subungual exostosis. The patient was a 13 year old girl who had had pain for a month over her left hallux without a prior history of trauma. An enlarged mass was seen, which had eroded through the dorsal aspect of the nail plate. The mass was hyperkeratotic, 12x10x10 mm, and fixed, firm, and tender to palpation. Subungual exostosis was diagnosed based on the well-defined pedunculated radio opaque mass arising from the dorsum of the distal phalanx as seen on radiographs. Marginal excision was selected as the treatment option. Also, histological analysis demonstrated a normal trabecular bone base with fibrocartilaginous tissue superficially,
consistent with exostosis. A portable VAC dressing with a pedicle to the exposed nail bed and distal phalanx was applied. The patient was followed up for one year and by six weeks she was asymptomatic. By the last follow up post resection, there was no evidence of recurrence. Morais et al. presented a case study of a 17 year old male with a 2 year duration of an enlarging mass underneath the right hallux without a history of previous trauma to the site of the lesion. Clinical findings included exophytic, non-tender, fixed, firm flesh-colored subungual nodule on the dorsal aspect of the right great toe. A 10 mm lesion was found, which was associated with nail plate deformity and onycholysis (Figure 5).

The clinical appearance and radiographic findings were used to confirm the diagnosis of SE. The authors considered surgical excision as the best management plan for this specific case. Histological analysis was used to confirm the diagnosis of subungual exostosis. It showed mature trabecular bone covered by hyaline fibrocartilage tissue, which is characteristic of SE. Stănescu et al. presented a case of a 14 year old boy who had a painful, bleeding nodular tumor. The patient had had this lesion for two years and was initially misdiagnosed with subungual verruca. He was again misdiagnosed with pyogenic granuloma and underwent several surgical interventions due to the reappearance of the tumor. The patient was a soccer player and correlated the lesion with a previous trauma. The excision of the lesion was performed and histopathological techniques were used to confirm the diagnosis of SE. The authors mentioned that the dermatological and histopathological examinations, as well as radiographic examinations, were performed to make sure there was no evidence of
achromatic malignant melanoma. The patient was followed up for 2 years with no evidence of recurrence. Stănescu et al. concluded that without histopathological and radiographic examination, SE could be misdiagnosed and mistreated. Stănescu et al. concluded that local excision and removal of the cartilaginous cap is the recommended elective treatment of the subungual exostosis.\textsuperscript{17}

Campanelli et al.\textsuperscript{18} presented a case of a 12 year old girl with a 10 mm nodule on the lateral nail fold of the right hallux for 3 months (Fig. 6-A). Initially, it was misdiagnosed as a wart and treated with salicylic acid. A calcifying projection on the dorsolateral part of the distal phalanx continuous with the underlying bone was revealed on the radiograph, which was a diagnostic characteristic of the SE (Fig. 6-B). The subungual exostosis was resected and histopathological studies showed a mature trabecular bone covered by hyaline fibrocartilage tissue (Fig. 6-C). The patient did not experience recurrence for the next 3 years.\textsuperscript{18}

Fig. 6: (Reproduced from the New England Journal of Medicine, case report\textsuperscript{18})

A case series was conducted by Storlazzi et al. to evaluate subungual exostosis at the molecular level. The authors examined the genome of 5 patients suffering from SE to identify the genes that are critical for neoplastic transformation. FISH analyses in this study were confirmed a clustering of the breakpoints to the regions harboring the collages genes COL12A1 and COL4A5 in chromosome bands 6q13-14 and Xq22, respectively. In 4 out of 5 genomes, both COL12A1 and COL4A5 were on the derivative chromosomes X and 6, which signified that at least one of them is consistently involved in the formation of a chimeric fusion gene, or in the exchange of regulatory sequences. Tissue remodeling requires collagen molecules during physiologic growth and differentiation, which is why both \textit{COL12A1} and \textit{COL4A5} are found as good candidate target genes in the pathogenesis of subungual
exostosis. The authors indicated that further studies are required to clarify the functional outcome of the t(X;6) translocation in subungual exostoses.9

**DISCUSSION**

A subungual exostosis is a rare condition in both the pediatric and adult populations. This literature review shows that most of the cases presented in children. Some physicians and families hesitate to have an x-ray examination of a child. However, this article, as well as the previously published papers, reinforces the importance of radiographic examination to minimize the misdiagnosis of SE. By reviewing the cases of those who were misdiagnosed, we are hoping that all physicians recognize the limitation of clinical appearance of subungual exostosis and rely more on radiological examination.

Moreover, this literature review sought to emphasizes the demographic findings associated with SE to introduce a guideline for a better management plan. This topic seems to be under-represented in the podiatric literature, based on Table 1, which suggests that SE has been diagnosed and treated more so by other specialists in the medical field.

Partial resection of the lesion was the main cause of recurrence in patients. It is another piece of evidence that indicates that these patients are not commonly treated for SE by a podiatrist. Complete excision of the lesion is the most preferred method of treatment. There are different wound management methods that still require more investigation. However, they can be promising alternatives to recommend for the best postsurgical cosmetic result and treatment plan.

In addition to radiographic findings, the histopathological examination may also be useful for further evaluation of the lesion and confirming the presence of SE.

Previously published articles suggested that hereditary abnormalities could be etiologic in the development of the SE. A translocation t(X;6)(q22;q13-14) was shown in Storlazzi et al. study and is associated with SE. Even though it is a promising study for evaluation of SE etiology, more studies need to be done to confirm a significant association between SE occurrence and the genome.

**CONCLUSION**

In conclusion, there are limited systematic reviews or prospective studies to present better recommendations for the evaluations and management of subungual exostosis. A subungual exostosis is a rare condition with high complication rates. In order to minimize the misdiagnosis of SE and deliver good patient outcomes, it is important to introduce podiatrists as specialized physicians in such cases. Further studies should attempt to identify predictors essential in diagnosis of SE. More studies are required to
emphasize the importance of radiograph and histopathological characteristics of SE and achieving the best treatment option.

AUTHORS’ CONTRIBUTIONS

Two authors contributed equally to the production of this article. All considered the topic, initial reviews, and contributed substantially to its revision. All authors read and approved the final submission of this draft.

STATEMENT OF COMPETING INTERESTS

None of the authors have any competing interests associated with this manuscript.

REFERENCES

Correlation Between Higher Body Mass Index and Plantar Fasciitis in Adults: A Literature Review

By: Marwa Hmady, BS

ABSTRACT

Introduction
Plantar fasciitis affects a large number of patients and is considered one of the most common causes for heel pain among adults. There is a lot of risk factors associated with plantar fasciitis. Obesity is contemplated to be a major risk factor in plantar fasciitis development, possibly due to increased mechanical loading of the foot due to excess weight.

Study design: Systematic Review of the Literature

Methods
A literature review investigating the correlation between the increased body mass index and plantar fasciitis in adults was evaluated. The literature was selected using the query of “Plantar Fasciitis” [MeSH] AND “BMI” [MeSH] in PubMed database.

Results
After applying our inclusion and exclusion criteria, five articles were included in this review. The articles chosen were a retrospective medical record review, two matched case-control studies, and two systemic reviews.

Discussion and Conclusion
All the articles included in this literature review imply a strong correlation between obesity and the diagnosis of plantar fasciitis.

Key Words: Plantar Fasciitis, Chronic Plantar Heel Pain, Obesity, Body Mass Index

Level of Evidence: 4
INTRODUCTION

Chronic plantar heel pain (CPHP) is one of the most common foot pathologies accounting for 15% of total complex foot complaints amongst adults. Of the various etiologies of heel pain, plantar fasciitis remains the most common cause of chronic heel pain in an outpatient setting, affecting about one million patients in the United States. Furthermore, almost 10% of all injuries amongst runners are due to plantar fasciitis. The plantar fascia is a thick fibrous band of connective tissue which originates from the medial process of the calcaneal tubercle (tuber calcanei) and inserts at the metatarsal heads. The plantar fascia is divided into three main structural components: medial, central (AKA plantar aponeurosis) and lateral bands, with the central band being the most significant component. Plantar fasciitis is the inflammation of the said fibrous ligament at its insertion. It’s characterized by an intense sharp pain at the plantar aspect of the heel which worsens after a period of offloading or with first steps in the morning.

Determining the etiology of plantar fasciitis is challenging due to the overlap and multiformality of the conditions mentioned. Although plantar fasciitis is the most common diagnosis, there are a wide variety of differential diagnoses that must be considered. Differential diagnoses include, but are not limited to, calcaneus injury, infection, sickle cell avascular necrosis, bone contusion, neuropathy, tendinitis/tendinosis, osteoporosis and malignancy.

Based upon the various hypotheses pertaining to the emergence of plantar fasciitis, the causes could be grouped into two categories, intrinsic and extrinsic. Extrinsic causes, which are environmental and circumstantial influences, include unhealthy lifestyle, lack of exercise, lack of supportive shoes, etc. Intrinsic factors, on the other hand, include individual predisposition such as obesity, equinus, limited ranges of motion or leg length discrepancy.

There are many risk factors contributed to the onset of plantar fasciitis, especially the repetitive overstretching and loading of the fascia. Patients who have higher body mass index, in particular those who fall in the obese category, are more susceptible to foot pathologies due to increased weight load.

Obesity is hypothesized to be one of the main contributors to the pathological overloading of the foot, causing over stretching of the fascia and subsequent inflammation aka fasciitis. Thus, a higher BMI is expected to be correlated to a higher incidence of plantar fasciitis. According to the national heart, lung, and blood institute (NHLBI), an individual with a BMI of 30 or higher is considered obese. All the articles used in this review measured and utilized the same parameters of BMI. This literature review examines the correlation between plantar fasciitis and BMI and aims to determine whether the diagnosis of plantar fasciitis is increased in the obese population.
METHODS

A search in PubMed with the query of “Plantar Fasciitis” [MeSH] AND “BMI” [MeSH], yielded thirty-five articles. Inclusion criteria comprised of higher body mass index (BMI) or obese patients, non-diabetics, adults, and articles that primarily discussed plantar fasciitis and associated foot pathologies such as overpronation. Articles that focused primarily on various treatment options for plantar fasciitis were excluded. The exclusion criteria included articles which evaluated diabetic patients (DM I and II) and discussed other etiologies of acute or chronic heel pain (e.g. Achilles tendinopathy). Although the exclusion criteria included “discussing treatment options”, we chose to include the retrospective medical review article based on that the main reason for conducting this review was to link obesity to plantar fasciitis rather than suggest bariatric surgery as a treatment option. Twenty-nine articles were excluded based on the inclusion and exclusion criteria outlined in figure 1, yielding five articles to be included in this literature.

RESULTS

The five articles reviewed included a retrospective medical record review, two matched case-control studies, and two systematic reviews respectively. Boules, Mena, et al. reviewed the effects of surgical weight loss on plantar fasciitis. The information was gathered from a database of the Cleveland Clinic Bariatric and Metabolic Institute. This study included a total of 163 patients diagnosed with plantar fasciitis (PF). Of the 163 patients, 146 underwent bariatric surgery, in turn removing them from the obese BMI category, and achieving complete resolution of plantar fasciitis.8

Mickle, Karen J, et al. is a case-control study which analyzed the effects of obesity in adult patients, in relation to foot pain and related functional limitation. The study compared overweight and healthy weight participants, and it was found that obese participants have a significantly higher prevalence of disabling foot pain. It was also
noted that obesity affects gait and is associated with increased foot length, shorter stride and step length, a bigger step width and more time spent in the stance and double support phases and less time in swing and single support phases of the gait cycle. Overweight participants were also found to generate an increased total force across the foot during stance, which was distributed over greater contact area. According to the findings, BMI increases soft tissue thicknesses at all sites except at the 1st metatarsal head, significantly reducing flexor strength of the hallux and lesser digits.9

The study by Irving, Damien B, et al. examined the correlation of obesity and foot pronation with PF and chronic heel pain along with a number of commonly hypothesized causative factors. The study included 80 participants with bilateral heel pain ranged in age from 20 to 82 with 59% women and the median duration of symptoms was 12 months. The control group also included 80 participants matching the case study’s participants with age and gender. The Foot Posture Index was used to assess foot posture and body mass index was calculated for each individual. Other measurements were also taken but we will not be mentioning those due to their irrelevance to this review. The results were then statistically analyzed, and the case group was found to have a significantly greater mean FPI score \( t = 2.93, P = 0.004 \), BMI \( t = 2.85, P = 0.005 \). Both univariate analysis and multivariate logistic regression revealed that the group with chronic heel pain had a more pronated foot posture than the control group.10

A systematic review and meta-analysis by van Leeuwen KDB, et al., looked into the various clinical and imaging risk factors to further examine the association between BMI and plantar fasciitis. The review included 46 case control, 4 cross sectional and 1 prospective case study studies, all of which evaluated a total of 104 variables. The pooled data concluded that higher BMI had the strongest effect in patients with plantar fasciitis as well as the only significant clinical association. The pooled imaging data drew an association between plantar fasciitis and having a significantly thicker, hypoechoic plantar fascia with increased vascular signal and perifascial fluid collection. Furthermore, those patients were found to have a thicker loaded and unloaded heel fat pat, and bone findings, including a subcalcaneal spur and increased Tc-99 uptake.11

Lastly, the systematic review by Irving, D.b., et al. was conducted to deduce the factors associated with chronic plantar fasciitis. The review included 16 articles and their methodological qualities were assessed and descriptively analyzed. Having a higher BMI and a calcaneal spur were the two most significant factors associated with chronic heel pain especially in non-athletic populations. Similar to what was mentioned in van Leeuwen KD, et al., increased weight and age and decreased ankle range of motion were significant in a non-athletic population.12 In athletic population however, weight and BMI were not associated with
chronic heel pain. Unlike the results obtained by the previously mentioned articles, Irving, D.b., et al. found a slight but present correlation between plantar fasciitis and other risk factors. These factors included increased age, decreased ankle dorsiflexion, decreased first metatarsophalangeal joint extension and prolonged standing.

**DISCUSSION**

Overall, there is a strong correlation between BMI and chronic heel pain, caused primarily by plantar fasciitis. This is considered to be the result of additional stress that excess weight exerts on the soft tissue of the lower extremities. Biomechanical studies have demonstrated the application of increased vertical force on the heel during stance phase of gait, resulting in a higher mean pressure on the longitudinal arch. In the obese population, pronated feet are more common, thus the combination of those two conditions lead to chronic plantar heel pain. Individuals that have an increased BMI generate a higher force with ambulation. The force is disseminated across a greater area, affecting pronated feet more than normal arch height feet. In obese individuals, there is an excess stress and strain on the musculoskeletal structures of the foot, specifically the plantar heel. This mechanical stress is proportional to the amount of excess weight, as proven by the proportional resolution of plantar fasciitis with surgical weight loss.

We found the studies included in this review are well conducted and good source of information pertaining to our hypothesis. There meta-analyses had a sufficient number of articles and the data obtained was carefully extracted and analyzed. The studies Mickle, Karen J, et al., and Irving, Damien B, et al. were all controlled case studies. The fact that these studies included a control group raises the credibility of the results deduced that BMI is in fact a significant risk factor of plantar fasciitis. Some limitations included: the specific inclusion criteria which were clinical definition of plantar fasciitis. Some cases might’ve had heel pain from causes other than the plantar fascia. If this was to be true, the data would not be completely accurate, and the factors found statistically insignificant (e.g. ankle ROM, age, etc..) might have been contributing factors associated with plantar fasciitis.

There are multiple study limitations in the literature review. A significant limitation was the small sample size of articles that comprised the inclusion and exclusion criteria, despite the results obtained. Moreover, two of the articles included in this literature review mentioned the fact that the causality cannot be deduced from correlation. In other words, an association between BMI and plantar fasciitis doesn’t indicate that obesity is a risk factor for heel pain emergence. The evidence obtained does not tell us whether the higher body mass index was present prior to emergence of plantar fasciitis or if it developed after the onset of pain and its subsequent activity restraint. The findings of this review should be used to guide the focus of prospective cohort studies, the results of which would ultimately provide a list of risk factors for CPHP. Such a list is essential in the development of new and improved preventative and treatment strategies for CPHP.

**CONCLUSION**

All the articles included in this literature review imply a strong correlation between obesity and the diagnosis of plantar fasciitis. A higher body mass index can be considered
as a risk factor for chronic heel pain due to the increased vertical forces directly under the plantar heel during gait, leading to increased mechanical stress on the musculoskeletal structures of the heel. The increased stress damages the soft tissue structures in the lower extremity and leads to symptoms associated with plantar fasciitis.10

AUTHORS’ CONTRIBUTIONS

Each author on this paper contributed in writing this manuscript. Each author drafted, read, and agreed on the completeness of this manuscript before submission.

STATEMENT OF COMPETING INTERESTS

The author(s) declare that they have no competing interests.

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Effectiveness of Onychocryptosis Treatments in the Pediatric Population: A Literature Review

By: Joann Li, BA; Alexander Malek, BA, BS, MPH; Emanoil Shafik, BA, MS

ABSTRACT

Introduction
Ingrown toenails or onychocryptosis is a common problem that affects both the pediatric and adult population. Onychocryptosis occurs when the lateral margins of the nail plate improperly grow into the dermis causing inflammation and infection. There are various treatment modalities for ingrown toenails ranging from conservative to surgical; however, because there is a lack of pediatric studies to demonstrate the best treatment methods for ingrown toenails in children, often times the treatment choice for pediatrics are guided by treatment protocols for the adult population. The purpose of this literature review is to analyze various management modalities for ingrown toenails and to discuss the recurrence rates and safety profiles of each treatment for the pediatric population.

Study Design: Qualitative Systematic Review of Literature

Methods
A PubMed search was completed using the query “Ingrown toenails AND treatments AND pediatrics.” Inclusion criteria included articles with onychocryptosis or ingrown toenail in the title, articles printed in English, and articles with full text availability through the New York College of Podiatric Medicine library or interlibrary loan. Exclusion criteria included non-English articles, articles not focused on ingrown toenail treatments, and articles inclusive of immune-deficiency participants.

Results
The PubMed search resulted in 24 articles. After applying the inclusion and exclusion criteria, 13 articles from the PubMed database were selected to be included in the literature review to discuss onychocryptosis treatment in the pediatric population. Treatment options included both conservative treatments such as soaking, nail packing, CO₂ laser, and nail bracing, as well as surgical options such as partial nail avulsions, nail avulsion with phenol, wedge excisions of the nail edge, excision of the nail fold, toenail splinting and surgical matrixectomy.

Conclusion
There is currently no set standard for the best method to manage ingrown toenails in children. However, there is a consensus that conservative treatments are generally used for Stage 1 and 2 of the disease and surgical treatments are recommended for patients with Stage 3 of the disease or patients who experience recurrence. Often, the best treatment varies between patients as there are multiple factors to consider when choosing the appropriate treatment.

Keywords: Onychocryptosis, Ingrown Toenails, Pediatrics

Level of evidence: 4
INTRODUCTION

Ingrown toenails or onychocryptosis is a common problem that affects both the pediatric and adult population; about 20% of patients who present for foot consultation are diagnosed with ingrown toenails.1 Onychocryptosis occurs when the lateral margins of the nail plate improperly grow into the dermis causing inflammation and infection.2,3 The highest incidence of ingrown toenails occurs in those patients between eleven and thirty years of age. However, children as young as two years old frequently suffer from this problem as well.1,2

Ingrown toenails can affect any digit, however, the hallux is almost exclusively affected.1,2,4 While one or both nail borders can be affected, it has been shown that the lateral border is 50% more commonly affected compared to the medial one.4 The exact etiology of ingrown toenails is currently unknown, however there are various contributing factors such as genetic predisposition, tight fitting shoes, improper nail cutting, etc.5,6

The pathology of ingrown toenail occurs when the lateral portion of the nail plate grows into the adjacent nail fold, acting as a foreign body, causing inflammation and infection.2,7 There are three different stages of onychocryptosis: stage 1 (inflammation) is mild swelling and erythema of the nail fold, stage 2 (infection) is increased swelling of the nail fold with seropurulent discharge and ulceration, and stage 3 (granulation) is chronic inflammation with granulation tissue formation and nail fold hypertrophy.4,6 Nail spicules, which are sharp lateral nail edges that penetrate the soft tissue, are commonly seen in patients with ingrown toenails and are believed to be the driving cause of ingrown toenails as well as a common cause of recurrence and pain if not properly removed.6

Ingrown toenails can cause significant discomfort and pain. This condition can also cause recurrent soft tissue infections, impair one’s ability to wear normal shoes and can affect participation in sports and other activities.5,8 During physical examination, the toe will likely show erythema and swelling and in more serious cases there can be discharge and granulation tissue present.4

There are various treatment modalities for ingrown toenails ranging from conservative to surgical. When the case is minor, conservative treatment such as soaking, nail packing, and nail bracing is often appropriate.5 However, for cases where there is drainage, granulation tissue or recurrence, non-conservative treatments are often needed.3,5 The common surgical options for ingrown toenails include partial nail avulsions, nail avulsion with phenol, wedge excisions of the nail edge, excision of the nail fold, toenail splinting and surgical matrixectomy.3,4,6 There are many factors to consider when choosing the appropriate treatment modalities such as the stage of the onychocryptosis, a history of ingrown toenails, and risk of invasive procedures. Due to a lack of pediatric studies to demonstrate the best treatment methods for ingrown toenails in children, often the treatment choice for pediatrics is guided by treatment protocols for the adult population.3 Surgical interventions are often stressful and off-putting for children, and may result in development of infection post operatively or ischemia.9 The purpose of this literature review is to analyze various management modalities for ingrown toenails in the pediatric and adolescent population and to discuss the recurrence rates and safety profiles of each treatment for the pediatric population.
METHODS

A literature search was performed on PubMed. The PubMed search was completed using the query “Ingrown toenails AND treatments AND pediatrics”, yielding 24 articles. Inclusion criteria included articles with onychocryptosis or ingrown toenail in the title, articles printed in English and articles with full text availability through New York College of Podiatry Medicine library or interlibrary loan. Exclusion criteria included articles not published in English, articles not focused on ingrown toenail treatments and articles inclusive of immune-deficiency participants. After applying the inclusion and exclusion criteria, 13 articles from the PubMed database were selected to be included in the literature review.

![Diagram]

Figure 1: Summary of article acquisition with inclusion and exclusion criteria

RESULTS

The PubMed search resulted in 24 articles. After applying the inclusion and exclusion criteria, 13 articles from the PubMed database were selected to be included in the literature review to discuss onychocryptosis treatment in the pediatric population. Treatment options included both conservative treatments as well as surgical...
options. Different treatment modalities are selected depending on patient presentation as indicated in the articles included in this review. The age range and study aim for each article is summarized in Table 1.

<table>
<thead>
<tr>
<th>Article</th>
<th>Treatment Modality</th>
<th>Age Range</th>
<th>Study Aim</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chitgopeker 2016&lt;sup&gt;7&lt;/sup&gt;</td>
<td>• Nail Tube Splinting</td>
<td>13 years old</td>
<td>Case report discussing the success of nail tube splinting in a patient with recurrent ingrown toenails</td>
</tr>
<tr>
<td>Ezekian 2017&lt;sup&gt;4&lt;/sup&gt;</td>
<td>• Antibiotics • Anesthetic • Nail Avulsion • Wedge Excision of Nail Edge • Nail and Germinal Matrix Excision • Matrixectomy</td>
<td>N/A</td>
<td>Discussion of different ingrown toenail treatments</td>
</tr>
<tr>
<td>Farrelly 2009&lt;sup&gt;10&lt;/sup&gt;</td>
<td>• Wedge excision of ingrown toenail with bipolar diathermy of nail bed</td>
<td>N/A</td>
<td>To compare the results, complications and patient satisfaction of the wedge excision with bipolar diathermy of nail bed with other procedures</td>
</tr>
<tr>
<td>Gera 2019&lt;sup&gt;2&lt;/sup&gt;</td>
<td>• Nail care advice, topical antibiotics and daily cleansing • Wedge resections • Total Nail Avulsion</td>
<td>~14 years old</td>
<td>Comparison of nonoperative treatments with operative treatments</td>
</tr>
<tr>
<td>Haricharan 2013&lt;sup&gt;11&lt;/sup&gt;</td>
<td>• Nail Fold Excision</td>
<td>&lt;18 years old</td>
<td>Evaluate the effectiveness of the procedure</td>
</tr>
<tr>
<td>Lazar 1999&lt;sup&gt;12&lt;/sup&gt;</td>
<td>• Soaking, application of EMLA 5% cream, cauterizing granulation tissue and parent</td>
<td>4 - 17 years old</td>
<td>To discuss the effectiveness of conservative treatment with patient education in treating pediatric ingrown toenails</td>
</tr>
<tr>
<td>Study</td>
<td>Procedure(s)</td>
<td>Age Range</td>
<td>Primary Outcomes</td>
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<tr>
<td>Livingston 2017&lt;sup&gt;5&lt;/sup&gt;</td>
<td>• Nail Fold Excision</td>
<td>4 - 20 years old</td>
<td>To evaluate patient-reported outcomes for pain, functional status and quality of life before, one, two- and six- months post-op</td>
</tr>
<tr>
<td>Mitchell 2011&lt;sup&gt;6&lt;/sup&gt;</td>
<td>• Avulsion of entire nail</td>
<td>1 - 16 years old</td>
<td>To determine average age of patients undergoing surgical treatment for ingrown toenails</td>
</tr>
<tr>
<td>Mitchell 2011&lt;sup&gt;6&lt;/sup&gt;</td>
<td>• Avulsion of entire nail with phenol</td>
<td>1 - 16 years old</td>
<td>To determine commonly used surgical procedures and their recurrence rates</td>
</tr>
<tr>
<td>Mitchell 2011&lt;sup&gt;6&lt;/sup&gt;</td>
<td>• Wedge excision of nail edge</td>
<td>1 - 16 years old</td>
<td></td>
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<tr>
<td>Mitchell 2011&lt;sup&gt;6&lt;/sup&gt;</td>
<td>• Wedge excision of nail edge with phenol</td>
<td>1 - 16 years old</td>
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<tr>
<td>Mitchell 2011&lt;sup&gt;6&lt;/sup&gt;</td>
<td>• Excision of nail bed</td>
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<tr>
<td>Mitchell 2011&lt;sup&gt;6&lt;/sup&gt;</td>
<td>• Excision of nail bed with phenol</td>
<td>1 - 16 years old</td>
<td></td>
</tr>
<tr>
<td>Perez 2012&lt;sup&gt;1&lt;/sup&gt;</td>
<td>• Nail Splinting</td>
<td>2 - 16 years old</td>
<td>To analyze the results of nail splinting as a treatment for pediatric ingrown toenails</td>
</tr>
<tr>
<td>Rueff 2010&lt;sup&gt;13&lt;/sup&gt;</td>
<td>• Emmert Procedure</td>
<td>10 year old</td>
<td>Case report discussing a rare ischemic complication of the Emmert Procedure</td>
</tr>
<tr>
<td>Serour 2002&lt;sup&gt;8&lt;/sup&gt;</td>
<td>• CO2 laser partial matrixectomy</td>
<td>10 - 75 years old</td>
<td>To evaluate the effectiveness of CO2 laser partial matrixectomy for recurrent ingrown toenails</td>
</tr>
<tr>
<td>Shih 2019&lt;sup&gt;9&lt;/sup&gt;</td>
<td>• Nail Brace</td>
<td>6 - 17 years old</td>
<td>To discuss the use of nail bracing as a form of treatment for pediatric ingrown toenails</td>
</tr>
<tr>
<td>Yang 2007&lt;sup&gt;3&lt;/sup&gt;</td>
<td>• Chemical matrixectomy with NaOH</td>
<td>2 - 16 years old</td>
<td>To compare the use of nail avulsion plus chemical matrixectomy with surgical matrixectomy in treating pediatric patients with ingrown toenails</td>
</tr>
</tbody>
</table>

Table 1: *Summary of Articles Reviewed*
Conservative

Soaking

An infected ingrown toenail could be treated conservatively by soaking the affected foot in warm water mixed with chlorhexidine and cetrimide for 15 minutes. Afterwards EMLA 5% cream is applied to the affected area for 30 minutes and the granulation tissue is cauterized with silver nitrate solution. Once the physician deems the affected area is clean, a Steri-Strip is applied obliquely under the ingrown nail corner and left in place. This procedure is continued at home until the nail grows beyond the side-grooves.  

Lazar et al. conducted a study on 20 pediatric patients who had ingrown toenails. The treatment duration ranged from 3 – 9 weeks. Some patients had previously undergone surgical intervention for their ingrown toenails, however their ingrown toenail returned. They found that the procedure had significant results and was tolerable in 19 out of the 20 patients.  

Nail Brace

The nail brace includes the application of a nail brace device to the patient’s affected nail plate. There are three different nail brace devices (hook device, adhesive device and composite device) that could be used depending on the accessibility of the nail plate. The hook nail device is placed under the bilateral nail plate and the wire is bent to apply an upward tension force. The adhesive device is applied to the dorsum of the nail plate using adhesives and the attached wire is twisted to apply the upward tension force. The composite device is applied by creating a hook in the wire and placing it under the nail edge; then adhesive is applied to fix it onto the dorsum of the nail plate. The nail brace application duration ranges from 15 minutes to 40 minutes depending on which device is applied.  

Shih et al. performed a study on 38 pediatric patients who presented with pain, swelling and erythema on the affected ingrown toenail. The treatment duration was less than 16 weeks for majority of the patients. They found that 27 patients showed positive response after the procedure and none of the patients experienced any postoperative morbidity. The recurrence rate was 21% with 8 patients who had recurrent ingrown toenails following the procedure.  

Surgical

CO2 Laser

Laser procedures are an adjunctive procedure that can be done alongside partial matrixectomy as treatment for recurrent ingrown toenails. The procedure is first done by doing a partial matrixectomy and then a laser with a 2 mm beam in continuous mode is directed to vaporize the matrix, lateral horns, lateral nail groove and granulation tissue. Once the first pass is complete, a dermal curette and a saline moisten applicator is used to remove the epithelium of the matrix and the lateral nail fold. Then the laser is passed through the same area for a second or third time. Once the procedure is complete, antibacterial ointment is applied to the toe and a dressing is applied. Patient’s parents are advised to change the dressing daily, cleaning the toe with saline or hydrogen peroxide during each change.  

Serour et al. performed a prospective study with 196 patients and 344 matrixectomies; the included patients previously underwent unsuccessful nail procedures. They reported a recurrence rate of 1.45%, but only in patients who had bilateral matrixectomies.
All patients healed within 15-30 days and did not report any infections or excessive drainage. Only mild erythema was noted.  

Toenail Splinting

Nail splinting involves the use of a flexible tube secured with a suture. Prior to the procedure, patients are prepped by taking antibiotics 48 hours prior to surgery. The procedure is completed under local anesthesia and the affected nail plate is freed on the anterior and posterior surfaces from the distal end to the proximal matrix. Then a flexible tube is placed on the outer edge of the nail; it is important to ensure that the ingrown edge must be incorporated into the channel of the tube. The tube is then inserted 1 to 2 mm below the eponychium and proximal nail folds and the tube is fixed to the nail plate proximally with a suture. Antibiotic ointment is then applied to the surgical site. Postoperatively, patients are given a course of antibiotics to be taken for a week or two after the procedure. Patients can walk after 24 hours if there is no discomfort. The tube is removed following eight to twelve weeks of nail growth and the patient’s parents are taught proper nail care to prevent future ingrown toenails.

Perez et al. conducted a study with 71 patients, all of whom had a Stage 3 ingrown toenail. The recurrence rate of the procedure was 12.6% and all the patients were able to return to school 48 hours following the procedure. Chitgopeker et al. discussed the use of toenail splinting in a 13-year-old patient who had bilateral recurrent ingrown toenails. The patient had previously tried chemical matrixectomies, electrodessication, and ablative CO2 laser; none of which have prevented recurrence. The patient underwent nail tube splitting on her right foot and an excision on her left foot. The tube was left on the patient for 3 months after the procedure and the patient has not had a recurrence in 1.5 years.

Wedge Excision with Bipolar Diathermy

Wedge excision with bipolar diathermy is a novel and simple technique to treat ingrown toenails. The procedure involves a wedge excision of the affected toenail followed by a bipolar diathermy to cauterize the nail bed. After the procedure, a simple dressing is applied and removed after 24 hours. Patients are recommended to not wear shoes or socks for one week following the procedure.

Farrelly et al. conducted a prospective study where 353 procedures were conducted on 302 patients. A recurrence rate of 9.9% was reported with no significant complications in any of the cases. A patient satisfaction questionnaire was returned by 73 of the patients and 97.2% of the patients stated that they were “satisfied” or “very satisfied” with the outcome of the operation.

Nail Fold Excision

Nail fold excision or the Vandenbos procedure is performed by only excising the skinfold, leaving the toenail and nail matrix intact. The procedure is done by creating an incision in the nail base, cutting out toward the side and then to the distal end of the digit. It is important to ensure that all of the nail fold skin is removed and the matrix proximal to the incision is not damaged. Following the removal of the nail fold skin, the open skin edge and subcutaneous tissue is cauterized. The patient is then instructed to elevate his or her foot on a pillow for 15 minutes following the procedure.

Haricharan et al. conducted a study in which 67 procedures were performed on 50 patients and found that patients were able to normally ambulate 7 days following the
procedure. The procedure produced excellent cosmetic results. In his study, there were 6 patients with postoperative complications including bleeding issues, nail deformity and excessive granulation. The majority of the postoperative complications were treated and patients did not have any long-term effects. Livingston et al. presented a study to evaluate the recurrence rates and patient satisfaction with the Vandenbos procedure. They had 39 participants and found that patients were able to return to school seven days after the procedure with no recurrences. Ninety-five% of patients and 100% of patients’ parents would recommend the procedure.  

**Surgical Matrixectomy**

Surgical matrixectomy is a common technique that involves the removal of the affected portion of the nail with a sharp excision of the underlying matrix using a scalpel. Afterwards, the physician will curette any remaining matrix. Often this procedure is done under either local or regional anesthesia. Patients are usually allowed to go home the day of surgery and are to follow up with their clinician in one week.  

Yang et al. investigated the recurrence rates of pediatric patients who underwent a surgical matrixectomy; of the 420 patients who underwent a surgical matrixectomy, 20% of the patients had a recurrence. In addition, there were 39 patients who experienced soft tissue infections following the procedure. Mitchell et al. found that out of 31 patients who had a surgical matrixectomy, there were 21.2% patients who had to undergo additional procedures for the same nail.

**Chemical Matrixectomy**

Chemical matrixectomy is a procedure that is used as an alternative to surgical matrixectomy. Phenol was previously used for this procedure; however, it has been found that NaOH has similar outcomes with a better safety profile. For chemical matrixectomies, a partial or complete nail avulsion is performed. Ten % NaOH (or phenol) is then applied to the germinal matrix and then the matrix is curetted away. Once the procedure is complete, glacial acetic acid is applied to neutralize the base and saline is then used to wash out the affected area.  

Yang et al. conducted a study to compare the effectiveness of chemical matrixectomy versus surgical matrixectomy. The study included 518 patients with 112 patients who underwent a chemical matrixectomy. It was found that there was a 12% recurrence rate. Mitchell et al. discussed a 10-year retrospective cohort study to look at the recurrence rates of various surgical treatments. They found that the use of phenol alongside surgical procedures decreased recurrence rates in the patients.

**DISCUSSION**

Conservative treatments for ingrown toenails are often used for patients who have a minor case of ingrown toenails. However, for patients who present with drainage, infection, or granulation tissue, surgical nail procedures are often recommended. Traditionally, physicians recommended starting with conservative treatment in patients who present with an ingrown toenail, especially in the pediatric population. Often, surgical techniques are considered once the patient has failed conservative treatment or has recurrent ingrown toenails. Surgical procedures all
carry their own risks ranging from infection to ischemia. Rueff et al. presented a case where a pediatric patient experienced distal necrosis of their hallux following a surgical procedure to remove his ingrown toenail which resulted in the loss of his distal phalanx. It is important to educate the patient’s parents on postoperative care following a surgical procedure and to inform the patient’s parents about the risk of recurrence with surgical procedures.

Conservative

Soaking

Ingrown toenails are an agonizing and common condition in children and young adults. Previous conservative treatment included cleaning the affected skin and inserting a cotton-wool pledget under the ingrown toenail edge. However, this method was often painful, and many pediatric patients did not tolerate it well. The soaking method is an alternative method which is almost painless and much more tolerable. Lazar et al. demonstrated that the soaking method produced results comparable to surgical procedures that carry morbidity risks.

Nail Brace

The nail brace application is a safe and simple non-invasive procedure that can be used to treat pediatric patients with ingrown toenails. Shih et al. found that the procedure had a short recovery time, rapidly relieved symptoms and was well tolerated by the patients. Additional studies would need to be done to compare the effectiveness of nail bracing and surgical procedures; however, nail bracing could be used as a conservative treatment alternative for ingrown toenails.

Surgical

CO₂ Laser

Laser procedures have been suggested as a treatment for nail pathologies since the 1980s, however there has been little research done attesting to their efficacy. In the study conducted by Serour et al. they found that CO₂ laser therapy can be effective in treating patients with recurrent ingrown toenails. The advantage of this procedure is low recurrence, decreased postoperative pain, less bleeding and less damage to the surrounding area compared to phenol or cold steel procedures. However, the laser wound takes longer to heal and requires 3-6 weeks of local care. Overall, CO₂ laser should be a procedure to consider if a patient continues to have recurrent ingrown toenails despite having undergone standard modalities.

Toenail Splinting

Nail tube splinting is an alternative surgical technique that can be used to treat ingrown toenails. There are currently limited data on the effectiveness of this technique. However, based on the Perez et al. and Chitgopekere et al. studies, nail tube splinting has similar recurrence rates compared to phenol procedures and conventional matrixectomies. In addition, nail tube splinting which does not cause injury to the nail matrix has decreased recovery time and better cosmetic results. Perez et al. recommended that nail tube splinting be considered as an initial treatment for Stage 3 ingrown toenails as since it is less traumatic compared to other matrixectomy techniques. Chitgopekere et al. has shown that nail tube splinting can be effectively used for recurrent ingrown toenails that have failed other treatment modalities.
Wedge Excision with Bipolar Diathermy

The wedge excision with bipolar diathermy is a technique that offers the advantage of being fast and simple. It is believed to be a technique that can be performed by inexperienced surgical clinicians in a primary care setting. Farrelly et al. found that the recurrence rates of this technique to be comparable to other techniques in literature. The procedure leads to minimal bleeding, minimal discomfort, low morbidity and does not require the use of a toxic chemical such as phenol, all while having a high level of patient satisfaction. The authors believe that this technique could be used in lieu of phenol as this technique has similar recurrence rate and requires minimal training to properly perform this procedure.10

Nail Fold Excision

The Vandenbos procedure was believed to be more painful and associated with longer recovery times as an open wound is being created; however, it was believed that the procedure is associated with low recurrence and better long term results.5 In both studies conducted by Haricharan et al. and Livingston et al. they found that the Vandenbos procedure had a similar recovery times compared to other surgical procedures, no recurrence and good cosmetic outcomes.5,11 It was also found that both patients and their parents were satisfied with the outcome of the procedure and would recommend it to others.5 Although, wedge excision and partial matrixectomy are more commonly used in practice, the Vandenbos procedure should be a technique to consider in a pediatric patient with ingrown toenails.

Chemical/Surgical Matrixectomy

The removal of the germinal matrix can be done either surgically or with chemical agents.4 Surgical matrixectomy involves the use of the scalp to remove the matrix whereas chemical matrixectomy involves the use of either phenol or sodium hydroxide. Matrixectomies are often done in addition to other surgical procedures such as nail avulsions or wedge excisions. It has been found that the removal of the germinal matrix can reduce the recurrence of ingrown toenails as the physician is removing the underlying risk factor.2,3 Yang et al. and Mitchell et al. both found that chemical matrixectomy had lower recurrence rates compared to the surgical matrixectomy.3,6 It is believed that surgeon experience is critical for surgical matrixectomy and failure to remove all of the germinal matrix will lead to recurrence or postoperative infection. Therefore, chemical matrixectomy is often used in the clinical setting as it has low recurrence and complication rates.3

CONCLUSION

Onychocryptosis is a common issue in the pediatric and adolescent population. Although it may seem like a small issue at first, if not properly treated it often results in severe pain that can negatively affect a child’s normal lifestyle.4 There is currently no set standard for the best method to manage ingrown toenails in children.1 However, there is a consensus that conservative treatments are generally used for Stage 1 and 2 of the disease and surgical treatments are recommended for patients with Stage 3 of the disease or patients who experience recurrence.2 Ultimately the best treatment method differs between patients as there are multiple factors to consider when choosing the appropriate treatment for a pediatric patient with ingrown toenails.
AUTHORS’ CONTRIBUTIONS

All three authors equally contributed to the design of the study and evaluated the available articles. All authors contributed equally in the writing of this literature review and reviewed the final version for submission.

STATEMENT OF COMPETING INTERESTS

The authors declare that they have no competing interest associated to this manuscript.

REFERENCES

Surgical vs. Functional Rehabilitation for the Treatment of Achilles Tendon Ruptures: A Literature Review

By: Thomas Milisits, BS, MPH; Mohammed Gheith, BS; Gregory Rose, BS; Kenan Redzematovic, BE

ABSTRACT
Acute Achilles tendon rupture introduces major structural and biomechanical defects in the lower extremity leading to insufficient transmission of force through the soleus, gastrocnemius and calcaneus. A number of surgical and non-surgical management options are available, with patient and case specific factors determining the best course of treatment. This systematic review will evaluate the efficacy of various treatment options based on post-treatment patient outcomes including pain, range of motion of ankle joint and return to activity. The PubMed search was conducted using the query “Achilles tendon rupture”, “functional rehabilitation”, “surgery”, using the “and”/”or” operators (i.e. ((achilles tendon rupture [MeSH Terms]) AND functional rehabilitation AND surgery)). The major findings of the review do not provide sufficient evidence to definitively conclude that one treatment plan is better than the other, but rather that patient lifestyle and daily life goals should be closely examined while determining the most effective intervention.

Introduction
Treatment of Achilles tendon rupture is a topic that invites much debate amongst medical practitioners. The recent literature has made headwind into moving the topic towards a more unequivocal agreement on surgery being the primary indication, as it is associated with significantly lower rates of re-rupture than conservative treatment with the numbers cited as 1.4% re-rupture rate with surgical treatment and 10-12% with conservative treatment.\(^1\)\(^-\)\(^2\)

In lieu of the current approach to Achilles tendon repair favoring an open surgical approach due to its lower re-rupture rates, there is new evidence that a conservative approach via novel casting techniques can provide for the proper healing and decreased re-rupture rates comparable to an open surgical approach. The aim of this paper is to explore the rationale and findings of the novel conservative approaches to Achilles tendon rupture treatment and compare it to the open surgical approach.

Study Design: Qualitative Systematic Review of Literature

Methods
Literature searches were performed using the PubMed database. The PubMed search was conducted using the query “Achilles tendon rupture”, “functional rehabilitation”, “surgery”, using the “and”/”or” operators (i.e. ((achilles tendon rupture [MeSH Terms]) AND functional rehabilitation AND surgery)), yielding 217 results. Authors used the inclusion criteria of articles printed within the last five years between 2015 and 2019, articles printed in English, human subjects, and articles with full text availability through the Icahn School of Medicine at Mount Sinai. Exclusion criteria included articles printed before 2015, printed in non-English languages, non-human subjects, and irrelevance to the treatment of Achilles tendon ruptures. Application of
inclusion and exclusion criteria yielded a total of 17 articles. The authors carefully reviewed the 17 articles and found that 7 of them pertained to the current study.

**Results**
The evidence shows conflicting evidence that the rate of re-rupture is slightly higher in the conservatively treated groups vs the surgically treated groups. However, the complication rates (i.e. infection) tend to be higher in the surgically treated groups. Post-operative functional rehabilitation seems to give the best option if surgery is absolutely indicated or desired by the surgeon and/or patient.

**Discussion/Conclusion**
While there is debate as to whether you should conservatively treat acute Achilles ruptures or primarily repair them surgically, there seems to be a growing interest in conservative care. Patient lifestyle and daily life goals should be closely examined while determining the best treatment for your patients. The results of conservative care, if the correct protocol is followed with proper patient compliance, seem promising and should be explored further.

**Keywords:** Achilles tendon, ruptures, surgical rehabilitation, functional rehabilitation, treatment

**Level of evidence:** 4
INTRODUCTION

Treatment of Achilles tendon rupture is a topic that invites much debate amongst medical practitioners. The recent literature has made headwind into moving the topic towards a more unequivocal agreement on surgery being the primary indication, as it is associated with significantly lower rates of re-rupture than conservative treatment with the numbers cited as 1.4% re-rupture rate with surgical treatment and 10-12% with conservative treatment.1-2

The current approach to the Achilles tendon rupture involves employing the Kuwada Classification system to determine the staging of the rupture, with stage 1 indicating a partial rupture, stage 2 a rupture less than 3 cm, stage 3 a rupture between 3 and 6 cm, and stage 4 a rupture greater than 6 cm.3 The anatomic site of rupture is typically 2-6 cm proximal to the tendon’s insertion at the calcaneus. This is thought to be due to either hypovascularity in the area or the twisting of the gastrocnemius and soleus complex becoming the Achilles tendon in this area.4-5 Reducing the torn tendon and reapproximating the ends with either a Bunnel, Kessler, or Krakow stitch is the recommended approach to open surgical reduction. Reinforcement grafts of the surgeon’s preference may be added based on the strength of the reattachment and quality of tendon itself.

In lieu of the current approach to Achilles tendon repair favoring an open surgical approach, there is new evidence favoring a conservative approach via novel casting techniques or functional rehabilitation, which can provide for the proper healing and decreased re-rupture rates comparable to an open surgical approach.9,11 The aim of this paper is to explore the rationale and the findings of the novel conservative approaches to Achilles tendon rupture treatment and compare them to the open surgical approaches.

METHODS

Literature searches were performed using the PubMed database. The PubMed search was conducted using the query ((("achilles tendon"[MeSH Terms] OR ("achilles"[All Fields] AND "tendon"[All Fields]) OR "achilles tendon"[All Fields]) AND "rupture"[MeSH Terms]) AND (functional[All Fields] AND ("rehabilitation"[Subheading] OR "rehabilitation"[All Fields] OR "rehabilitation"[MeSH Terms]))) AND ("surgery"[Subheading] OR "surgery"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR ("surgical"[All Fields] AND "procedures"[All Fields] AND "operative"[All Fields]) OR "operative surgical procedures"[All Fields] OR "surgery"[All Fields] OR "general surgery"[MeSH Terms] OR ("general"[All Fields] AND "surgery"[All Fields]) OR "general surgery"[All Fields])) yielding 180 results. Authors used the inclusion criteria of articles printed within the last five years between 2015 and 2019, articles printed in English, human subjects, and articles with full text availability through the Icahn School of Medicine at Mount Sinai. Exclusion criteria included articles printed before 2015, printed in non-English languages, non-human subjects, and irrelevance to the treatment of Achilles tendon ruptures. Application of inclusion and exclusion criteria yielded a total of 17 articles. The authors carefully reviewed the 17 articles and found that 7 of them pertained to the current study.
**RESULTS**

<table>
<thead>
<tr>
<th>Article</th>
<th>Treatment Modality</th>
<th>Study Aim</th>
<th>Conclusions</th>
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<tr>
<td>Lin et al. (2019) 6</td>
<td>Surgery: V-Y Tendon Plasty (n=20)</td>
<td>To evaluate and better understand clinical outcomes of V-Y tendon plasty for Achilles tendon reconstruction</td>
<td>V-Y tendon plasty should be used for chronic Achilles ruptures as it yields good functional results and low chance of complication rates</td>
</tr>
<tr>
<td>Ochen et al. (2019) 7</td>
<td>Surgery + Functional Rehabilitation: 29 studies included 15,862 patients, 9,375 treated operatively and 6,487 treated nonoperatively</td>
<td>To compare re-rupture rate, complication rate, and functional outcome after operative versus nonoperative treatment of acute Achilles tendon ruptures</td>
<td>Surgical correction reduced the risk of Achilles re-rupture (not statistically significant) but had higher risk of other complications such as infection. The treatment modality should be patient specific</td>
</tr>
<tr>
<td>Zhao et al. (2017) 8</td>
<td>Surgery: 6 articles included comparing functional rehabilitation post-operatively versus traditional cast immobilization post-operatively</td>
<td>To compare early functional rehabilitation and traditional immobilization following surgical Achilles tendon repair after an acute rupture</td>
<td>Early functional rehabilitation yielded better results than cast immobilization and is recommended postoperatively after acute Achilles ruptures</td>
</tr>
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</table>
Table 1: Articles used in this systematic review with the authors' treatment modality, study aim, and conclusions.

### Studies on Surgery Alone

In the study by Lin et al, the authors believed that a V-Y tendon plasty was an appropriate first line of treatment for acute Achilles tendon ruptures up to approximately 9cm. The twenty patients in this study were placed in a below-knee cast in plantar flexion up to 20 degrees for 4 weeks. After 4 weeks, the patients were allowed to be partial weight-bearing and physical therapy was initiated. The patients were able to return to daily activity with no restrictions at 10 to 12 weeks. At follow up, none of these patients had recurrent Achilles tendon rupture, or had serious complications such as sural nerve entrapment or DVT. However, one incident of superficial infection was reported but was resolved with debridement and antibiotic use. The authors reported that the patients in the study were able to perform the same activities as they were before, such as walking, running, and jumping.

Several meta-analyses in the last five years have looked at early functional rehabilitation post-operatively as opposed to traditional cast immobilization. Both of these studies found that early functional rehabilitation post-operatively does not increase the re-rupture rate of the Achilles tendon, increases patient satisfaction, and initiates an early healing response.

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**Wu et al. (2016)**  
Surgery + Functional Rehabilitation: 9 meta-analyses studies included  
To conduct a systematic review of overlapping meta-analyses on surgical versus non-surgical treatments for acute Achilles tendon ruptures  
There is inconsistency in the literature regarding ideal treatment option for acute Achilles ruptures, however functional rehabilitation may be superior if the treatment center offers this modality

**Valkering et al. (2016)**  
Functional Rehabilitation post-operatively  
To evaluate whether functional weight-bearing mobilization by means of increased metabolism could improve both early and long-term healing  
Functional weight-bearing mobilization initiates an early healing response in treatment of acute Achilles ruptures by upregulation of glutamate

**Zhang et al. (2015)**  
Surgical + Conservative treatment of acute Achilles rupture: 9 studies included in review  
To perform a systematic review of meta-analyses for surgical versus conservative treatment of acute Achilles tendon rupture, to assist decision makers in selection among conflicting meta-analyses, and to offer intervention recommendations by the best available evidence  
Conservative treatment with functional rehabilitation should be considered in treatment of acute Achilles tendon ruptures because it offers similar rerupture rates with significantly lower complications rates when compared to surgical treatment
A recent 2019 systematic review and meta-analysis looked at the surgical vs conservative management of acute Achilles tendon ruptures. These authors found that there were significantly more re-ruptures in the conservative group (3.9%) compared to the surgical group (2.3%) (risk difference 1.6%; risk ratio 0.43, 95% confidence interval 0.31 to 0.60; P<0.001). However, the operative group had significantly higher complication rates, mainly infection at the incision (2.8%) than the conservative group (4.9% vs 1.6%; risk difference 3.3%; risk ratio 2.76, 1.84 to 4.13; P<0.001). The authors found that there was no significant difference in re-rupture rate in the operative group that underwent functional rehabilitation with early range of motion compared to studies of surgery alone (risk ratio 0.60, 0.26 to 1.37; P=0.23).

Another group of recent systematic review of overlapping meta-analyses compared surgery to conservative management of acute ruptures. These authors found when functional rehabilitation was not used in the postoperative setting, conservative management was similar to surgical treatment of acute Achilles ruptures in terms of re-rupture, return of range of motion, infection and functional outcomes. If functional rehabilitation was not used in the conservative treatment group, the risk of re-rupture was significantly increased.

DISCUSSION

There is much debate in current literature pertaining to the conservative treatment of acute Achilles ruptures versus the traditional open surgical approach. We often see in the news and in the sports world, many top-level athletes having primary repair of an Achilles rupture. This may influence surgeons to perform primary repair more often. Perhaps the ideal way to determine the best course of treatment for patients with an Achilles rupture is to thoroughly examine their lifestyle and activity level in their daily lives.

Historically, functional rehabilitation has not been utilized as a treatment for acute Achilles ruptures. It is important to remember that conservative treatment does not equate to no treatment. Numerous protocols have been published as of late pertaining to functional rehabilitation for these types of midsubstance Achilles ruptures with excellent results. One example of a recent protocol was published in January of 2019 by Glazebrook and Rubinger. Their protocol is initiated within the first week following the rupture. A plaster cast is applied and the patient remains with plaster cast immobilization completely non-weight bearing for two weeks. At the two week follow-up visit, the patient is placed in an Achilles-specific walking boot with 40 degree heel lifts. The patient begins physiotherapy which includes a gradual increase in weight bearing for the next four weeks. During the period, weight bearing progresses from 25% to 100% at six weeks. Additional physiotherapy activities include active plantar and dorsiflexion range of motion exercises, inversion/eversion below neutral, icing, electrical stimulation and non-weight bearing physical activity such as swimming. Most importantly, the patient must use pain as their guideline and refrain from activities if the pain gets too severe. During weeks six to eight, physiotherapy is continued two times per week, heel lifts are gradually removed, weight bearing is permitted to the patient’s tolerance level, and gradual resistance exercises are added. Through week twelve, the patient must understand that the tendon is still very vulnerable and that any sudden load of the tendon (i.e. trip or fall) can cause a re-rupture. The patient can
slowly begin to wean off of the boot and begin exercises such as calf stretching and balance board activities. After week 16, the patient can increase dynamic weight-bearing exercises such as jogging and weight training. At six to nine months, the patient may return to normal non-contact sporting activities and by one-year post rupture, the patient may return to full sport activity if 100% of their strength has been regained.

The above protocol is just one example of a conservative functional rehabilitation modality for patients with an Achilles rupture. While surgery has always been the traditional treatment of choice, this type of conservative treatment may be ideal for the non-professional athlete who simply wants to return to their regular everyday activity.

If a patient surgical candidate, surgery should not be considered. However, if surgery is preferred by the patient and the surgeon, it may be best to ensure that the patient is treated in a facility that offers functional rehabilitation post-operatively as many studies have shown the best outcomes under these circumstances.

There are limitations to our review. We limited our review to the last five years and only included seven articles. However, the results of these articles are quite similar in that conservative treatment may be the best option for the ideal candidate and that if surgery is indicated, the best results have been proven with postoperative functional rehabilitation. Another limitation is that there are not many articles that discuss these different protocols for conservative functional rehabilitation. Future research should focus on casting techniques and how they rehabilitate their patients in these circumstances.

CONCLUSION

There is much debate whether conservative management or surgical treatment of acute Achilles ruptures provide the best patient outcomes. There appears to be a growing interest in conservative care via functional rehabilitation. Patient medical history, lifestyle and daily life goals should be heavily considered in deciding which treatment plan would be best for the individual patient. Surgical intervention may be the most viable option for younger patients or high performance athletes, while conservative treatment appears to be the best option for the weekend warrior. The results of conservative care seem promising if the appropriate protocol is followed with a high degree of patient compliance and should be explored further, particularly since the results in the literature thus far seem to have similar healing and re-rupture statistics and does not expose the patient to surgical complications such as infection.

AUTHORS’ CONTRIBUTIONS

Each author on this paper contributed equally in writing this manuscript. Each author drafted, read, and agreed on the completeness of this manuscript before submission.

STATEMENT OF COMPETING INTERESTS

The authors state that there were no competing interests in completing this manuscript.
REFERENCES


The Psychological Effects of Lower Extremity Amputations on Patients with Diabetes
By: Mujtaba Qureshi, BS; Lindsay Short, BA; Mike Chang, BA; Sami Ahmed, BA

ABSTRACT
Introduction
The decision to amputate a part of the lower extremity is difficult for both the clinician and the patient. Following an amputation, there are a multitude of factors that affect the patient’s health, including the psychological and social ramifications of the amputation on the patient’s well-being. Currently, there is a multidisciplinary approach for a patient undergoing an amputation involving the surgeon, nurses, prosthetist, physical therapist, occupational therapist, social worker, and a vocational counselor. The current treatment regimen does not indicate a psychiatric consultation or therapy for patients undergoing an amputation unless the patient experiences a severe psychiatric episode post-operatively. Our objective is to identify the psychological complications, risk factors, and the proper psychological care needed for diabetic patients.

Study Design: Qualitative Systematic Review of Literature

Methods
A search on the PubMed database was conducted using the search terms ‘psycho-social effects of foot amputation’, ‘psychological effects of foot amputation’, and ‘psychological effects of lower limb amputation’.

Results
A total of 88 articles were found. After applying the inclusion criteria, 8 articles remained, and all 8 articles were used.

Conclusion
Proper psychological evaluation and support for these patients should be an essential aspect that is included in the continuum of care and managed after the amputation procedure, to improve the patient’s mental and emotional well-being. Psychological support postoperatively will continue to empower the patient to return to the workforce and perform activities they enjoyed prior to the amputation. In addition, it will enable better quality of life to prevent further deterioration of health, especially of the contralateral limb.

Keywords: lower extremity, amputations, diabetes mellitus, psychological effects

Level of evidence: 4
INTRODUCTION

Epidemiology of Diabetes Mellitus and Amputations

Every year diabetes mellitus is becoming an increasingly widespread problem, with potentially dire consequences. The prevalence of diabetes rises with age and is increased in minority populations\(^1\). Across all race and ethnic groups, men have a 2-fold higher incidence of amputation when compared to women. In the United States, there are 185,000 amputations that occur every year, with vascular disease being the predominant cause for amputations in individuals 65 years old and above. Due to the systemic manifestations of diabetes, these patients also have a high prevalence of peripheral neuropathies, ulcers, infections, and amputations. Diabetic patients are 8-24 times more likely to undergo lower limb amputation than non-diabetics\(^2\). In 2005, 592,000 patients with diabetes were living with a lower extremity amputation, 60% of which were major amputations (proximal to the tarsometatarsal joint). The number of patients living with an amputation is expected to increase by 70% by 2020. When a patient has one limb amputated, the other limb is at risk for a future amputation as well\(^1\). The decision to amputate a part of the lower extremity is a difficult decision for the clinician and the patient. Amputations affect both the patient’s physical well-being and their mental health. These patients are susceptible to anxiety and depression with concerns regarding their sexuality, social acceptance, and body image\(^3\).

Diabetes Mellitus and Mental Illnesses

Diabetics may be diagnosed with mental illnesses prior to the appearance of their complications. In a prospective analysis study conducted by Bajwa et al, about 1/3 of the study population of diabetics had psychiatric symptoms, primarily being depression and anxiety\(^4\). Depression adds an increased concern to diabetic patients because it can lead to deterioration of glycemic control, thus increasing risk of late complications. This perpetuates a cycle of health complications and a decreased quality of life, leading to exacerbation of their depression\(^5\). Furthermore, after a surgical amputation of their limb, some patients have shown to experience posttraumatic stress disorder and psychiatric delirium\(^4\). Studies have also revealed that diabetics with amputations report more indicators for depression and weaker psychosocial adaptation than diabetics without amputation\(^6\).

The Multidisciplinary Approach of Treating Amputations

Amputation affects many different aspects of a patient’s life, thereby causing a need to address the myriad of emotions patients experience throughout their adjustment process. Yet despite this, the current treatment regimen only involves a psychiatric consultation if the patient experiences a severe psychiatric episode post-operatively. This indicates that deterioration of their mental health often goes untreated, for the average amputee. The purpose of this study is to review the various effects of amputation on a patient’s psychosocial well-being by isolating specific mental health scores and to highlight the role of psychiatric support in the postoperative management of patients.

METHODS

The search was conducted on the PubMed database. Three searches were performed, and all articles relating to human subjects and written in English were screened.
Articles were then screened by 'Best Match'. The first search using the term “psychosocial effects of foot amputation” yielded 15 unique articles. The second search using the term “psychological effects of foot amputation” yielded 29 unique articles. The third search using the term “psychological effects of lower limb amputation” yielded 44 unique articles. All three searches in total yielded 88 articles. Articles that were unrelated to the psychological or social effects of foot or leg amputations were excluded. Articles relating to pain management, physiological complications, medical care, prosthetic care, therapy models in rehabilitation, and with an insufficient sample size were further excluded. Additionally, articles that conducted assessments using subjective interview format without a documented and recognized questionnaire or assessment tool were excluded. After applying the exclusion criteria, the first search term yielded 2 articles, the second search term yielded 3 articles, and the third search term yielded 3 articles, for a total of 8 articles. All 8 articles were used.

Figure 1: Summary of article acquisition with inclusion and exclusion criteria
**RESULTS**

The review evaluates 8 published articles that studied the effect of limb salvage amputations and combat amputations. The symptoms and complications post-amputations, methods of reducing psychological symptoms, predictors and risk factors for psychological complications, and screening tools were analyzed in this literature review.

*Symptoms and Complications*

**STRESS READAPTATION.** In a case-control study by Fejfarova et al., 104 diabetic patients with symptomatic diabetic feet were compared to a control group of 48 diabetic patients without symptomatic diabetic feet. Symptomatic diabetic feet were defined at patients with diabetic foot ulcers and/or charcot neuroarthropathy. Notably, the results indicated that amputated patients had “significantly worse stress readaptation in contrast to other patients with the diabetic foot and diabetic controls” (P < 0.01) (Table 1).

**BODY IMAGE.** In a case-control study conducted by McDonald et al., an experimental group of 50 diabetics with an amputation were compared to a control group of 240 diabetics without an amputation to identify psychosocial impacts of amputation on diabetics. Through univariate analysis, it was noted that the amputees had statistically significant higher levels of depression, decreased physical quality of life and body image disturbance, when compared to the control group. In multivariate analysis, amputation did not add statistically significant differences between the two groups for depression and physical quality of life. Most significantly, presence of amputation remained statistically significant for body image disturbance (P = 0.005) (Table 1).

**QUALITY OF LIFE.** Willrich et al. examined two focus groups in order to assess health related quality of life, cognitive function, and depression in diabetic amputees. The authors randomly selected 20 patients with no complications as a control, 20 patients into focus group 1 who were diabetics with neuropathy or Charcot arthropathy without amputation, and 20 patients into focus group 2 who were diabetic amputees for at least 6 months. The results indicated that the diabetic amputees’ group displayed decreased perceived functional status and quality of life as compared to the control group (P < 0.00) (Table 1).
### Table 1: Summarized findings of psychological complications in Amputees from the Fejfavora et al., McDonald et al., and Wilrich et al. studies

<table>
<thead>
<tr>
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<th>Fejfavora et al.</th>
<th>McDonald et al.</th>
<th>Wilrich et al.</th>
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<tbody>
<tr>
<td><strong>Tools</strong></td>
<td>WHOQOL-BREF</td>
<td>BIDQ, WHOQOL-BREF</td>
<td>SF-36 Health Survey</td>
</tr>
<tr>
<td><strong>P value</strong></td>
<td>P &lt; 0.01</td>
<td>BIDQ: P &lt; 0.005</td>
<td>P &lt; 0.000</td>
</tr>
<tr>
<td><strong>Summarized Finding</strong></td>
<td>Worse Stress Readaptation in Amputees</td>
<td>Decreased Quality of Life, Greater Body Image Disturbance in Amputees</td>
<td>Decreased Functional Health and Quality of Life in Amputees</td>
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**Reduction in Psychological Symptoms**

Melcer et al. conducted two retrospective studies examining the psychological complications of patients with combat related amputations and combat limb salvage patients, based on whether they had an early amputation, late amputation, or had successful limb salvage procedure (no amputation).

The first study in 2013 screened for the presence of psychological diagnostic codes for visits up to 24 months after amputation in three groups. Group EA (early amputation) had 587 patients, group LA (late amputation) had 84 patients, and group LS (limb salvage) had 117 patients. Patients were then screened for presence of psychological diagnostic codes for visits up to 24 months after amputation. After adjusting for group differences, it was found that early amputees had lower rates of psychological diagnoses (especially posttraumatic stress disorder & substance abuse), and late amputees had higher rates for 5 out of the 6 measured psychological disorders compared with both early amputees and limb salvage patients.

The second retrospective study in 2017 was conducted using 518 patients with unilateral lower limb amputation (440 early amputation, 78 late amputations) and 107 limb salvage patients. In the early amputation group, the distribution of the amputation were 37% above the knee and 63% below the knee. For the late amputation group, the distributions of the amputation were 12% above the knee and 88% below the knee. For the late amputation group, the distributions of the amputation were 12% above the knee and 88% below the knee. There were no differences in four-year prevalence of at least one psychological disorder between all three groups, unlike the 2013 study, and ranged from 82% to 89%. Both the early amputation group and the limb salvage groups had significantly fewer psychological diagnoses than the late amputation group (p < 0.05), similar to the 2013 study. Although these retrospective studies by Melcer et al. evaluated combat-induced amputation injuries rather than diabetic amputations, they are included in this review to highlight the case of early amputation mitigating psychological effects of amputation.
A randomized clinical trial conducted by Imeni et al. evaluated the effect of spiritual care on body image in diabetic amputees. The study had a total of 54 diabetic participants (41 males and 13 females) between the ages of 40-72, who had their amputation 3 months prior to the study. The experimental group contained 28 participants, while the control group consisted of 26 participants. Prior to the spiritual intervention, there was no significant difference between the groups (p = 0.72). After the intervention, the experimental group showed a significant increase in body image score (p < 0.001) while the control group showed no significant increase in body image after the intervention (p = 0.08).

**Predictors, Risk factors, and Screening**

A longitudinal study was conducted by Pedras et al. in 2018 to create a predictive model of post-amputation anxiety and depression in diabetic patients. The study was conducted with 179 patients with diabetic foot ulcers proceeding to amputation with no prior history of psychiatric disorders. They were screened for the presence of anxiety and depression symptoms prior to amputation, and screened again one month after surgery. Two findings were reported. The first finding indicated that anxiety and depression pre-amputation were significant predictors of depression post-amputation. The second finding linked anxiety pre-amputation as a significant predictor for anxiety post-amputation.

In the Eurodiale study, Siersma et al. evaluated whether the HRQoL tool (Health-Related Quality of Life) can have prognostic significance in diabetics with foot ulcers. The longitudinal study followed 1088 patients who presented with new onset of DFUs up to a maximum of 1 year. Results indicated that a high HRQoL score did not have a correlation with ulcer healing, but a low HRQoL score correlated significantly with major amputation and death. The domains that were major predictors from EQ-5D for amputation were mobility, self-care, and usual activities (ie. work, study, housework, leisure activities). The domains that were major predictors for death were self-care, usual activities, and pain/discomfort.

**DISCUSSION**

**Symptoms and Complications Post-Amputation**

The current management of patients’ post-amputation does not include robust care for their emotional and mental well-being despite the reported increase in anxiety and depression in diabetic amputees. The articles highlighted in this review further expanded and discussed the known psychological complications that diabetic amputees face; namely a decrease in stress re-adaptation ability, an increased body image disturbance, and decreased functional status and quality of life.

Stress re-adaptation is the ability to overcome a difficult situation when afflicted by a stressful event. Fejfarova et al. emphasized in their study the importance of diabetic amputees to have a good adaptability to stress to overcome anxiety and depression. Their study reports that diabetic patients with foot symptoms had a higher stress load (31%), with a higher risk of somatization compared to controls (17%). Additionally, the study used the Social Re-adaptation Scale questionnaire to evaluate adaptation to stress; the results showed that diabetic amputated patients had worse stress re-adaptation than non-amputated diabetics. The authors equate these results with the
higher psychological pressures associated with amputees. A limitation in this study is that the data in the sub-group analysis was not directly reported in the article, only focusing between the general diabetic group and the non-diabetic control groups. Further analysis between the non-diabetic amputees and the diabetic amputees was conducted, the data did not show a marginal difference between the two groups. This may limit further studies in finding how significant the difference in stress adaptation is. Overall, their study highlights an important finding that must be considered in the treatment and management of the well-being of diabetics’ post-amputation. Specifically, the question arises whether a lower stress re-adaptation ability hints to a lower threshold of how much anxiety and depression is pathological for diabetic amputees. If so, it could indicate that anxiety and depression may be more detrimental to an amputee than the current thought, thereby requiring special considerations in their mental health management.

Body image disturbance is associated with a multitude of mental health outcomes, including depression and eating disorders. McDonald et al. evaluated various physiological disturbances in diabetic amputees, including higher levels of depression as well as decreased physical quality. The study measured psychological distress using the Hospital Anxiety and Depression Scale (HADS), quality of life using WHOQOL-BREF, and body image using the Body Image Disturbance Questionnaire (BIDQ). Most notably, body image disturbances were increased despite controlling for demographic and medical variables, indicating that it is influenced by amputation itself. Recognizing a patient’s body image disturbance could be advantageous in sourcing their psychological disorders. Failing to manage these psychological symptoms may delay healing, and cause recurrence in physiological symptoms as indicated by Monami et al.\textsuperscript{15}

Health Related Quality of Life is an important measure in influencing policy and aids in understanding the success of treatment and level of care required for patients. Wilrich et al. provides evidence that diabetic amputees had decreased perceived functional status and quality of life. Health related quality of life was tested using the SF-36 Health Survey. This brings to question what efforts in medicine and healthcare are needed to allow an amputee to function at the level and quality of life that the patient wants or needs. As stated by the authors, there is little literature about whether a decreased HRQOL score is indicative of a lower mental and cognitive state. This study found no correlation between decreased quality of life and depression, but further studies may be necessary. This study had notable limitations, specifically the low sample size, lack of knowledge concerning length and control of diabetes, and lack of distinction and control for amputation or duration of ulceration.

**Reduction in Psychological Symptoms**

Patients who undergo amputations are at risk for psychological disorders. This holds true not just for diabetics but for combat amputees and trauma amputees as well. Melcer et al. examined the difference in incidence of psychological complications of combat amputees based on when they had their amputation.\textsuperscript{8-9} It was found that early amputation was associated with fewer adverse psychological health outcomes when compared to patients with late amputations. The aim of the 2017 Melcer et al. study was to re-visit the findings of the
2013 study via a four-year outcome study. New results indicated that the incidence of psychological disorders were not lower for the early amputation groups in comparison to the late amputation groups after the first year post-amputation, but there was a decreased incidence in the number of average psychological disorders in the early amputation group. Currently, amputation is commonly considered a last resort, but as evidenced in this study, clinicians may need to re-evaluate when an amputation is the right decision while considering the patient’s mental well-being and quality of life. There appears to be a window of opportunity when an amputation is the better option for the patient and should be considered earlier in the treatment timeline.

One of the study limitation was that it was conducted for combat amputees rather than diabetics, therefore similar studies need to be conducted for diabetic amputees. Additionally, another limitation in the study includes the study design since case studies were evaluated retrospectively instead of a randomized control study.

Post-operative management for amputees may include therapy and counseling. A study by Imeni et al. found that there may be an element of spiritual therapy that can reduce psychological complications\textsuperscript{10}. The tool used to assess body image was Breakey’s Amputee Body Image Scale (ABIS). The participants answered the questionnaire prior to spiritual intervention and then at the end of 4 weeks, when the intervention concluded. The experimental group conducted three sessions of meditation, whereas the control group underwent three sessions of diabetic foot ulcer prevention. The experimental group participants were then asked to perform meditation exercises for one month. The study found a positive impact on body image by implementing a 4-week meditation regimen in the lives of diabetic amputees.

When considering the complete care and treatment of a diabetic patient, it may be important to screen whether spiritual therapy can be used as a tool to manage post-amputation psychological complications. Whether or not patients are receptive to forms of spiritual therapy, including meditation, can be a factor in forming the decision on how, when, and if an amputation is best for a patient. One limitation for this study may be the cultural background, as this study was not conducted with U.S. participants and thus may not have a similar effect on U.S. diabetic amputees.

Predictors, Risk Factors, and Screening

Pedras et al. screened for the presence of anxiety and depression symptoms prior to amputation in diabetics and one month after their amputation\textsuperscript{11}. The findings indicated that anxiety and depression pre-amputation were significant predictors of post-amputation depression, and anxiety pre-amputation itself was a predictor for anxiety post-amputation. Screening for patients at risk of anxiety, depression, and sequelae of other psychological conditions may help predict and mitigate these conditions by putting accurate services in place for at-risk patients. In the Eurodiale study by Siersma et al., the HRQoL screening tool EQ-5D was found to be another way of determining whether a patient was at risk for major amputation\textsuperscript{12}. Screening patients with new onset of diabetic foot ulcers and patients indicated for amputation may be two additional points that would need to be a part of the treatment plan in treating diabetic patients not just as foot ulcer-carriers but as patients as a whole. Limitations in these two studies include the need for repetition with larger sample sizes and comparison between other screening tools to evaluate the efficacy of the tools and predictors used.
CONCLUSION

As the incidence of diabetes continues to increase, there is an increased need to manage various aspects of medical care for diabetic patients. Studies have shown that diabetics with foot complications of neuropathy, ulcers, and Charcot arthropathy have higher incidences of psychological complications. The studies highlighted in this review have revealed that diabetic amputees have even greater incidences of psychological and social complications when compared to diabetic patients without amputations, including increased anxiety, depression, stress adaptation, body image disturbances, and functional health perception and quality of life.

Including risk-prediction screening tools such as EQ-5D, alternative forms of mental and spiritual care therapies, and re-evaluating the current amputation timeline, could provide overall well being of the diabetic patient. Proper psychological evaluation and professional support for these patients should be an essential aspect that is included in the continuum of care and managed after the amputation procedure in order to improve the patient’s mental and emotional well-being. Psychological support post-amputation will continue to empower the patient to return to the workforce and perform activities they enjoyed prior to the amputation. It may also enable better quality of life to prevent further deterioration of health, especially of the contralateral limb.

AUTHORS’ CONTRIBUTIONS

All authors contributed equally to this literature review. All authors were involved in forming the topic and agreed upon the final manuscript.

STATEMENT OF COMPETING INTERESTS

All authors declare that there are no competing interests.

REFERENCES


Understanding the Pathogenesis and Progression of Chronic Achilles Tendinopathies

By: Wolfgang Kienzle, BS; Elias Logothetis, BS; William Stallings, BS; Megan Mitchell, BS; Ahmad Saad, BS; Kadir Saravanan BS

ABSTRACT

Introduction
Achilles tendinopathy is a common musculoskeletal complaint that presents in podiatric medical offices across the world. This is a condition that causes swelling, stiffness and pain to the Achilles tendon. It is usually a chronic condition that presents in middle aged and elderly populations specifically in patients who have a tight posterior heel cord. Many comorbidities can be associated with an increased risk of developing insertional type Achilles tendinopathies. Some of these include patients with obesity, high cholesterol, high blood pressure, certain arthritides or in patients taking certain antibiotics. Additionally, mid portion tendinopathies can be seen in more active individuals from overuse injuries. The purpose of this review is to understand the progression of Achilles tendinopathies in contrast to more acute Achilles tendonitis injuries, to provide better clinical care for those at risk of developing this disease.

Study Design: Systematic Review of Literature

Methods
A search was performed on PubMed using search terms/criteria: Tendinopathy and Achilles. The results were sorted by best matched which yielded 2178 articles. A search modifier was added to make the new search phrase Tendinopathy and Achilles and Pathogenesis while still sorting results by best match. This narrowed the results to 762 prior to applying inclusion and exclusion criteria. The inclusion criteria included articles that were written as literature reviews as well as the articles must be free to access through NYCPM Library website. Exclusion criteria included articles published after 2009. After applying this criterion to the search, 15 articles were selected for review.

Conclusion
Achilles tendon pathology is a very common problem presenting in podiatric offices on a regular basis that affects a wide variety of people. Achilles tendon pathology is usually a clinical diagnosis of which a patient presents with debilitating pain near the heel that is aggravated during activity. Treatment consists of conservative modalities such as activity modification, NSAIDs, and injection therapy, and surgical intervention such as debridement of the diseased tendon, flexor hallucis tendon transfer, and gastrocnemius recessions. Although the clinical presentation and treatment of the pathology is mostly understood, the pathogenesis of the condition remains relatively unclear. It is clear that chronic Achilles pathologies tend to be due to overuse injuries and that individual characteristics such as obesity, increased age, male sex, and the use of fluoroquinolones and corticosteroids have been shown to lead to increased incidence of Achilles tendon pathology. With the increasing incidence of Achilles tendon pathology in the population and the critical role it plays in ambulation it is important that we gain a better understanding of the etiology and pathogenesis of its pathology.

Key Words: Achilles, Tendon, Heel Pain, Pathogenesis, Etiology

Level of evidence: 4
INTRODUCTION

Achilles tendinopathy is a chronic degenerative process which often affects young active adults and 6-18% of recreational athletes. Unfortunately, conservative care is often ineffective resulting in approximately 50% of Achilles Tendinopathy patients proceeding with surgical intervention. While the presentation and treatment of Achilles Tendinopathy is widely understood, the pathogenesis of the condition is less clear. The Achilles tendon insertional complex is composed of three parts: the entheseal fibrocartilage at the tendon bone insertion, the sesamoid fibrocartilage in the deep surface of the tendon, and the periosteal fibrocartilage which covers the opposing surface of the calcaneal wall. One hypothesis is that the various degenerative processes in each of these three parts play a role in the progression toward Achilles tendinopathy. Another hypothesis is that Achilles tendinopathy originated from compression of the Achilles tendon-bone insertion against the calcaneus. Another hypothesis is that over time, degenerative changes within the Achilles will build up, and this is thought to be the hallmark of Achilles tendinopathy. These changes are marked by loss of parallel collagen structure, loss of fiber integrity, fatty infiltration, and capillary proliferation. Recent evidence has also shown the possible anatomical involvement of the course of the plantaris tendon in the development of Achilles tendinopathy.

In order to properly treat Achilles Tendinopathy, a physician must understand the various biomechanical causes and presentations. There are many potential etiologies of this condition, with no concrete primary causative agent identified. The primary purpose of the study is to do a systematic review of studies surrounding the pathogenesis of Achilles Tendinopathy in order to narrow down the various etiologies and understand the common presentations. This will enable physicians to more accurately diagnose and effectively treat this condition.

METHODS

An in-depth, systematic literature review was performed utilizing the NYCPM PubMed linked database. The process of article selection is displayed in Figure 1. The initial search included MESH terms “Tendinopathy” and “Achilles” which yielded 2178 potential articles. This was narrowed down by adding the MESH term “Pathogenesis” which led to 762 potential articles. The review material was narrowed even further by incorporating inclusion and exclusion criteria. The inclusion criteria included papers in a literature review format, as well as those that were free to access through the NYCPM library search engine. The exclusion criteria included only articles written after 2009 to ensure the research represents the most up to date information. 15 articles met all criteria. These articles were then reviewed, and the material was synthesized.
RESULTS

Diagnosis

Achilles tendinopathies are caused by overuse injuries that put strain on the tendon. The symptoms for Achilles tendinopathy include swelling and tenderness around the Achilles tendon area. Patients will have complaints of intense foot pain near the heel that is most intense in the morning and is exacerbated by activity. Patients will report stiffness that is aggravated by prolonged rest and will also often report that their symptoms limit their activity at work and participation in sports. Individuals with Achilles tendinopathy can experience struggles finding comfortable and supportive shoe wear. Specific tendon area problems can be evaluated through physical examination as well as various imaging modalities such as X-rays, MRI, or ultrasound.

Upon physical examination, a positive Thompson test (when squeezing the triceps...
surae muscle does not elicit plantar flexion of the same foot) is indicative of tendon rupture which can be confirmed by musculoskeletal ultrasound or MRI, but will not be present in patients suffering from an associated Achilles tendinopathy. 18

Causes

In a 2012 study titled “Physiopathology of Intra-tendinous Calcific Deposition”, the authors discuss what’s commonly referred to in literature as Non-insertional Achilles Tendinopathy. The Non-insertional, or calcific, tendinopathy is located in the body of the tendon which, while it is seen in the Achilles, it is more commonly seen in the rotator cuff tendons. The authors are quick to point out that there are many terms in literature that may have been used in the past to describe calcific tendinopathies but note that it is paramount that local degeneration precedes the calcification process of the tendon regardless of the position of the deposit. The calcification process is similar in both the Achilles and patellar tendons, where endochondral ossification processes take place. The mechanism is more related to a slow ossification process of the fibrocartilage at the enthesis of these tendons compared to the microtear and repair pattern of the calcification that is seen in the tendon body. 17 In these more insertional forms, the fibrocartilage insertion is worn down and allows blood vessels to invade from the underlying bone marrow past the fibrocartilage cells. Bone is then deposited, and calcific spurs are formed where the original insertion of the tendon was. This process creates greater surface area for the tendon insertion that may be due to increased mechanical loads. Even with the proliferation of blood vessels there is no indication that this is an inflammatory process. While the authors are not able to pinpoint direct pathogenesis, they’re able to conclude from their review that calcium carbonate apatite crystals are the only concrete component that is found in the calcification of tendons that undergo this degenerative process however, this has only been extensively studied in the rotator cuff tendons. 17

Eggar and Berkowitz’s noted in their 2017 review that the Achilles tendon is one of the most important multifunctional tendons in the human body. The etiology of injury to the Achilles tendon is described as consisting of both intrinsic and extrinsic factors. Intrinsic factors are mainly biomechanical in nature as well as systemic conditions, while extrinsic factors include excessive overload and training areas. 8 Some examples of intrinsic and extrinsic factors include increased age, male sex, obesity, diabetes and the use of fluoroquinolones and corticosteroids. Each one of these factors has a positive correlation with the Achilles tendon pathology. 7

While many articles discussed possible factors that “may” lead to degeneration of tendons, one focused specifically on the degenerative process caused by a class of broad-spectrum antibiotics that treat a variety of infections. Over the last few years it has become increasingly clear that Fluoroquinolones (FQs) usage can be associated with tendinopathy and tendon ruptures especially in elderly patient populations. Achilles tendinopathy or rupture is one of the most serious adverse effects of FQs use and was first reported in 1984 in a 56-year-old treated with norfloxacin for a urinary tract infection. Since then, about 100 cases of FQ related tendinopathy or tendon rupture have been published, with the mean age of affected patients being 64, with a male to female
ratio of 2:1, and only 27% of patients having bilateral issues. In addition Ciprofloxacin have been correlated with 90% of FQ related tendon disorders. Histological findings in patients include necrosis, degenerative lesions, neovascularization, fissures, and interstitial edema.

Nourissat et al. describes obesity as a major public health issue and associated the condition with increased risk of Achilles tendon pathology. Obesity is an increasing problem in the United States and across the world. The authors state that more than 30% of the population are obese in approximately one-third of the national states and that the most affected age group is between 55-65 years old. Obesity is defined as having a BMI > 30. Obesity is associated with many concomitant pathologies such as cardiovascular diseases, diabetes, and osteoarthritis. The authors state that obesity induces considerable mechanical stress on the lower limb and go on to state that there is a definite association obesity and the onset of Achilles tendinopathy.

Another important factor to note is that males are more susceptible to Achilles Tendon injuries compared to females. The incidence of injury increases in males aged 30 to 49, making up approximately 75% of Achilles tendon ruptures. A rupture is more likely to happen when there is acute trauma to a tendon that has shown signs of degradation over time. This trauma usually occurs while one is engaging in strenuous physical activity or playing sports. Tendon injuries throughout the body are classified as either extra-synovial or intra-synovial, with Achilles tendon injuries in the former grouping.

Even though the true etiology of Achilles tendon injuries remains widely unknown, two major theories that have been proposed by Eggar and Berkowitz. The degenerative theory proposes that chronic degeneration of the tendon can lead to rupture without excessive loads being applied. This is based on a study that saw degenerative changes in all 74 patients with acute Achilles tendon ruptures. The mechanical theory states that different movements and forces exerted on the tendon can lead to failure. The authors described the etiology of chronic Achilles tendinopathy as being a result of repetitive overuse injuries, metabolic or vascular imbalances, and disorganized collagen structure. The authors described the etiology of Insertional Achilles Tendinopathy being due to the degeneration of the Achilles tendon fibers at the insertion on the calcaneus and being associated with older age, steroid use, obesity, diabetes, inflammatory arthropathies, Haglund’s deformity, and calcification at the insertion site.

A study by Li and Hua designates that the histological changes in insertional Achilles tendinopathy are specified into linear steps that occur during the degenerative process. The authors highlight three unique stages: reactive tendinopathy, tendon disrepair, and degeneration. Histological studies “revealed an increased number of tenocytes and concentration of glycosaminoglycans in the ground substance, disorganization and fragmentation of the collagen, and neovascularization which is in stark contrast to the normal histology of the tendon.” It’s important to note that these stages do not include an inflammatory phase. There were no macrophages, neutrophils or other inflammatory cells present in patients that suffer from Achilles tendinopathy.
Treatment

Conservative treatment options for Achilles tendinopathies are non-invasive methods that include activity modification, heel lift and orthotics, massage, varying temperatures of compresses, strength training methods (specifically eccentric training), extracorporeal shock wave therapy, sclerosing therapy, topical glyceryl trinitrate, aprotinin injections, low level laser therapy, platelet rich plasma injections, NSAIDs and corticosteroids. With the exception of oral medications or injections, a large majority of these highlights just how influential extrinsic factors are on the degenerative process of a tendon due to forces that are biomechanics in nature.

The history of Corticosteroid injections, oral corticosteroids and NSAIDs and other anti-inflammatory treatments don’t have the greatest effect because the root of the issue of Achilles tendinosis is not inflammation, but instead degeneration of the tendon itself. Eccentric training following a 12-week program which strengthens and lengthens the tendon simultaneously showed the most hopeful results with 90% reduction in pain with mid-portion Achilles tendinosis and 30% reduction in pain with insertional Achilles tendinosis. There are two schools of thought on how to treat Achilles tendinosis via the process of neovascularization. One is to stimulate healing factors and neovascularization with the use of platelet rich plasma injections which inserts the patient’s own plasma with healing factors back into the tendon. This works similarly to extracorporeal shock wave therapy which causes micro trauma to stimulate neovascularization promoting healing and providing pain relief. The other school of thought is to prevent neovascularization and the accompanying sensory nerve growth to reduce patient pain levels. This can be done by three sclerosing techniques, prolotherapy, electrocoagulation, and polidocanol. Aprotinin injections are used to slow the degeneration of the tendon by inhibiting matrix metalloproteinases. Therapy enhances ATP production, enhances cell function, reduces inflammation, increases protein and collagen synthesis, and promotes angiogenesis.

The impact of conservative (non-surgical) treatment options for Achilles tendinopathy should not be overlooked. To figure out if exercise had a positive impact on treatment on Achilles tendinopathy, randomized controlled trials with heavy-load exercise treatment was performed in a study that focused solely on the conservative management on Achilles tendinopathies. The exercise group had a 60% success rate compared to only a 24% success rate in the control group regarding improvement in the Achilles condition. It was also noted that eccentric exercises that lengthen muscles were found to be more helpful compared to concentric exercises that contract the muscles. Significant improvement was seen in patients after 12 weeks of regular exercise for those in the exercise group. If the exercises are not performed properly or patients over work themselves, it can worsen the Achilles condition. If a patient has a biomechanical abnormality in their Achilles tendon, orthotics may be helpful in improving their condition, which further exemplifies the importance of extrinsic factors affecting gait as well as everyday life that leads to intra-tendon damage. Additionally, randomized controlled trials were performed, and it was found that 89% of the patients described a reduction in pain or soreness after 4 weeks of wearing the custom designed foot orthoses.
Braces and splints were not found to be effective in alleviating the Achilles tendon condition. Through randomized controlled trials, physiotherapy was also found to be an effective treatment option. Also, there was not enough concrete clinical evidence to support the continued effectiveness of injection therapies (ex. Corticosteroid injections) or extracorporeal shock wave therapy. There were two randomized control trial studies conducted that analyzed the effectiveness of placing glyceryl trinitrate patches on the Achilles mid portion in order to alleviate pain and discomfort. There was a clinically significant decrease in pain with the glyceryl trinitrate group when compared to the control group.

Operative treatments may always be explored after conservative treatment options have failed and it depends on severity and the patient’s goal. These treatments may include the removal of damaged tissues and lesions, small longitudinal incisions on the affected tendon, as well as stripping the paratenon and the “scraping” method. The scrapping method is less invasive than traditional surgical approaches and utilizes the findings of ultrasound and doppler diagnostics. While the classic method of repair required a full 4 to 12-month rehabilitation period, this new method describes full loading of the tendon within just 2 to 6 weeks post-treatment. Open tendon debridement and repair with or without augmentation is only used in the most severe cases. While percutaneous longitudinal tenotomy, minimally invasive tendon stripping, and endoscopic procedures are less invasive, and patients can sooner return to sport or weight bearing activities. We as healthcare providers need to recognize the varying levels of success of surgical procedures. The exact etiology of what started the degeneration of the tendon and the predisposing factors are extremely important pieces of information when deciding the treatment options for an individual patient.

Recovery

One of the biggest issues is in the way Achilles tendinopathy heals. Remodeling of the tendon injuries will lead to fibrous bundling of Type III collagen fibers which have smaller and less elastic fibrils compared to Type I collagen fibers in healthy tendons. The new more disorganized tendon is more likely to rupture in the future, especially if the factors that led to the original injury are not removed or negated. Pain, swelling, and impaired performance in physical activities are expected in a patient with a diseased Achilles tendon.

The recovery steps for Achilles tendinopathy include the short inflammatory phase, the proliferative phase, and the remodeling phase. Recent studies have shown that having a regulated and controlled amount of inflammation after a tendon repair led to better healing and clinical results. Inflammation is mainly stimulated by macrophages of two classes M1 and M2. This careful balance between both cell types is imperative to successful tendon repair. An overproduction of either macrophage types could be detrimental to overall healing. Some of the most pertinent information regarding Achilles tendon injury and repair has been studied in animal models. While there are numerous parallels that can be made between the animal models and humans, there is still a need for further studies to strengthen the connection between them. Currently they are not considered perfect, but they may be reliable for use in further study.
**DISCUSSION**

There are many differentials to keep in mind when assessing Achilles tendinopathy including, but not limited to, calcaneal apophysitis, Haglund deformity, plantar fasciitis, flexor hallucis longus synovitis, calcaneal bursitis, posterior tibial tendon dysfunction and much more. These are common problems presenting in podiatric offices on a regular basis. These conditions are aggravated during activity with patients presenting with pain to the Achilles tendon and its related anatomical structure. There are a large number of additional intrinsic and extrinsic factors that can cause and/or exacerbate Achilles tendinopathy. In order to prevent conditions like Achilles tendinopathy from occurring, it is important to maintain a healthy weight and not over-strain the leg/foot area with exercises and excessive activity. Since fluoroquinolone use plays a part in the degeneration of tissue in the Achilles, it is important to educate the patient on the increased risk of Achilles tendinopathy and rupture. It is also crucial to note it in the patient’s medical record when prescribing these medications. Physicians who prescribe FQs should be mindful of the possible Achilles Tendon injury especially when treating elderly patients, and any patients that do show signs and symptoms should discontinue FQs immediately. This should be followed by proper treatment of the Achilles’ tendon including immobilization which should be swiftly initiated to reduce the chances of a complete Achilles’ tendon tear.

When diagnosing Achilles tendinopathy, thorough history and physical, clinical examination with use of imaging modalities are needed. It is important to consider conservative treatment options first before opting for surgery. There are still gaps in knowledge regarding treatment options for Achilles tendinopathy and how different patient populations may respond to treatments differently. Filling in these gaps could help provide more effective care for patients across the world with Achilles tendinopathy. Treatment consists of conservative modalities such as activity modification, NSAIDs, and injection therapy, and surgical intervention such as gastrocnemius recessions. Although the clinical presentation and treatment of the pathology is mostly understood, the pathogenesis of the condition remains relatively unclear. With the increasing incidence of Achilles tendon pathology in the population and the critical role it plays in ambulation, it is important that we gain a better understanding of the etiology and pathogenesis of its pathology.

An important opportunity for future study would be to determine if the more insertional forms of these disorders contain the same inorganic substances as those that predispose to the bodies of their respective tendons. Without more studies it cannot be concluded that these processes are the same as those studied more recently in the rotator cuffs as compared to the Achilles and patellar tendon. The most important reason that these pathologies may be different is that in the calcific tendinopathies, where the deposits are in the body of the tendons, there seems to be inflammatory cells in the resorptive and post calcific phases. More research is needed in order to better understand the distinct differences between these processes.

**AUTHORS’ CONTRIBUTIONS**

Each author on this paper contributed equally in writing this manuscript. Each author drafted, read, and agreed on the completeness of this manuscript before submission.
STATEMENTS OF COMPETING INTEREST

The authors state that there were no competing interests in completing this manuscript.

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“Unusual Causes Of Plantar Foot Pain”: A Systematic Literature Review

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ABSTRACT

Introduction

Plantar foot pain is one of the most common complaints in the podiatry clinic with a majority being diagnosed and treated as plantar fasciitis. However, if a patient’s symptoms continue despite prolonged therapy, then more rare causes of plantar foot pain should be considered. Our review aims to explore unusual causes of plantar foot pain to expand a physician's differential diagnosis when initial treatments fail. This review includes a wide range of etiologies of plantar foot pain including hematologic, neurologic, and malignant causes.

Study design: Qualitative Systematic Review of Literature

Methods

The authors performed one independent English language PubMed search. The search included MeSH terms “Plantar Pain” AND “Unusual”, which produced 38 articles. The inclusion criteria included “English”, publications after the year 2010, and human subjects. Human subjects were determined by thorough evaluation of all articles, as not every article using human subjects was tagged as “human subjects”. The exclusion criteria was based on a thorough review of the literature to exclude articles describing injuries as a mechanism of plantar pain, clear clinical presentations pointing to the etiology, and studies that did not contribute to the differential diagnosis of plantar pain.

Results

The search generated a total of nine articles that presented unusual cases of plantar pain in 11 patients. Three of the articles presented cases of plantar vein thrombosis, a condition that has only been reported a handful of times. Three articles described an osseous or soft tissue mass including a calcaneal osteochondroma, heel lipoma, and multiple plexiform schwannomas. Two articles described a form of neuropathy; one case described a case of bilateral Baxter’s neuropathy and the other described edema of the abductor digiti quinti muscle secondary to subacute denervation in two patients. One article presented malignant lung cancer that manifested in the foot.

Discussion

Though it is important to first rule out common etiologies of plantar pain such as plantar fasciitis, it is always important to consider other etiologies of plantar pain when conventional treatment fails. Plantar foot pain that doesn't resolve may be attributed to rare etiologies or systemic conditions. This review included plantar foot pain secondary to a plantar vein thrombosis, bilateral Baxter’s neuropathy, edema of the abductor digiti quinti, calcaneal osteochondroma, heel lipoma, multiple plexiform schwannoma, and metastasis from lung cancer. Widening the physician’s differential diagnoses to these etiologies may help prevent inaccurate diagnoses and improper treatment of a patient’s medical condition.
Keywords: Unusual causes, Plantar pain, Plantar vein thrombosis, Neuropathy, Calcaneal osteochondroma, Lipoma, Schwannomas, Lung cancer metastasis, Lower extremity, Plantar fasciitis

Level of evidence: 4
INTRODUCTION

Plantar foot pain is a common complaint of many patients presenting to the physician. In a study by Garrow, foot pain was experienced by 24% of women and 20% of men on a daily basis. The differential diagnosis of plantar foot pain is extensive due to many etiologies that may manifest as the non-specific finding of pain, including: biomechanical, vascular, neurological, traumatic, and degenerative. Though a majority of plantar pain can be attributed to trauma or plantar fasciitis, it is important to consider the various other etiologies with plantar pain as a presenting symptom.\(^1\) Furthermore, the plantar surface of the foot was the most common area of pain. Additionally, the study showed that those with pain also suffered from functional limitations causing them to avoid walking long distances.\(^2\)

The location of a patient’s pain can help the physician narrow down the cause to a few etiologies. For example, the majority of plantar heel pain can be associated with plantar fasciitis. This high incidence of plantar fasciitis as the cause of plantar heel pain may influence the physician to treat an unknown condition using a presumptive and inaccurate diagnosis, with the physician failing to explore other potential etiologies. This misdiagnosis of plantar foot pain can result in the patient receiving inappropriate treatment, and therefore, unresolved pain. The physician should be aware of these alternate diagnoses at the initial presentation in order to minimize the chances of improper treatment of the patient.\(^1\)

A detailed report of the patient’s history and physical examination findings may be sufficient in properly diagnosing a patient for their foot pain if it is due to a common etiology, such as plantar fasciitis. However, if the initial presentation is inconsistent with the presumed diagnosis, then more rare and unusual etiologies should be considered. Reported cases of unusual etiologies of plantar pain include benign masses, musculotendinous edema, rare neurovascular processes, and systemic conditions manifesting in the foot.\(^3\) This study describes these reported cases to demonstrate the importance of considering a wider set of differential diagnoses to decrease the incidence of improper treatment resulting from an inappropriate diagnosis.

METHODS

The authors utilized PubMed to perform a search for cases of unusual causes of plantar heel pain. A search with the key words “plantar pain” AND “unusual” yielded a total of 38 articles. Inclusion criteria required the articles to be written in English, published after the year 2010, and the subjects were human. Not every study was labelled “human subjects” as per filter by PubMed, therefore the PubMed filter for subjects was not utilized. Instead, a thorough review of the literature was performed to only include studies with human subjects. Exclusion criteria involved thorough review of the literature to rule out articles that did not pertain to “unusual causes of plantar pain”. This included injuries resulting in plantar pain, clear clinical presentations and history relating the etiology to the plantar pain (such as an ulcer and infection causing plantar pain), articles describing a clinical presentation that did not involve plantar pain, or any other studies that did not contribute to the differential diagnosis of plantar pain. After inclusion and exclusion criteria were applied, a total of nine articles were chosen, describing 11 patients presenting with unusual causes of plantar pain.
RESULTS

There were nine articles chosen that fulfilled the inclusion and exclusion criteria. Of the nine articles, a total of 11 patients were described with unusual causes of plantar pain. Four of the patients described were male and five were female. The average patient age was 65 years old, with the oldest patient being 82 years old and the youngest being 19 years old.

The patients described in the study presented with a wide variety of etiologies to their plantar foot pain. Three articles described four patients with a hematological cause of their plantar pain, all of which were plantar vein thrombosis. Two articles described three patients with a neurological cause of plantar pain; one of these articles described a case of bilateral Baxter’s neuropathy, and the other article described two patients with edema of the abductor digiti minimi muscle secondary to subacute denervation. Three patients were described to have hard or soft tissue masses that resulted in plantar pain. One patient was described with a systemic condition, metastatic lung cancer, that manifested as plantar pain.

Plantar vein thrombosis was the most common unusual cause of plantar pain among the articles reviewed, with a total of four patients out of the 11. All cases of plantar vein thrombosis was diagnosed with the aid of some form of ultrasound (duplex or color sonography), while two patients had an additional magnetic resonance imaging (MRI) to aid in the diagnosis. Vansevenant and Vanhoenacker reported
treat their patient with a change in footwear (bump on the inner sole corresponding with the site of chief complaint) and prescribing non-steroidal anti-inflammatory drugs; their patient had no residual thrombus two months later on ultrasound. Karam et al reported two patients that were both treated with anti-vitamin K therapy for three months. Both patients underwent ultrasound three months later, with one patient having partial resolution and the other having complete resolution of the plantar vein thrombosis. Karam et al further reported that one patient did not have any findings consistent with cancer at the moment but adenocarcinomatous lesions were discovered one year later on colonoscopy. Furthermore, hypercoagulation investigation of the other patient showed slightly positive anticardiolipin antibodies and a heterozygous mutation of the MTHFR gene and G20210A mutation of the prothrombin gene, both of which are known to increase the risk of deep venous thrombosis.

Barros et al. reported a patient that did not initially present with plantar pain. Their patient presented with a chief complaint of varicose veins but admitted to plantar pain during the physical examination. The patient was referred for a duplex ultrasound and a plantar vein thrombosis was found. Further single-photon emission computed tomography (SPECT) imaging with inhaled radioaerosol (99mTc-phytate) and intravenous radiopharmaceutical (99mTc-MAA) were performed and results were consistent with a pulmonary thromboembolism. This patient is the first known case of a pulmonary embolism secondary to a plantar vein thrombosis. The patient was hospitalized for anticoagulation therapy (intravenous heparin for five days with long term oral warfarin for six months) and discharged seven days later. Duplex ultrasound at six-month follow-up revealed partial resolution of the plantar vein thrombosis. Barros et al. reported that the patient’s hematological workup revealed no hypercoagulable state. The patient’s history was significant for hormonal therapy for dysmenorrhea.

A total of two articles reported three patients presenting with a neurological etiology resulting in plantar foot pain, both of which involved the lateral plantar nerve and the abductor digiti minimi muscle. Jaring et al. reported a patient presenting with chronic foot pain due to bilateral Baxter’s neuropathy secondary to planter fasciitis. Nerve conduction studies revealed delayed motor responses in the tibial nerves bilaterally while ultrasound and MRI findings were consistent with plantar fasciitis and fatty atrophy of the abductor digiti minimi muscles. These findings are consistent with the authors’ diagnosis. The patient underwent lifestyle modifications including orthotics and physiotherapy to reduce the nerve impingement. After nine months, the patient reported significantly less symptoms in both feet and did not require invasive surgery. Chimutengwende-Goron et al. reported two patients with edema of the abductor digiti minimi muscle secondary to subacute denervation, with one patient having concurrent plantar fasciitis while the other did not. Diagnosis was confirmed as MRI studies revealed fatty atrophy of the muscle bellies, indicating subacute denervation and resulting in the painful edema. One patient was treated with rest, footwear modification, anti-inflammatory drugs, stretching, and physical therapy, while the other was treated with physiotherapy, insoles, and a night splint. Both patients’ symptoms were completely
resolved at follow-up 18 months after the initial presentation.

Three articles reported three patients presenting with a mass as the etiology of their plantar foot pain. Koh et al. reported a patient presenting with chronic plantar heel pain due to an osseous body protruding from the posterolateral plantar aspect of the calcaneus. MRI findings were consistent with an osteochondroma of the posterolateral plantar calcaneus. The patient was treated with surgical resection of the osteochondroma to reduce plantar heel pain. They reported to be pain free 12 months following the surgery. Taweel et al reported a patient presenting with sharp, focal heel pain secondary to a lipoma of the plantar foot that was pressing the abductor hallucis muscle. Diagnosis was confirmed using an MRI and studies revealed a fusiform, encapsulated lipoma, resulting in a potential mass effect on the abductor hallucis muscle. The patient was treated with surgical excision of the mass and reported no pain three months following the surgery. Li et al. reported a patient presenting with complaints of plantar foot pain that had been ongoing for approximately 18 months secondary to three soft tissue nodules. MRI diagnosis and further pathology studies on the masses following excision surgery confirmed them to be multiple plexiform schwannomas in the plantar foot, resulting in a potential mass effect on both the flexor digitorum brevis muscle and superficial fascia of the third metatarsophalangeal joint. The patient was treated with surgical excision of the masses. They reported hypoesthesia in the distant third and fourth toes following the operation; however, they were followed for three years with no recurrence of pain.

One article reported a patient presenting with a systemic etiology resulting in plantar foot pain. Dai et al. reported a patient presenting with plantar heel pain without any inducing factors. X-ray findings showed a spur and osteolytic lesion of the calcaneus; further CT and MRI studies showed the lesion to contain bone destruction. The osteolytic lesion was then considered to be a malignant tumor. Additionally, a chest CT revealed a lesion in the lung. Biopsy of the calcaneal lesion showed a poorly differentiated adenocarcinoma. The patient received curettage of the lesion and replacement with bone cement in addition to the biopsy. The patient succumbed to the cancer six months later.

**DISCUSSION**

Plantar foot pain is one of the most common complaints for which a patient seeks medical attention. Of all the possible causes of plantar foot pain, plantar fasciitis is the most common. However, it is important for a clinician to have several differential diagnoses in mind. When normal treatment measures for plantar foot pain are ineffective, it is important to include the possibility of other disorders manifesting as foot pain. In this review, we presented cases of plantar foot pain which were initially treated as plantar fasciitis but were misdiagnosed after further testing was ordered. Plantar heel pain is a symptom which can be caused by manifestations of hematologic, neuropathic, growths, and systemic disease.

Plantar vein thrombosis is a very rare hematologic cause of plantar pain; often presenting acutely, with non-specific symptoms. Clinical symptoms can include local swelling as well as increased pain with walking and certain shoe gear. In similar
cases presented, two geriatric males presented with plantar pain similar to plantar fasciitis.\textsuperscript{4,5} After failed initial treatment, an ultrasound was performed and evidence of non-compressible plantar veins were shown. Though an extremely rare case, it is important to utilize further imaging modalities such as ultrasound and MRI to get a clearer clinical picture. Diagnosis is very difficult due to the insidious onset of symptoms and with patients presenting often with no history of previous thrombosis. The similarity in clinical symptoms to plantar fasciitis also makes the diagnosis of plantar vein thrombosis difficult. This diagnosis is usually an incidental finding after an ultrasound or MRI is ordered in the area of thrombosis.\textsuperscript{4} Treatment of the condition is also controversial, ranging from NSAIDs to antithrombotic therapy. Symptoms generally resolve within 2-3 months of treatment, with little evidence of recurrent thrombosis.\textsuperscript{5} Furthermore, it is imperative to treat plantar vein thrombosis due to possible complications. In a case study by Barros et al., the patient diagnosed with plantar venous thrombosis also had a pulmonary embolism, which is a medical emergency.\textsuperscript{6}

One of the most common manifestations of plantar pain can be due to a neurological etiology. The plantar pain is often secondary to compression of a nerve or denervation of a muscle resulting in pain. This type of pain elicits symptoms very similar to chronic plantar pain. The main differentiating factor in neurological heel pain is the presence of sensory abnormalities or radiation of the pain.\textsuperscript{13} In a report by Jaring et al., the author presents a case of a 56-year-old female with bilateral plantar pain. MRI showed evidence of bilateral signal abnormality with fatty atrophy of the muscle, which led to a diagnosis of bilateral baxter’s nerve neuropathy.\textsuperscript{8} Chimutengwende-Gordon et al. presented a similar case with prolonged histories of plantar pain. MRI evaluation was used to show fatty infiltration of the abductor hallucis muscle consistent with bone and soft tissue edema indicating denervation.\textsuperscript{9} Both of the authors presented cases where patients experienced pain unresolved with analgesia and consistent with “first step pain” associated with plantar fasciitis. Because the symptoms mimicked those of plantar fasciitis, the patients were treated accordingly. In both cases, symptoms did not resolve which prompted the clinicians to order MRIs. In both these separate cases the patients had symptoms identical to plantar fasciitis, it was only the persistence of symptoms along with changes in sensation which helped the physicians decide to order further testing. Once neurological pain is suspected, more specific diagnostic tests can be administered such as clinical maneuvers, electrodiagnosis, and further imaging.\textsuperscript{14}

Abnormal growth of masses in the foot such as lipomas or schwannomas often only have pain as the major symptom. In many cases, the presiding symptoms are insidious and are often persistent regardless of conventional treatment modalities. It usually requires the use of further imaging, such as MRI to identify and properly diagnose the patient. The presence of the mass is often an incidental finding.\textsuperscript{11} In a study by Koh et al., a patient had symptoms identical to plantar fasciitis, along with gastrocnemius equinus. After multiple failed gastrocnemius releases and a plantar fascial release, clinicians ordered an MRI in which evidence of a calcaneal osteochondroma was seen.\textsuperscript{10} Similar cases were presented by Taweel et al. and Li et al., in which presenting symptoms were very similar with pain on palpation to the calcaneus, along with tenderness in the arch. In the case of Taweel
et al, an MRI discovered a heel lipoma. Though rare, heel lipomas can cause pain similar to plantar fasciitis, which initially led the physicians to an incorrect diagnosis of plantar fasciitis.\textsuperscript{12, 15} In the case presentation by Li et al, the patient had persistent heel pain for 18 months along with numbness. MRI revealed multiple plexiform schwannomas, which were treated with surgical recession \textsuperscript{15}. In these cases, the presence of a mass was an incidental finding after failed conservative treatment and further imaging was ordered.

In certain instances, systemic diseases can manifest as heel pain. Oftentimes, the plantar pain is the first symptom of the disease in an otherwise insidious presentation. Certain tumors can metastasize to bone in the feet causing symptoms similar to common heel pain. An example is a case of a 58-year-old female that presented with left heel pain without any inducing factors. Initial X-rays showed an osteolytic lesion in the calcaneus and a follow-up CT scan of the calcaneus showed evidence of bone destruction consistent with a malignant tumor. A subsequent chest CT scan confirmed small cell cancer of the lung.\textsuperscript{16} Bone metastasis might be the first sign of lung cancer, though spread to the calcaneus is rare.\textsuperscript{7} In this case the first symptoms were calcaneal pain, without any prior symptoms. The patient had pain worse in the morning, which can commonly be misdiagnosed as chronic plantar heel pain. Though a rare case of metastasis, the cancer was initially misdiagnosed due to no radiographs upon initial visit and the patient ultimately succumbed to the cancer. It is imperative that routine heel pain is thoroughly examined and that radiographs are taken to rule out any other underlying conditions.\textsuperscript{16}

Though very rare, unusual etiologies for plantar heel pain which may present with common symptoms can be identified with proper examination, ultrasound, and advanced imaging modalities. In many of the cases presented, either ultrasound or advanced imaging was needed after months of repeated failed conservative treatment to properly diagnose each patient. When treatment of the initial diagnosis fails, it is vital to reassess one's diagnosis with further testing. Though most cases of plantar foot pain may be routine, a thorough initial exam can often save the patients months of pain under the wrong assessment and treatment.

\textbf{AUTHORS’ CONTRIBUTIONS}

All authors contributed equally to the production of this article. All conceived the topic, performed initial literature reviews, and authored the introduction, results, discussion, and conclusion. All authors drafted, read, reviewed, and agreed upon the final manuscript.

\textbf{STATEMENT OF COMPETING INTERESTS}

The authors declare that they have no competing interests.

\textbf{REFERENCES}


Complications Associated with Transmetatarsal Amputations in Diabetic Patients

By: Margaret Schadegg, BS; Joseph Pagnotta, BS; Jonathan Kelly, BS

ABSTRACT

Introduction
Diabetes in the United States is currently the cause of a majority of non-traumatic amputations due to complications associated with it such as peripheral neuropathy and peripheral vascular disease. In recent years, transmetatarsal amputation (TMA) has become one of the preferred methods of surgical intervention for the treatment of forefoot ulcers, gangrene, and infections caused by complications of diabetes. However, the procedure is often accompanied by various complications. Minimal research has been done on the effectiveness of treatments in order to prevent such post-operative complications. The objective of this paper is to conduct a systematic review of literature in order to highlight the complications in diabetic patients after a TMA procedure.

Study Design: Systematic Review of Literature

Methods
Three Pubmed searches were conducted. The first systematic search was performed using the query: (("metatarsal bones/surgery"[Mesh Terms] OR "metatarsus/surgery"[Mesh Terms]) AND "diabetic foot/surgery"[Mesh Terms]) AND "amputation/methods"[Mesh Terms]). The second was performed using the query: ("amputation/adverse effects"[Mesh Terms] OR "amputation/rehabilitation"[Mesh Terms]) AND "foot/surgery"[Mesh Terms] AND ("metatarsal bones"[MeSH Terms] OR ("metatarsal"[All Fields] AND "bones"[All Fields]) OR "metatarsal bones"[All Fields]). The third was performed using the query: ("amputation"[MeSH Terms] OR "amputation"[All Fields]) AND ("diabetes mellitus"[MeSH Terms] OR ("diabetes"[All Fields] AND "mellitus"[All Fields]) OR "diabetes mellitus"[All Fields])) AND "metatarsus/surgery"[Mesh Terms]). After inclusion and exclusion criteria were applied 5 articles were selected to be fully assessed for this review. One ScienceDirect database was conducted: "Diabetes" "Amputation" and "Transmetatarsal amputation". After inclusion and exclusion criteria were applied one article was selected for review.

Results
Among the 6 articles reviewed, it was universally found that there was a high percentage of complications associated with the TMA procedure in diabetic patients. The studies we reviewed compared percentage of patients with post-operative complications such as wound dehiscence, skin breakdown, reamputation, and both mortality and healing rates.

Conclusion
The literature reviewed yielded a wide range of statistical outcomes for diabetic patients post operatively. It was found that patients with a low ABI, weak distal pedal pulses, peripheral neuropathy and/or peripheral vascular disease were more likely to have complications including skin breakdown or reamputation.

Keywords: Transmetatarsal amputation, Diabetes, Reamputation, Skin breakdown

Level of evidence: 4
INTRODUCTION

Diabetes mellitus, which commonly leads to diabetc foot disease, is a condition which affects millions of people in the United States, with an increasingly large prevalence among individuals over the age of 60.\textsuperscript{1,2} The most common predisposing factors associated with diabetic foot disease include peripheral vascular disease (PVD) and diabetic peripheral neuropathy.\textsuperscript{3} Peripheral neuropathy allows for increased chance of injury to the patient’s extremities due to lack of recognition of injury and PVD prevents the adequate blood supply needed to properly heal the injury.\textsuperscript{1} These symptoms then lead to high rates of ulceration, infection, and gangrene with resultant poor wound healing.\textsuperscript{1,3}

Diabetic neuropathy is one of the most common long-term complications of diabetes, with distal bilateral symmetrical neuropathy being the most common form of neuropathy seen among patients.\textsuperscript{1} There are two subtypes of diabetic neuropathy with some patients experiencing loss of sensation and others experiencing increased pain. Patients affected by painful diabetic neuropathy may experience burning and tingling sensations along with hyperalgesia. Those patients experiencing loss of painful sensation may also experience loss of vibration sense and impaired deep tendon reflexes. Diabetic neuropathy that results in sensation loss can result in skin breakdown with minimal trauma and is considered an initiating factor in the development of foot ulceration. About 45% to 60% of all ulcerations are mainly caused by the presence of neuropathy in diabetic patients.

Peripheral vascular disease, which includes disease of both major vessels and lower extremity arteries and arterioles, is predominantly caused by atherosclerosis—and is further influenced by the diagnosis of diabetes mellitus in the patient.\textsuperscript{4} With an estimated 200-360 million affected people world-wide, patients diagnosed with both PVD and diabetes have been subjected to a guideline-directed medical therapy that has ultimately proven subpar with regards to clinical outcomes—though this dual diagnosis is both highly prevalent and regarded as having high morbidity rates.\textsuperscript{4} The compounding of intermittent claudication, or absence of peripheral pulses in the lower extremity, together with peripheral neuropathy commonly diagnosed in diabetic patients, further exacerbates a linear progression towards multiple foot pathologies including ulceration and gangrene. These pathologies can then ultimately lead to varying types of amputations. Diabetes serves as the cause of up to 50% of all non-traumatic amputations in the U.S.. However, primary amputations often lead to a secondary amputation within several years, often resulting in poor health outcomes for the patient.\textsuperscript{5}

15-25% of diabetic patients have a lifetime risk of developing ulcers which often do not heal on their own, requiring physicians to intervene with a variety of treatment modalities.\textsuperscript{1} For patients with forefoot pathologies, a common and increasingly used treatment is transmetatarsal amputation in which the distal foot is removed from the metatarsal shafts at the union of the metatarsal heads and proximal phalangeal joints.\textsuperscript{6} The justification for TMAs as opposed to above or below the knee amputations is that they are capable of adequately removing forefoot ulcers, infection, gangrene, and/or ischemia while preserving enough of the extremity to allow
for ambulation with proper recovery, leading to overall lower mortality rates.\(^7\) While these procedures have proven effective, there is also a high incidence of reamputation, subsequent skin breakdown, and decreased wound healing.\(^6,8\) The purpose of this paper is to review the possible complications associated with transmetatarsal amputations in diabetic patients.

**METHODS**

Three English language literature searches were conducted using the PubMed database. The first systematic search was performed using the query: ("metatarsal bones/surgery"[Mesh Terms] OR "metatarsus/surgery"[Mesh Terms]) AND "diabetic foot/surgery"[Mesh Terms]) AND "amputation/methods"[Mesh Terms]). This search yielded 21 items. The second systematic search was performed using the query: ("amputation/adverse effects"[Mesh Terms] OR "amputation/rehabilitation"[Mesh Terms]) AND "foot/surgery"[Mesh Terms] AND ("metatarsal bones"[MeSH Terms] OR ("metatarsal"[All Fields] AND "bones"[All Fields]) OR "metatarsal bones"[All Fields])). The second search yielded 10 items. The third systematic search was performed using the query: ("amputation"[MeSH Terms] OR "amputation"[All Fields]) AND ("diabetes mellitus"[MeSH Terms] OR ("diabetes"[All Fields] AND "mellitus"[All Fields]) OR "diabetes mellitus"[All Fields]) OR "metatarsus/surgery"[Mesh Terms]). The third search yielded 32 items.

The inclusion criteria for the three queries included articles published from 01/01/1995 to 12/31/2019, full-text articles, articles written in English, and articles using Human subjects. Following implementation of inclusion criteria, the first query yielded 17 items, the second query yielded 6 items, and the third query yielded 11 items. Exclusion criteria included articles written before 1995, non-English articles, non-full text articles, articles pertaining to non-Human species, studies not reporting outcomes or complications following TMA, as well as articles omitting information related to diabetes mellitus or diabetic foot. Following implementation of the exclusion criteria, 3 articles were selected from the first query, 1 article was selected from the second query, and 1 article was selected from the third query for further review. In total, five articles from PubMed were selected for this literary analysis.

Using the ScienceDirect database, the keyword search: "Diabetes" "Amputation" and "Transmetatarsal amputation" returned 711 items. The ScienceDirect database query was further refined by “Article Type” (Review articles & Research articles), and “Publication title” (The Foot & Diabetes Research and Clinical Practice) and “Years” (2002-2019), yielding 30 results. The inclusion criteria for the ScienceDirect query included articles published from 2002-2019, publication titles relating to the foot, or diabetes research and clinical practice, review articles, and research articles. The exclusion criteria for the ScienceDirect query included articles written before 2002, conference abstracts, book chapters, as well as publication titles that omitted information related to diabetes mellitus or diabetic foot. Application of the keyword search, inclusion
criteria, and exclusion criteria yielded 30 results, of which one was selected that best met our research criterion for this literary analysis. The results of our PubMed and ScienceDirect queries are displayed in Figure 1.

![Diagram showing article acquisition using PubMed database]

**Figure 1**: Summary of article acquisition using PubMed database

![Diagram showing article acquisition using ScienceDirect database]

**Figure 2**: Summary of article acquisition using ScienceDirect database
RESULTS

Among the 6 articles reviewed, it was conclusively discovered that there is a high percentage of complications associated with the transmetatarsal amputation (TMA) procedure in diabetic patients.\textsuperscript{2,6-10} The percentage of patients with wound dehiscence, skin breakdown, reamputation, and both mortality and healing rates were reviewed post operatively. The summary of reamputation rates and additional complications from cases in each publication can be found below in Table 1.

Hosche et al. conducted a study on the outcomes of transmetatarsal amputations (TMA) in patients with Diabetes Mellitus (DM). Results were extracted using data from 35 patients, all of whom were diagnosed with DM, as well as received a TMA over a 6-month period. The mean age of this patient population is 54.7 years, and the follow up period took place over 8.3 years. Of the 35 patients in this population, 22 patients (63\%) required revision or higher amputation of the affected limb, 6 patients (24\%) developed an ulceration of the stump, and 8 patients (33.3\%) developed ulceration of the contralateral limb (4 of these went on to amputation).

Pollard et al. conducted a retrospective review of 91 patients who underwent transmetatarsal amputation and later developed postoperative complications associated with TMA. The mean age of this patient population is 64.3 years, the average follow-up for the procedure was 2.1 years, and it was concluded that of the 91 patients diagnosed with Diabetes Mellitus, 87.1\% exhibited post-operative complications following TMA. The \(x^2\) tests of association were used in order to determine whether a diagnosis of Diabetes Mellitus would serve as predictive or associative with wound healing. Of the 91 patients, 2 patients (2.2\%) died within 30 days post-operation, 31 patients (34.1\%) required higher amputations, 52 patients (57.1\%) had wound dehiscence, 21 patients (23.1\%) required surgical revision of the stump, 31 patients (34.1\%) had chronic stump breakdown, and 19 patients (20.9\%) developed postoperative wound infection.

Mueller et al. conducted a study on patients with transmetatarsal amputation (TMA) with the purpose of determining the incidence of higher amputation and subsequent skin breakdown, as it relates to rehabilitation, treatment, and outcomes for 107 patients, 77\% of which had diabetes mellitus (DM). The mean age of this patient population is 62.4 years, and the follow up period took place from April 1989 to September 1993 (4.5 years). The results of the study indicated that patients with TMA and DM were at a higher risk for skin breakdown or higher amputation, especially within the first 3 months. Mueller et al. found that of the patients with TMA (107), 17 patients (16\%) died, 29 patients (27\%) developed subsequent skin breakdown, 30 patients (28\%) needed subsequent higher amputation on the same extremity (25 below-knee amputation and 5 above-knee amputations). Mueller concludes his results by indicating that individuals with DM experience lower-extremity amputation 15x greater than individuals who do not have DM.

Thorud et al. conducted a systematic review and meta-analysis on the reoperation and reamputation after transmetatarsal amputation (TMA). Within this review, 24 studies were analyzed. Reported reoperation rate ranged from 8.3-63\% and reamputation
rate ranged from 0-55.8%. After applying a random effects model, the reoperation rate was found to be 24.43% and the reamputation rate was 28.37%.

McKittrick et al. conducted a study on the progress and surgical management of lesions, gangrene, and infections following transmetatarsal amputation (TMA) in patients with diabetes mellitus (DM). McKittrick highlights the significance of using chemotherapeutic agents and antibiotics in order to control infection, and ultimately reduce the mortality rate of this population, thus introducing a new approach to control invasive infection in these patients. Of the 202 patients included in this study, 35 patients (17%) healing did not occur following TMA, 32 patients (16%) had one or more local symptoms resulting in limited use of their lower extremity which was deemed unsatisfactory, and 135 patients (67%) had satisfactory results. They showed that the functional results of TMA in DM patients ultimately revealed mixed results in regard to successful surgical outcomes.

Joyce et al. conducted a 12-year retrospective case review of surgical outcomes in DM patients following TMA. The results of this case review examined 27 right and 27 left TMA surgical outcomes, 7 of which were bilateral. The mean age of the patient demographic was 60 years-old, and TMA procedures were performed on 40 males (85%) and 7 females (15%). Joyce et al. concluded that full wound healing was achieved in 42 patients (78%), six patients (11%) died before the TMA healed, and six patients (11%) required further surgical debridement and major limb amputation. With regards to mortality rates, the highest incidence was found to be between years 1 and 3 post-TMA. From 3 years post-TMA, the mortality incidence reduced, and the lowest mortality rates were determined for patients who survived 5 years post-TMA. Though TMA has favorable healing and mortality rates, Joyce et al. suggests post-operation TMA outcomes and mortality are both highly variable.
<table>
<thead>
<tr>
<th>Study</th>
<th>Number of Cases</th>
<th>Mean Patient Age</th>
<th>Incidence of Reamputation</th>
<th>Complications Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hosch et al.</td>
<td>35</td>
<td>54.7 years</td>
<td>63%</td>
<td>Ulceration of stump, ulceration of contralateral limb</td>
</tr>
<tr>
<td>Pollard et al.</td>
<td>91</td>
<td>64.3 years</td>
<td>30.7%</td>
<td>Wound dehiscence, surgical revision needed, chronic stump breakdown, post-operative wound infection</td>
</tr>
<tr>
<td>Mueller et al.</td>
<td>107</td>
<td>62.4 years</td>
<td>28%</td>
<td>Skin breakdown of stump</td>
</tr>
<tr>
<td>Thorud et al.</td>
<td>1146</td>
<td>NR</td>
<td>33.1%</td>
<td>NR</td>
</tr>
<tr>
<td>McKittrick et al.</td>
<td>215</td>
<td>61.5 years</td>
<td>15.3%</td>
<td>Local symptoms resulting in limited use of the affected limb</td>
</tr>
<tr>
<td>Joyce et al.</td>
<td>54</td>
<td>60 years</td>
<td>11%</td>
<td>Revision debridement needed, post-operative wound infection, sepsis</td>
</tr>
</tbody>
</table>

Table 1: Reported Complications of TMAs in the Six Publications Analyzed

**DISCUSSION**

Serving as 50% of all cause of amputations unrelated to trauma of the lower extremity, Diabetes Mellitus (DM) is the major cause of diabetic foot disease amongst patients ages 60 and older.\(^5\) With the growth of data and significant research pertaining to the prevalence of secondary amputation occurring amongst DM patients who initially received the transmetatarsal amputation (within several years after primary amputation), it has become clear that a correlation exists with regards to poor health outcomes.\(^5\)

According to Mueller et al., patients with risk factors associated with poor wound healing such as peripheral neuropathy or peripheral vascular disease were much more likely to develop subsequent skin breakdown and reamputation. Additionally, they reported 42% of patients had subsequent re-ulceration and Thorud et al. found that up to 22% of patients had incidence of re-ulceration after a TMA procedure. McKittrick et al. noted a smaller percentage of patients that developed either skin necrosis at the incision site or gangrene formation leading to further...
amputation. Patients with co-morbidities such as end stage renal disease were found to have a much lower rate of stump healing at 44%. Pollard et al. found that among 101 TMA patients, 88 developed either stump breakdown, reamputation, or infection.

Although the poor health outcomes have been observed amongst patients who receive secondary amputation to the transmetatarsal area, a higher level amputation is often regarded as more predictable when it comes to healing\(^2\). Though the healing process becomes more manageable, it comes at a cost, resulting in a necessary increase of energy expenditure for walking, and could ultimately compromise the cardiac and pulmonary function present in DM patients.\(^2\) More proximal amputations also compromise patient mobility and increases the metabolic demand of the patient—as a result, it is recommended that more distal amputations would improve the patient’s overall morbidity.\(^2\) TMAs preserve the patients' ability to ambulate without the need of a prosthetic device. In addition, following a more proximal level amputation, incidence of contralateral amputation and mortality increase dramatically.\(^2\)

**CONCLUSION**

The objective of this systematic literature review was to discuss the complications associated with transmetatarsal amputations in diabetic patients and compare results of patients with varying risk factors. Of the six articles reviewed, despite the statistical discrepancies, it was unanimously stated that there was high incidence of complications in patients including wound dehiscence, surgical revision, ulceration of the stump, infection, sepsis, limited use of limb, and secondary amputation in patients. Pollard et al. concludes that patients with additional dangerous risk factors such as end stage renal disease and absent pedal pulses had a higher chance of impaired wound healing and subsequent reamputation. After careful review of the literature, we have determined that although transmetatarsal amputations in diabetic patients have lower mortality rates than the more proximal amputations, and a better quality of life post operatively; there is a conclusive high incidence of complications that result from the procedure.

**AUTHORS’ CONTRIBUTIONS**

All authors contributed equally in the formation of this review and extraction of data. All authors agreed upon the final submission.

**STATEMENT OF COMPETING INTEREST**

All authors state they have no competing interest.

**REFERENCES**


Limb Salvage in Patients with Foot and Ankle Tumors: A Literature Review

By: Nayab Khan, BA; Nichole Mgboji, BS; Navid Rostamian, BS

ABSTRACT

Introduction
Soft tissue sarcomas of the foot and ankle occur infrequently and can be difficult to diagnose. All too frequent once they are diagnosed, treatment plans result in amputation of the foot or leg. This is the result of the difficulty in finding the balance between clean excision margins that lessen tumor recurrence and distant metastasis while not compromising the functionality of the foot and ankle. Our review aims to evaluate the current surgical treatment protocols for management of foot and ankle sarcomas and whether the limb salvage sparing options resulted in local tumor recurrence.

Study Design: Quantitative Systematic Review of Literature

Methods
We conducted our search using PubMed search term “limb salvage foot tumor [MeSH]”. This search yielded 82 articles. The inclusion criteria included articles dating five years back or less, articles in English, articles focusing on the subjects of cancer and those written as systematic review, articles with the focus of adults 19+ years in methods, and articles with the keyword “limb salvage” in title or abstract. Exclusion criteria removed articles prior to 2014, not relating specifically to the foot, not in English and full text not available. This yielded a result of 4 articles that fit the criteria for sparing options in local tumor recurrence.

Discussion
Three out of the four articles reported on limb salvage procedures which did not result in local tumor recurrence. The treatment plans in those articles included wide excision margins without losing functionality of the foot. The fourth article regarding osteosarcoma yielded a 20% local tumor recurrence. This recurrence may be due to a high-grade metastatic sarcoma afflicting the patient requiring additional aggressive treatment.

Conclusion
Foot and ankle sarcomas are challenging to diagnose and treat. Depending on the type of sarcoma, its histopathology and initial presenting stage and grade, the treatment option must be a patient specific. In the case of soft tissue sarcomas, wider excision margins may lessen the chance of local tumor recurrence. In the case of osteosarcoma, it may be beneficial to adjust the treatment plan toward more aggressive surgical intervention. This case study was limited by the wide spectrum of sarcomas studied with smaller patient populations evaluated. In further studies, focusing on one sarcoma and its outcomes may be beneficial to creating a sarcoma specific protocol to determine whether limb salvage or amputation results in lower incidence of local recurrence and disease-free survival.

Key words: Soft tissue sarcoma; limb salvage; foot; ankle

Level of evidence: 4
INTRODUCTION

Most tumors of the foot and ankle are benign. Soft tissue sarcomas (STS) account for approximately 1% of total cases and of that 1%, 10% of STS occur in the lower extremities. Due to the limited number of STS, they are frequently confused with benign tumors, often resulting in misdiagnosis and inappropriate treatment. Inappropriate treatment includes inadequate preoperative workup. These often include unclear imaging and biopsy resulting in “unplanned excisions,” which may leave residual tumor cells and distant spread. Therefore, the risk of local tumor recurrence is high, and the patient may require more surgery. These “re-excisions” have been associated with overall worse outcomes.

In many cases, the goal during STS surgery is to find clear sufficient wide tissue margins while keeping functionality of the foot. Upon confirming diagnosis with biopsy and staging the patient, treatment is dependent on the balance of two choice. The first choice is using marginal excisions which may have a high risk of local tumor recurrence. The second choice is using wider margins which may compromise the foot and ankle. If wide enough margins are not possible then the foot need amputation to prevent local and distant recurrence.

The aim of this literature review is to evaluate current surgical treatment for sarcomas. The focus will be on understanding the differences in outcomes of limb salvage surgery is chosen versus amputation is chosen. More specifically, evaluating how advances in medical imaging, histological assessment, updated reconstruction techniques leading towards increased foot functionality and quality of life may point towards an increase in the use of limb salvage surgery.

METHODS

A literature review was conducted on PubMed using the search term “limb salvage foot tumor [MeSH]”. This search yielded 82 articles. The inclusion criteria included articles dating five years back or less, articles in English, articles focusing on the subjects of cancer and those written as systematic review, articles with the focus of adults 19+ years in methods, and articles with the keyword “limb salvage” in title or abstract. Exclusion criteria removed articles prior to 2014, not relating specifically to the foot, not in English and full text not available. This yielded a result of 4 articles.
**DISCUSSION**

Historically, treatment of lower extremity STS was with amputation. Currently, from advances in medical imaging, histological assessment, and improved techniques in resection and reconstructive options, there is an increased rate of preserving the affected limb. Generally, larger tumor size was associated with higher rate of proximal amputation and local recurrence. In the analysis of acral and soft tissue sarcomas, the most common foot sarcoma was synovial with commonly 3 cm long high grade tumors. The primary treatment was radiotherapy with 24% of patients having partial amputations versus 19% with limb sacrificing amputations. In this case, 19% of patients had five-year local recurrence rate, while 82% had a five-year survival rate. Overall, the increased rate of amputations was in the inadvertent excision group versus the intentional excision group. This was due to larger tumor size. In terms of limb preserving surgery, there was no increase in local recurrence rate in those who underwent limb salvage. This suggests, should there be an amputation or a limb preserving surgery, the risks are the same. However, there was a difference between mortality of the two groups. Mortality was higher in the limb amputation surgery versus limb sparing surgery. This might have been due to a number of factors, but the association should be further explored to test in which case limb sparing is beneficial. The most useful diagnostic threshold in foot sarcomas would be the size of the tumor. Notating size and excision margins should be taken in consideration by clinicians coming across such cases. Nonetheless, the results exemplified that limb salvage surgery (at least in the case of acral soft tissue sarcomas) did not increase the rate of recurrence versus proximal amputations. Increased tumor size led to increased rate of lower recurrence. Those who underwent proximal amputation with larger tumor size were more likely to succumb to their illness than any other group in this study. Therefore, deciding on limb salvage surgery as a treatment option in one case of acral foot sarcoma has proven to not be detrimental.

In the case of STS involving the major nerves of lower extremities such as recurrent malignant peripheral nerve sheath tumors (MPNST), limb salvage surgery shows promising outcomes. MPSNTs make up about 10% of soft tissue sarcomas. This case
A report focused on a 65-year-old female with recurrent MPNST of the first interdigital nerve. The treatment plan was limb salvage surgery with wide margins and reconstruction with an autogenous fibula graft. The patient initially presented with a palpable mass between the first and second metatarsals of the right foot, otherwise her history was unremarkable. Histology of the tumor revealed a grade 1 MPNST. There was a discussion then between limb salvage or limb amputation. The decision was as stated above. A wide margin excision treatment was chosen to excise the tumor and the patient’s fibula was used as a graft to replace the bone defects on the first two metatarsals post tumor excision. The follow up showed no local tumor recurrence or metastasis in the six and twelve month period examinations. In this case, limb salvage was chosen over amputation for MPNST and did not result in local tumor recurrence thereby signifying limb salvage may be used as a primary treatment option for sarcomas.

In the case involving a chondrosarcoma of the 2nd and third metatarsals of 24-year-old patient similar findings to above were seen. The patient reported swelling in the left foot for 16 months with pain associated for the 6 months. There was no history of trauma to the foot or changes in sensation or erythema. He did have multiple nodular swellings present since childhood but otherwise no systemic illnesses. Upon examination, there was 4 X 3 cm bilobed swelling in the left foot. The swelling was up to the mid-diaphysis and MRI showed a likely destructive lesion between the 2nd and 3rd metatarsals. The course of action taken was a bloc tumor mass resection in the 2nd and 3rd metatarsal preserved to the bases. This prevented instability of the forefoot and maintained function and anatomic integrity of the limb. A fibula graft was used to replace the defect in the left foot. The 1-year follow-up showcased the graft was incorporated into the foot and the patient had normal gait. Once again, limb salvage surgery was chosen over amputation. We believe this treatment was chosen based on the immediate frozen section analysis showing clear margins therefore a lower chance of recurrence.

In the case involving osteosarcoma, the results are not as clear. Between 2007 and 2012, five patients were followed of which were diagnosed with high-grade osteosarcoma of the distal tibia. The patients underwent tibiotalar arthrodesis limb-salvage using ipsilateral vascularized fibula transfer. The study evaluated the effectiveness and feasibility of this surgical technique. Upon 5-year follow-up, one out of the five patients, or 20% developed local recurrence and had an amputation to prevent metastasis. The other four patients showcased no signs of distant metastasis or local recurrence. All patients could walk and stand with normal gait. All five patients were alive as of the last follow up. Based on these results, limb-salvage surgery and reconstruction as the primary method of treatment was beneficial to the patient for full use of the foot. Patients exhibited normal gait and were able to continue normal use of foot. That being said, however, this was a small case study. A greater patient population should be investigated to further this association.

CONCLUSION

Three out of the four papers stated that excision of tumors, particularly sarcomas, with limb preservation did not result in increased risk of local recurrence. Treatment in one of the four however, showed local reoccurrence in their results when treating osteosarcoma of the distal tibia. Whether this was due to the grade or stage of the tumor is
unclear. Future in-depth studies involving a greater patient population should be done to increase this association.

It can be stated, however, that it is critical to consider limb salvage as a treatment option before opting toward amputation surgery. The limitations to this literature review included the wide array of foot sarcomas studied and its retrospective nature. Future literature reviews would focus on specific carcinomas of the foot and whether limb salvage or amputation would be the ideal treatment option or even what exact criteria should be considered while choosing between the two options.

AUTHORS’ CONTRIBUTIONS

All three authors equally contributed to the design of the study and evaluated the available articles. All authors contributed equally in the writing of this literature review and reviewed the final version for submission.

STATEMENT OF COMPETING INTERESTS

The authors declare that they have no competing interest associated to this manuscript

REFERENCES

Cytokine Recruitment and Wound Healing Capabilities of Vitamin D Supplementation on Diabetic Foot Ulceration: A Quantitative Systematic Literature Review

By: Alex Fleischman, BS

ABSTRACT

Introduction

A diabetic foot ulcer (DFU) is defined as a non-healing or poorly healing, full-thickness, dermal penetrating wound that is present below the ankle on patients with diabetes mellitus. A typical immunological response to ulceration would be the recruitment of cytokines, e.g. IL-6, IL-1β, TNF-α, and INF-γ. 25-hydroxyvitamin D (Calcifediol) is a pre-hormone produced in the liver through the hydroxylation of vitamin D3 that is used to measure vitamin D serum levels. The goal of this paper is to conduct a literature review detailing a quantitative explanation to how vitamin D supplementation affects the wound healing abilities of diabetic ulcerations.

Study Design: Quantitative Systematic Review of Literature

Methods

Two independent English language PubMed searches were conducted. The primary search used MeSH terms “diabetic foot ulcer” AND “vitamin D deficiency.” The search yielded 18 articles. The secondary search using MeSH terms “diabetes mellitus” AND “vitamin D” AND “cytokines” AND “clinical trials.” The search yielded 24 articles. The inclusion criteria for article analysis selection consisted of papers with statistical evidence and analysis in relation to the subjects of diabetes mellitus, vitamin D concentration, and cytokine recruitment. Articles were excluded from the literature review if published prior to 2014, written in a language other than English, or involving species other than humans. After the employment of the inclusion and exclusion criteria, a total of 22 articles were selected to be used in the systematic review of literature.

Results

Eight out of the 22 articles used in the quantitative systematic review of literature were further analyzed. The study design, sample size, variables, and conclusions for each of these articles were summarized.

Conclusion

Diabetes mellitus has an effect on the downregulation of certain cytokines in an inflammatory response. This results in the overexpression of angiogenic factors and fibroblast activation, which stifle the wound healing duration as well as the effectiveness of the wound healing process. Vitamin D has a inhibitory effect on proinflammatory cytokines responsible for angiogenesis as well as fibroplasia. Vitamin D supplementation patients with DFUs was shown to have a positive effect on the wound healing duration and effectiveness.

Keywords: Diabetes mellitus, diabetic foot ulcer, vitamin D, 25-hydroxyvitamin D, cytokines, IL-6, IL-1β, TNF-α, INF-γ, wound healing

Level of Evidence: 4
INTRODUCTION

Diabetes Mellitus and the Wound Healing Process:

Diabetes mellitus is disease by which the resulting hyperglycemia causes neuropathy in the lower extremities. Abrasions to the lower extremities can result in severe ulcerations unbeknownst to the patient (DFU). Diabetes mellitus inhibits the downregulation of certain proinflammatory cytokines, which adversely affect the wound healing process. The consistent influx of proinflammatory cytokines increases the likelihood of impaired wound healing and osteoporosis.

The normal physiological response to wound healing is initiated by the vasoconstriction of lesioned blood vessels to promote the aggregation of thrombocytes and platelets to form a fibrin matrix for inflammatory cell migration. Leukocytes migrate to the lesioned area to trigger a macrophagic response to the incoming bacteria. The response initiates the release of mastocytes, gamma-delta cells, and Langerhans cells to the area for cytokine release. At this moment, certain cytokines, e.g. IL-1β, trigger neutrophils to migrate through the endothelial cells of blood vessels to the site of the lesion.

Patients with diabetes mellitus are unable to downregulate this step of the wound healing process. Therefore, the patient exhibits a spike in angiogenic factors as well as onset neutropenia. As the recruitment of inflammatory proteins continues, angiogenesis, fibroplasia, and re-epithelialization occur to heal the lesions in a normal inflammatory response. Patients with diabetes mellitus experience a longer and less effective wound healing process as compared to patients without diabetes mellitus due to the increase in recruitment of inflammatory protein.

Vitamin D and the Wound Healing Process:

Vitamin D is a fat-soluble vitamin obtained by UV exposure, food groups, or supplementation. Vitamin D3 is hydroxylated in the liver to form 25-hydroxyvitamin D (Calcifediol) that enters the bloodstream to be later activated by a second hydroxylation to form 25-dihydroxyvitamin D3 (Calcitriol). 25-hydroxyvitamin D3 is used as a measurement of blood vitamin D levels that 1,25-dihydroxyvitamin D due to its longer half-life.

Vitamin D promotes absorption of calcium in the intestinal lining to maintain osteoblast bone mineralization. In addition, vitamin D has a significant role in the regulation and differentiation of inflammatory response proteins. Vitamin D had an inhibitory response on IL-6. IL-1β, TNF-α, and other cytokines. Therefore, vitamin D plays an important role in the rate of wound healing by monitoring angiogenesis and fibroplasia brought about by an inflammatory response.

Objective and Hypothesis:

The objective of this paper is to conduct a systematic literature review detailing the quantitative data that details the theory that vitamin D supplementation has a positive effect on the wound healing capabilities of diabetic foot ulceration. In addition, the paper strives to systematically detail data regarding vitamin D levels and cytokine levels in patients with and without diabetic mellitus and/or diabetic foot ulceration.
METHODS

Two independent English language PubMed searches were conducted. The primary search used MeSH terms “diabetic foot ulcer” AND “vitamin D deficiency.” The search yielded 18 articles. The secondary search using MeSH terms “diabetes mellitus” AND “vitamin D” AND “cytokines” AND “clinical trials.” The search yielded 24 articles.

The inclusion criteria for article analysis selection consisted of papers with statistical data relating to diabetes mellitus, vitamin D concentration, and cytokine recruitment. Articles were excluded from the literature review if published prior to 2014, written in a language other than English, or involving species other than humans. After the employment of the inclusion and exclusion criteria, a total of 22 articles were selected to be used in the systematic review of literature.

Figure 1: Literature Search using Pubmed Database
RESULTS

Feldkamp et al. determined a significant difference (p < 0.001) in vitamin D serum concentration in patients with DFU and healthy individuals. 25-hydroxyvitamin D3 levels were measured in 104 patients with DFU and 99 healthy patients. The 25-hydroxyvitamin D3 levels in patients with DFU (11.8±11.3 ng/mL) was significantly lower than healthy patients (27.2±12.2 ng/mL) (p<0.001). Additionally, it was determined that the 25-hydroxyvitamin D3 levels are negatively correlated (r=-0.241 p<0.001) to the Armstrong Classification of DFUs.

Afarideh et al. measured the cytokine concentration in patients with DFU (n=30), with diabetes mellitus II without DFU (n=30), and healthy patients (n=30). Each group was comprised of representatives with no significant difference in age, BMI, cholesterol levels, and HbA1c concentration to standardize the results. Patients with grade 2 Armstrong DFUs comprised the study. Afarideh et al. determined that there was a significant difference of MCP-1 and IL-6 concentrations (p<0.001) between all three subgroups. There was a significant difference of IL-8 concentrations (p<0.05) between patients with DFU and healthy representatives. There was no significant difference of IL-8 concentration between diabetic patients with and without DFU (p>.05). Reference Table A for specific concentration values and significance.

Razzaghi et al. measured the affects vitamin D supplementation has on patients with DFU. 60 patients with grade 3 Armstrong DFU classification were used in this trial. Patients were randomly split into 2 groups, one of which was given 50,000 IU vitamin D supplements and the other given placebos every 2 weeks for 12 weeks. The average change in ulcer length, width, and depth was calculated for both groups. Razzaghi determined a statistically significant (p<0.05) difference all three dimensions between subgroups. Through error propagation of the data presented, the change in volume over the 12 week period was -0.605±0.004 for the placebo group and -3.990±0.004 for the vitamin D group. Reference Table C for specific dimensions and significance.

Tiwari et al. analyzed the cytokine concentration in type II diabetic patients with and without DFUs. Tiwari et al. used a total of 219 patients, 112 with DFU and 107 without DFU, over the course of calculation. To standardize the results, both groups did not have a statically significant difference in age, HbA1c levels, and BMI. Tiwari et al. determined that there was a significant difference in IL-6, IL-1β, and TNF-α concentration between subgroups (p<0.05). There was no significant difference in IFN-γ concentration (p>0.05). Reference Table B for specific concentration values and significance.
TABLE A: Afarideh et al. – Cytokine Concentration and Significance

<table>
<thead>
<tr>
<th></th>
<th>Healthy Control (n=28)</th>
<th>Type II Diabetes Mellitus controls (n=30)</th>
<th>DFU (n=30)</th>
<th>P value DFU vs. Healthy</th>
<th>P value DFU vs. T2DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCP-1 (pg/mL)</td>
<td>264.5</td>
<td>431.5</td>
<td>612.0</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IL-6 (pg/mL)</td>
<td>2.5</td>
<td>6.5</td>
<td>19.7</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IL-8 (pg/mL)</td>
<td>147.5</td>
<td>60.5</td>
<td>78.0</td>
<td>0.049</td>
<td>0.188</td>
</tr>
</tbody>
</table>

TABLE B: Tiwari et al. – Cytokine Concentration and Significance

<table>
<thead>
<tr>
<th></th>
<th>DFU Cases</th>
<th>Diabetic Controls</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-6 (pg/mL)</td>
<td>128.7 ± 7.4</td>
<td>87.3 ± 9.0</td>
<td>0.001</td>
</tr>
<tr>
<td>IL-1β (pg/mL)</td>
<td>101.5 ± 20.8</td>
<td>49.3 ± 10.8</td>
<td>0.02</td>
</tr>
<tr>
<td>TNF-α</td>
<td>182.3 ± 20.8</td>
<td>96.5 ± 22.9</td>
<td>0.006</td>
</tr>
<tr>
<td>INF-γ</td>
<td>18.1 ± 3.2</td>
<td>13.7 ± 1.5</td>
<td>0.2</td>
</tr>
</tbody>
</table>

TABLE C: Razzaghi et al. – Ulceration Dimensions and Significance

<table>
<thead>
<tr>
<th></th>
<th>Placebo Group (n=30)</th>
<th>Vitamin D Group (n=30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D (ng/mL)</td>
<td>-0.005 ± 1.8</td>
<td>11.1 ± 1.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ulcer length (cm)</td>
<td>-1.1 ± 0.2</td>
<td>-2.1 ± 0.2</td>
<td>0.001</td>
</tr>
<tr>
<td>Ulcer width (cm)</td>
<td>-1.1 ± 0.2</td>
<td>-1.9 ± 0.2</td>
<td>0.01</td>
</tr>
<tr>
<td>Ulcer depth (cm)</td>
<td>-0.5 ± 0.1</td>
<td>-1.0 ± 0.1</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

DISCUSSION

Feldkamp et al. determined that the vitamin D serum concentration, 25-hydroxyvitamin D3, is significantly lower in patients with DFU referenced to healthy representatives. Under further analysis, the patients with worse Armstrong grade DFU have lower vitamin D serum concentrations; furthering the theory that the severity of the ulceration and the inability of the wound healing process to proceed is inversely regulated by the vitamin D serum concentration.

Afarideh et al. concluded that there is a significant difference in MCP-1 and IL-6 concentration between healthy patients, and diabetic patients with and without DFU. In addition, there was a significant difference in IL-8 levels between healthy patients and
diabetic patients with DFU. Tiwari et al. determined that there is a significant difference in IL-6, IL-1β, and TNF-α concentrations in diabetic patients with and without DFU. There was no significant difference in INF-γ concentration between both subgroups. The data presented by Afarideh et al. and Tiwari et al. allows for the conclusion that cytokine levels are elevated in patients with diabetes mellitus and/or DFU as compared to healthy representatives.

Razzaghi et al. concluded that vitamin D supplementation significantly increases the rate of DFU healing processes. The difference for change in length, width, and depth were statistically significant as a result of a statistically significant increase in vitamin D concentration brought about by vitamin D supplementation. The rate increase suggests that vitamin D supplementation positively impacts the rate of the wound healing process in diabetic ulceration.

**CONCLUSION**

The data provided suggests that there is statistical evidence reinforcing the theory that the decrease in vitamin D serum levels in patients with diabetes mellitus and/or DFU negatively impacts the rate of the wound healing process as a result of the inhibition of cytokine downregulation. It would be advantageous for physicians to consider vitamin D supplementation for patients suffering from DFU and diabetes mellitus for ulceration healing and ulceration prevention, respectively.

**LIMITATIONS**

The studies referenced in the systematic review of literature was limited to the patients’ variation in DFU classification rating under the Armstrong scale. Patients with grade II and grade III were used in the data presented by Afarideh et al. and Razzaghi et al., respectively. Tiwari et al. used a mixed patient set of DFU grading. Further research must be done to determine the significance of vitamin D supplementation on the healing process for each grade subset of Armstrong DFU classification. Other factors, such as BMI, height, age, were held constant under the analysis of each trial under analysis.

**STATEMENT OF COMPETING INTERESTS**

The author declares that he has no competing interest associated with this manuscript.

**REFERENCES**


Efficacy of Assisted Fractional Carbon Dioxide Laser Therapy for Treatment of Onychomycosis

By: Laurin Larian, MA, MA, BA

ABSTRACT

Introduction
Onychomycosis, also known as tinea unguium, is a nail fungal infection. Many topical antifungal agents and oral medications are used to treat onychomycosis. Because of the inability of many topical antifungal agents to penetrate the nail bed and the many side effects of oral medications, treatment now includes laser therapy. Specifically, fractional carbon dioxide laser treatment with topical agents are being used together to treat fungal toenails.

Study Design: Systematic Review of the Literature

Methods
A PubMed database search was performed to include the following terms “Fractional carbon dioxide laser AND cream AND onychomycosis”. Inclusion criteria were English, male and female, and publication dates between 2014 and 2019. All 4 articles yielded were used.

Results
Efficacy of treatment with laser therapy and topical cream were analyzed by measuring clinical efficacy and mycological clearance. Additionally, comparative evaluation among the various types of onychomycosis was performed. Subjects were also surveyed to determine satisfaction as well as to evaluate the degree of pain to treatment.

Conclusion
The four articles analyzed showed that co-treatment with fractional carbon dioxide laser therapy and topical cream greatly improves both clinical efficacy as well as mycological clearance. Additional research is needed to include more participants as well as control and treatment groups.

Key Words: onychomycosis, fractional carbon dioxide laser, fungal infection, topical therapy

Level of Evidence: 4
INTRODUCTION

General Background

Onychomycosis is the most common nail disease in adults, comprising at least half of all documented nail disorders. Onychomycosis is a fungal infection of the nail bed and is mainly caused by dermatophytes, non-dermatophyte fungi and yeasts. These pathogens remain between the nail plate and nail bed and are extremely difficult to eradicate, especially due to the slow growth of nails.

Classification and Pathology

There are four types of onychomycosis which are characterized based on clinical presentation and path of invasion. The most common one is distal lateral subungual onychomycosis (DLSO). It invades the nail bed and hyponychium and spreads through the nail matrix. As a result, there is nail thickening as the nail bed and nail plate detach from one another. Proximal subungual onychomycosis (PSO) invades from the cuticle through the nail plate. It is the least common form of onychomycosis in individuals but may be an indicator of immunosuppressive diseases such as HIV. Superficial white onychomycosis (SWO) invades the nail plate directly and has the appearance of “white islands.” Lastly, total dystrophic onychomycosis (TDO) characterizes end stage nail disease. All types of onychomycosis are diagnosed by direct microscopy using potassium hydroxide or cultured in media.

Epidemiology

Several risk factors to onychomycosis include increased age, poor circulation, trauma, obesity, smoking, and athlete’s foot. One important risk factor is tinea pedis, which can also result in various secondary infections; specifically osteomyelitis and cellulitis. Individuals with repressed immune systems such as those with HIV or those receiving immunosuppressive therapies have a higher risk of getting infected.

Treatment

There are various treatment options for onychomycosis. Topical drugs include ciclopirox, amorolfine, efinaconazole, and tavaborole. However, these agents are typically ineffective in completely treating the nail fungus due to their limited ability to penetrate the nail plate and reach the nail bed. Systemic oral drugs include terbinafine, fluconazole, itraconazole, and griseofulvin. These agents, although effective, tend to have adverse effects such as gastrointestinal side-effects and liver abnormalities. They also interact with other drugs, which can be dangerous for patients with certain comorbidities. Recent research has looked into photodynamic therapy and laser therapy in treating onychomycosis. Specifically, fractional carbon dioxide laser therapy has demonstrated minimal side effects, maximal treatment effects, and shorter recovery time. This laser works by creating microscopic treatment zones which are several columns of openings into the tissue. By working via vaporization and tissue decomposition, the toenail fungi are more likely to be destroyed. Co-treatment of onychomycosis with laser therapy and topical medications allows for better treatment and a lower chance of recurrence. This literature review aims to discuss the efficacy of using fractional carbon dioxide laser therapy with topical cream to successfully treat onychomycosis in the lower extremity.
METHODS

A PubMed database search was performed to include the following terms “Fractional carbon dioxide laser AND cream AND onychomycosis”. Inclusion criteria were English, male and female, as well as publication dates between 2014 and 2019. The search yielded four results. There were no exclusion criteria. All four articles were used. The figure below shows a summary of the methods for this paper.

RESUL

RESULTS

In a study by Zhou et al., 60 patients were enrolled in a randomized and controlled trial where one group received fractional carbon dioxide laser treatment alone and the other group received laser treatment and topical antifungal cream (luliconazole). The clinical efficacy rate was measured 3 months and 6 months post treatment. Patients receiving both laser and topical treatment had improved significantly when compared to baseline. Additionally, they also had a significantly higher clinical efficacy rate when compared to patients receiving only laser treatment at both 3 and 6 months post-treatment. The mycological clearance rate was also significantly higher in the co-treatment group (57.4%) than the laser only group (38.9%). Three factors were found to significantly influence the treatment outcome in the co-treatment group: onychomycosis severity index score, nail thickness, and involved nail. Four factors were found to significantly influence treatment outcome in the laser only group: clinical type, onychomycosis severity index score, nail thickness, and involved nail. Patient satisfaction and adverse effects were also measured.7

A study by Bhatta et al. also used laser therapy with topical cream to treat toenail mycosis in 75 patients who completed the study. Three months post treatment, 14.66% of patients showed a complete response, 58.66% showed a significant response, 25.33% showed a moderate response, and 1.33% showed no response. Additionally, 94.66% of patients were potassium hydroxide negative and 92% were culture negative. Six months post treatment, 33.33% of patients showed a complete response, 40% showed a significant response, 6.66% showed a moderate response, and 20% showed no response. However, 84% of patients were potassium hydroxide negative and 80% were culture negative as this was due to fungal recurrence. Moreover, the Scoring Clinical Index for Onychomycosis was used to further evaluate treatment response. Using this index, it was determined that in 3 months of post-treatment, 98.18% of patients showed a response to treatment, and in 6 months of post-treatment 78.18% of patients showed a response to treatment. These results, using the index indicate that patients who were ideal subjects for systemic therapy were observed to have a positive clinical response.
to the laser assisted topical therapy. The researchers also evaluated the response rates among the four types of onychomycosis. Specifically, the response rate of patients with DLSO was greater than patients with TDO. Patients also reported their satisfaction and pain levels during the study.\textsuperscript{8}

Lim et al. tested laser therapy with a topical antifungal cream on 24 patients all of whom were unable to take oral antifungal medications. Significant clinical improvement occurred. At the end of the study, the visual appearance of most of the treated nails improved when compared to the beginning of the study. After each follow-up visit, the area of toenail infection significantly decreased and after 12 weeks only 19.4\% of the toenail area was still infected. Ultimately, 92\% of patients indicated some clinical response while half of all patients indicated a complete response where microscopy was negative. The latter reflected patients having no fungal recurrence for the 3 months post-treatment. Two major factors that motivated treatment outcome were the clinical type of onychomycosis as well as baseline nail thickness. All patients with SWO showed a complete response but patients with TDO did not. Moreover, 75\% of patients who had a nail thickness of 2.2 millimeters or less showed a complete response but patients with a thickness of more than 2.2 millimeters did not. Patient satisfaction was also measured where post-treatment, 59\% of patients were very satisfied and 8\% were not satisfied. Additionally, most patients could withstand the treatment and no major side effects were observed.\textsuperscript{9}

Lastly, the most recent study is by Shi et al. and colleagues who tested laser therapy and topical terbinafine hydrochloride 1\% cream on 30 patients over the course of 6 months. These researchers observed clinical improvement directly at the end of treatment, 1 month post-treatment, and 3 months post treatment. During this time frame, there was an increase in the percentage of nails showing complete and significant responses but there was a decrease in the mycological clearance rate from 1 month post-treatment (77.42\%) to 3 months post treatment (74.19\%). Of the 4 clinical types of onychomycosis, the clinical efficacy rates of DLSO, PSO, and SWO were significantly different when compared to TDO. The researchers indicated 5 influencing factors which may influence treatment outcome: age, clinical type of onychomycosis, thickness of nail, involved nail, and fungal species. Like the other studies, participant satisfaction and adverse effects were observed.\textsuperscript{10}
DISCUSSION

Toenail onychomycosis is not only difficult to treat but also has a high rate of recurrence. Treatment can include both topical and oral antifungals. However, topical creams have difficulty penetrating the nail plate and oral pills have major side effects and cannot be used in individuals with certain comorbidities. Recently, laser treatment of toenail onychomycosis has become another treatment option. Both photodynamic therapy and yttrium aluminum garnet laser have shown success. Fractional carbon dioxide laser allows for shorter recovery and less pain. When used in conjunction with topical antifungals, recovery is quicker.

Bhatta et al. summarized the effectiveness of the various treatment therapies used in different studies. Topical treatments have an effectiveness of 16%-46%. Oral treatments have an effectiveness of 38%-76%. Topical and oral co-treatments have an effectiveness of 71%-86%. Laser treatments have an effectiveness of 33%-70%. Lastly, laser and topical co-treatments have an effectiveness of 80%.

CONCLUSION

From this literature review, it can be concluded that fractional carbon dioxide laser treatment with topical antifungal medication is a safe and effective treatment of toenail onychomycosis. However, referencing only four articles is a limitation to this literature review and more research is needed to indicate that there is a correlation between laser therapy and improvement in toenail onychomycosis. Future studies should include more randomized controlled trials as well as more patients. Furthermore, specific settings for the laser system should be indicated as well as additional follow up visits. Doing so will help to further validate the obvious positive effects of laser and
topical therapy so that patients will have faster cures, less pain, and lower recurrence rates of toenail onychomycosis.

**STATEMENT OF COMPETING INTERESTS**

There are no competing interests.

**REFERENCES**


The Benefits of Podiatry Interventions in Fall Prevention

By: Zain-ul Sulheri, BS; Vikal Singh, MPH, BS

ABSTRACT
Introduction
Falls are the leading cause of injury-related deaths among seniors 65 years of age and older. Falls are also the leading cause of non-fatal injuries for seniors, threatening their independence, mobility, and safety. Staggering statistics related to falls among seniors make fall prevention a priority for them. The goal of this paper is to conduct a systematic review of the literature regarding podiatry specific multifactorial interventions in fall prevention.

Study Design: Qualitative Systematic Review of Literature

Methods
PubMed MeSH database was used for this systematic literature review. The MeSH key term “podiatry” was used in the search entry. Then into the search builder box, the following entry was copied and pasted, (fall[All Fields] AND ("prevention and control"[Subheading] OR ("prevention"[All Fields] AND "control"[All Fields]) OR "prevention and control"[All Fields] OR "prevention"[All Fields])) AND "Podiatry"[Mesh]). This search entry yielded a total of 7 articles. The articles search was further filtered using inclusion and exclusion criteria. The inclusion criteria included human subject and free full-text availability. The exclusion criteria included articles published before 2017 only. After the inclusion and exclusion criteria was applied, the search yielded 3 articles, however, 2 were summarized for this paper. Figure 1 depicts a flow chart that summarizes the methods.

Results
The studies selected for this paper demonstrate that podiatry related interventions lead to a lower fall rate in intervention groups. Wylie et al. discussed podiatry lead interventions to reduce falls, which can be delivered to home care residents. Cockayne S. et al. demonstrated a reduction proportion that was borderline statistically significant in older adults who experienced a fall. Furthermore, the economic evaluation suggests that the fall rate intervention could be cost-effective.

Discussion and Conclusion
Multifaceted and multifactorial interventions involving podiatry produced a significant decrease in the rate of falls in the elderly population. These interventions included patient education, footwear/and or orthoses, if required, foot and ankle at-home exercises, and a routine visit to a podiatrist office. Podiatry referral and a multidisciplinary team approach were emphasized. The study data used for this paper mostly applies to senior citizens in the community, and further research on these interventions in care homes, such as nursing facilities, is necessary.

Key Words: Care homes; Falls; Fall prevention; Older people; Podiatry; Podiatric treatment

Level of Evidence: 4
INTRODUCTION

Over one-third of adults over 65 years of age fall each year with one-half of these falls resulting in injury. From bruises and strains to broken bones and lasting trauma, falls threaten the health and safety of seniors, as well as their economic security and independence. According to the United States Senate Special Committee on Aging 2019 annual report, an older adult is treated in the emergency room for a fall every 11 seconds, and every 19 minutes an older adult dies because of a fall. Falls and related injuries also bear enormous financial implications for individuals, families, and the health care system. Each fall-related hospital stay costs an average of $30,000 each year, and Americans spend a total of approximately $50 billion in medical costs alone for fall injuries. Adults that are 65 years of age or older are at increased risk of falling as the risk increases with age. Common risk factors associated with aging includes changes in muscle strength, deterioration of vision, a diagnosis of osteoporosis, arthritis, dementia, and vitamin D deficiency. Certain medications also increase fall risks such as antidepressants and benzodiazepines. Falling can result in physical injuries, such as fractures, disability, and head trauma, as well as psychological and functional consequences such as loss of independence, social isolation and institutionalization, and even death.

However, falling does not have to be a natural part of aging. After decades of targeted trials, researchers have developed evidence-based programs to prevent falls among seniors. One of these programs that aid the elderly is with the intervention of podiatric medicine. There are various podiatric interventions in fall prevention, such as lower extremity treatment and routine care, exercise education, and footwear/ orthotic recommendations. Exercise in fall prevention also plays an important role. With the help of a podiatrist, seniors can learn about weight training, toe grasping, and foot range of motion to strengthen their lower extremities muscles that can lead to improved balance. Thus, podiatrists play a vital role in the comprehensive approach of preventing falls. In regards to senior’s health, social, and economic impact, podiatric interventions play a significant decisive role in improving these outcomes. The goal of this paper is to conduct a systematic review of the literature regarding podiatry specific multifactorial interventions in fall prevention.

METHODS

PubMed MeSH database was used for this systematic literature review. The MeSH key term “podiatry” was used in the search entry. Then into the search builder box, the following entry was copied and pasted, (fall[All Fields] AND ("prevention and control"[Subheading] OR ("prevention"[All Fields] AND "control"[All Fields]) OR "prevention and control"[All Fields] OR "prevention"[All Fields]) AND "Podiatry"[Mesh]). This search entry yielded a total of 7 articles. The article search was further filtered using inclusion and exclusion criteria. The inclusion criteria included human’s species and free full-text availability. The exclusion criteria included articles published before 2017. From the inclusion and exclusion criteria, the search yielded 3 articles, from which 2 were summarized for this paper because these 2 reported the benefits of podiatry interventions in fall prevention. Figure 1 depicts a flow chart that summarizes the methods.
RESULTS

Wylie et al. conducted a single-blind, pilot randomized controlled trial in six different care homes in the East of Scotland. Study participants included adult subjects of 65 years of age or older, a permanent residence in a care home for older people, have had at least one or more falls in the previous year, and a foot problem (defined as within the scope of practice of UK trained podiatrist). Patients with lower limb amputations,
terminally unwell, confined to a wheelchair, or temporary residents of a care home for older adults were ineligible for the study. Participants were randomly assigned to either the control group (n=20) or the intervention group (n=23). The control group received core podiatry only, which included regular nail and callus maintenance. The intervention group included the core podiatry treatment that the control group received, and in addition, they received foot orthoses, a foot assessment, and a course of foot and ankle exercises. Fall outcomes data were collected at four different time points: before the start of the intervention (T1), at the end of the 3-month intervention (T2), 3-months after the end of the intervention (T3), and 6-months after the end of the intervention (T4).5

Wylie et al. found that in the intervention group, 48% (10/21) experienced at least one fall, while in the control group, 71% (12/17) experienced at least one fall. There were also repeated falls assessed in this study, of which 33% (7/21) were seen in the intervention group and 53% (9/17) in the control group. From T1 to T4, the intervention group experienced a total mean of 2.3 falls, while the control group experienced a mean of 2.7 falls. The median time to the first fall was observed longer in the intervention group (91 days, range from 42 days to 257 days), compared to the control group median first fall time (64 days, range from 2 days to 160 days).5

Cockayne et al. used a cohort randomized control study of 1010 participants. Participants were randomly placed into two different groups. One group received intervention consisting of footwear advice, an orthotic insole or review of insole prescription, a program of foot and ankle balance exercise, and a leaflet for fall prevention. The other group received a fall prevention leaflet and usual care from a podiatrist and general practitioner (control group). Participants enrolled in the study were adults aged 65 years or older who have attended routine podiatry services within the past 6 months of the study date. Participants were required to have had one fall in the past 12 months, a fall that required hospitalization in the past 24 months, reported worrying about falling within the past 4 weeks of completing a baseline questionnaire, are community-dwelling and able to speak and read English. Participants that were current residents in nursing homes were ineligible from the study. In addition, participants were ineligible for this study if they reported any neuropathy, dementia or another neurological condition (Alzheimer’s disease, multiple sclerosis, Lou Gehrig’s disease, or Huntington’s disease), required a walking aid for walking more than 10 meters, such as a walker or a person to assist them, had a lower limb amputation, or if they were unwilling to attend their podiatry office for a reform appointment. The routine podiatry care consisted of treatment of conditions such as corns and calluses, which have been associated with increases in the risk of falls. Results were collected following 12-months of post-randomization of the study. The participants were also sent a follow-up questionnaire at the 6-months into the study and another at 12-months. Additionally, the participants in the intervention group were assigned an exercise and orthosis compliance questionnaire at 3, 6, and 12 months of the study.6

The primary outcome of the study conducted by Cockayne et al. was self-reported fall incidence from the participants at the end of the 12 months. Of the 1010 participants total, 493 were assigned to the intervention group, and 517 were assigned to the control group. The intervention was more costly but was seen to be more beneficial in terms of health-related quality of life of the patients. At the
end of 12 months, 992 (98.2%) participants of the study reported at least one fall. In the intervention group, there were 484 (98.2%) falls reported as compared to the control group having 508 (98.3%) falls. A total of 1,432 falls were reported, which included greater than one falling episode. In the intervention group, there were a total of 661 (median 1, range 0 to 23) falls, and in the control group, there 762 (median 1, range 0 to 28) fall reported over the 12 months course. Most of the falls were caused by a trip (n=457, 39.0%), and an injury was sustained from the fall (n=655, 55.9%). The injuries included 31 broken bones, including 17 from the intervention group and 14 from the control group. The most common bone broken included the hip bone and the bones of the hands (n=5 in both the intervention and control group). Few participants in the intervention group had one or more falls (n=245, 49.7%) compared to the control group (n=284, 54.9%). Besides, a longer median time to the first fall was seen in the intervention group of 314 days compared to the control where the median time to the first fall was seen at 257 days.

**DISCUSSION**

Wylie et al. noted a decrease in the fall rate of the participants assigned to the intervention group compared to those in the control group. The number of overall falls in participants in the intervention group was lower than in the control group. In addition, the median time to the first fall time was longer in the intervention group as compared to the control group. However, Wylie et al. stated since this was a pilot trial with such a small sample group (n=43), the full effectiveness of the intervention treatments might not be fully determined. Cockayne et al. stated there was a small reduction in falls seen in both groups. The intervention group participations received a falls prevention leaflet and routine care from their podiatrist and general practitioner, in addition, they also received footwear advice, footwear provision, foot orthoses, and foot and ankle-strengthening exercises. It was also discussed that even though the participants in the intervention groups may benefit more from the treatment options, it may be cost effective as the purchase of the footwear and orthoses components are the most expensive aspects of the treatments. Overall there were fewer falls seen in the intervention group participants compared to those in the control group, observed by a small margin. Also, compared to the patients in the intervention group, there was an occurrence of more than one fall in the control group. Finally, the median time to the first fall was longer for the participants in the intervention group compared to the control group.

The limitations stated by Wiley et al. begins with the study’s low power and relatively short follow up time, so the statistical analysis should be treated with caution. Additionally, due to the multifaceted type of research, it was impossible to blind participants to their group, nor was it possible to identify the contribution of each intervention component. Finally, care home residents that were unable to provide informed consent were excluded from the study, thus limiting the external validity of the study. Cockayne et al. reported several limitations for their study including lack of having additional participants contact a podiatrist in the qualitative interviews and the possibility of study participants to enroll in other fall prevention programs. Additionally, study participants were recruited from podiatry clinics; therefore, the estimated impact of the intervention may be different among patients who do not regularly see a private podiatrist. Lastly, Cockayne et al. stated that their study intervention is a complex one; therefore, their design does not
allow them to estimate the different contributions of changes in footwear, the addition of orthotic insole or the undertaking of foot and ankle exercises.6

CONCLUSION

The podiatric interventions mentioned in this paper were safe and potentially useful. The study by Wiley et al. demonstrates that a podiatry intervention to reduce falls can be delivered to care home residents. Their preliminary data provides a path for future research for a larger trial, incorporating a full process of evaluation to determine whether their intervention can significantly reduce falls in the high-risk population. According to Cockayne et al., although the primary outcome measure was not statistically significant, a lower fall rate was observed in the intervention group. Future research can examine whether the response could be delivered in group sessions, by physiotherapists, or in high-risk patients. Thus, podiatry interventions mentioned in this paper establishes the vital role of podiatrists in addressing - , shoes, orthotics, strengths, flexibility, and neurological functions to preventing falls. Podiatric interventions can play a significant role in improving the health, social, and economic impact of falls. While further research is necessary, podiatry interventions convey the importance of addressing fall prevention in the elderly.

AUTHORS’ CONTRIBUTIONS

All authors contributed equally to the production of this manuscript. All authors conceived on the topic and preformed literature searches. All authors drafted, read, reviewed and agreed upon the final submission of this manuscript.

STATEMENT OF COMPETING INTERESTS

The authors declare that they have no competing interests associated with this manuscript.

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A Comparison of Foot Orthoses and Rocker-Sole Footwear for Non-Surgical Treatment of First MTP Joint Osteoarthritis: A Qualitative Systematic Review of Literature

By: Shanay Fischer, BS; Ayushi Deshwal, BS

ABSTRACT

Introduction
Osteoarthritis (OA) is one of the most common causes of pain in older adults; yet osteoarthritis of the foot is under-researched when compared to osteoarthritis of the knee or hand. The main joint in the foot affected by osteoarthritis is the first MTP joint (MTPJ), resulting in stiffness, pain, and difficulty ambulating. Treatment options include both surgical methods, such as replacement of the joint, and non-surgical methods, such as foot orthoses (orthotic devices). The purpose of this literature review is to compare the non-surgical methods, specifically the use of foot orthoses versus rocker-sole shoes for the treatment of first metatarsophalangeal joint osteoarthritis.

Study Design: Qualitative Systematic Review of Literature

Methods
A literature search was conducted on PubMed. The search used the term ("Foot Osteoarthritis"[Mesh]) AND ("Foot Orthoses"[Mesh]) and yielded 164 articles. The exclusion criteria included articles written in a language other than English, a focus on surgical interventions, and written before January 1, 2005. This search yielded 137 articles. The inclusion criteria was articles that compare Rocker-Sole to Foot Orthoses and include the term "metatarsophalangeal joint". After applying the aforementioned inclusion and exclusion criteria, 11 papers were found. Of those 11, 4 research articles were used in this literature review because they specifically compare the rocker sole to foot orthotics. Another literature search was conducted on PubMed. The search used the term ("MTP Joint"[Mesh]) AND ("Foot Orthoses"[Mesh]) and yielded 13 articles. The exclusion criteria included articles that were written in a language other than English, a focus on the design of orthoses, and written before January 1, 2005. This search yielded 5 articles. The inclusion criteria was articles that focus on the effectiveness of Rocker-Sole and Foot Orthoses. After applying the aforementioned inclusion and exclusion criteria, 3 papers resulted from the search. Two of those articles were used in the previous search, so the remaining 1 article was used in this literature review.

Results
Both foot orthoses and rocker-sole shoes were effective for reducing pain associated with first MTPJ OA between baseline and post-intervention. The slight differences in the results, however, stem from different pain reduction mechanisms. After finding low compliance and more adverse effects with the rocker-sole shoe, the preferred modality is foot orthoses for individuals with MTPJ OA.
Conclusions
Prefabricated foot orthoses are a superior non-surgical intervention for treating those with first MTPJ OA due to both the effective reduction in pain at the first MTPJ and greater adherence to the intervention itself.

Keywords: orthoses, rocker-sole footwear, conservative treatment, osteoarthritis

Level of evidence: 4
INTRODUCTION

Background

Osteoarthritis (OA) is one of the most common causes of pain in older adults, prominently occurring in the knee. However, osteoarthritis is also commonly seen in the foot. Foot OA affects more than 15% of adults older than the age of 50. This condition is characterized by the breakdown of cartilage in joints and in more severe cases is characterized by the eventual loss of cartilage. The pain associated with osteoarthritis is related to bone rubbing together after cartilage has thinned out and deteriorated. The prevalence of first metatarsophalangeal joint (MTPJ) OA is higher in women, older people, and those from lower socio-economic classes.

Pathogenesis

The main joint in the foot affected by osteoarthritis is the first MTPJ, resulting in stiffness, pain, and difficulty ambulating. The first MTPJ plays a significant role in the propulsive phase of gait; therefore, people with osteoarthritis of this joint will often adopt an apropulsive gait. During the propulsive phase of gait, the foot maintains supination, with maximum forefoot loading occurring just prior to the lower limb moving into the swing phase. This maximum loading would account for the localized pain to the first MTPJ. Despite the number of adults suffering from osteoarthritis of the foot, it is under-researched in comparison to osteoarthritis of the knee or hand.

Treatment

The treatment options for first MTPJ OA include surgical methods (replacement of the joint) and non-surgical methods (foot orthoses or therapeutic footwear, such as rocker-sole shoes). Foot orthoses are customized inserts for shoes. In the case of first MTPJ OA, the inserts would involve a cut-out section below the first metatarsal and cutting the distal edge to the same level as the second to fifth toe sulci. Rocker-sole footwear is a shoe notable for its rounded sole in the anterior-posterior direction with a soft cushioned heel. Rocker-sole shoes are also commonly referred to as rocker bottom shoes. There is limited research which directly compares these two methods; yet individually, both treatments have been shown to reduce joint pain related to OA in the first MTPJ.

Objective

The purpose of this paper is to review the current literature available to compare the non-surgical methods of treatment, specifically the use of foot orthoses versus rocker-sole shoes for the treatment of first metatarsophalangeal joint osteoarthritis.

METHODS

A literature search was conducted on PubMed. The search used the term ("Foot Osteoarthritis"[Mesh]) AND ("Foot Orthoses"[Mesh]) and yielded 164 articles. The exclusion criteria included articles written in a language other than English, a focus on surgical interventions, and written before January 1, 2005. This search yielded 137 articles. The inclusion criteria was articles that compare Rocker Sole to Foot Orthoses and include the term "metatarsophalangeal joint". After applying the aforementioned inclusion and exclusion criteria, 11 papers were found. Of those 11, 4 research articles were used in this
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Figure 1: summary of article acquisition
RESULTS

Foot Orthoses

Welsh et al. performed a two-part clinical trial in order to explore changes in mechanically induced first MTPJ pain and foot and ankle kinematics in response to the use of foot orthoses. Welsh et al. was able to investigate increases in first MTPJ dorsiflexion by assessing changes in pain level following the use of foot orthoses. In the second phase of the study, they attempted to deduce a relationship between first MTPJ pain level and any changes regarding the mechanical effect of orthoses. Originally starting with the screening of 110 referrals, 35 were considered eligible. In addition to other criteria, the 35 subjects' first MTPJ pain was at least 40 mm out of a 100 mm visual analogue pain scale (VAPS). Of the 35, 3 were not able to tolerate the foot orthoses and did not qualify to proceed to the follow-up stage. Of the remaining 32, 10 were willing to attend the exploratory phase of the analysis at the 8-week period. 9 remained after 1 was lost to incomplete data. Of the 32 subjects, significant reduction in median pain score from baseline to 24 weeks was observed (@ baseline: 48 mm -> @ 24 weeks: 14.5 [z=-4.88, p<.001]. At 8 weeks the pain score was 29 mm. At 12 weeks the pain score went down to 20.4 mm. However it was found during the exploratory analysis that pain reduction was not accompanied by systematic changes. No changes were observed in first MTPJ dorsiflexion during the walking cycle of gait analysis (no orthoses median = 8°, IQR = 22.1 vs orthoses median = 7°, IQR = 23.3, p = 0.954) nor were they observed with maximum ankle/subtalar complex eversion (no-orthoses median = 1°, IQR = 8.9 vs orthoses median = 1°, IQR = 6.4, p = 0.672).

Foot Orthoses vs. Rocker-Sole Shoes

Menz et al. was responsible for the first study to ever compare the effect of foot orthoses versus rocker-sole shoes on subjects with first MTPJ OA. The protocol itself is the subject of one article while the remaining analyze the results. Through a
parallel-group, randomized trial comparing 2 interventions, Menz et al. evaluated the effects of both based on spatiotemporal parameters, hip and knee kinematics, and plantar pressures. 97 participants ultimately underwent the gait analysis portion of the study (n = 52 foot orthoses group, n = 46 rocker-sole group). All gait assessments were performed at the baseline assessment. The results of the spatio-temporal and kinematic data following use of foot orthoses indicated a minimal reduction in velocity (Cohen's $d = .14$; negligible effect) as well as a minimal reduction in knee ROM ($d = .44$; medium effect). The rocker-sole shoes led to reduced cadence ($d = .26$; small effect), a reduced percentage of the gait cycle spent in stance phase ($d = .44$, medium effect), and also a reduced sagittal plane hip ROM ($d = .44$; medium effect).

The plantar pressure data was compared as well during the peak pressure recordings. These recordings were analyzed in relation to the pressure data of the participants own footwear. The foot orthoses increased peak pressure under the lesser toes ($d = 50.59$; medium effect) and midfoot ($d = 50.45$; medium effect), and decreased peak pressure under the first MTPJ ($d = 50.55$; medium effect) and heel ($d = 50.72$; medium effect). The rocker-sole shoes decreased peak pressure under the first MTPJ ($d = 50.44$; medium effect), second to fifth MTP joints ($d = 50.92$; large effect), and heel ($d = 50.91$; large effect).

Menz et al. also conducted a follow-up of the study. Subjects were brought in at the 4, 8, and 12-week mark. In the follow-up study, the orthoses group had n = 53 whereas the rocker-sole group had n = 46. It appears the subjects in the orthoses group reported using their treatment modality for a greater amount of time than the rocker-sole group (mean±SD total hours worn over study period: 448±238 in the orthoses group versus 287±192 in the rocker-shoe group; $P<0.001$). At the 4 and 8 week marks, an increase in FHSQ pain domain was reported for both treatment modalities. An increase of 17 points occurred in the foot orthoses group and increase of 22 points occurred in the rocker-sole group. A higher increase in FHSQ score indicates greater improvement in foot health. At the 12-week follow-up there was not a significant difference between the two groups (ANCOVA-adjusted mean difference of 2.05 points; 95% CI -3.61, 7.71; $P = 0.477$).

At the completion of the study, the 15-point Likert scale was used in the assessment of the perception of global improvement and the foot orthoses group reporting a higher score (62% versus 39%; RR 0.63, 95% CI 0.41, 0.99; $P = 0.043$). Also, an NNH score of 5 (95% CI 2.3, 43.9) was determined for the rocker-sole group which means that 1 in 5 subjects using the rocker-sole modality had an unsuccessful outcome compared to the group receiving foot orthoses. At the conclusion of the study it was also found that subjects in the rocker-sole group were more likely to report adverse effects compared to the foot orthoses group (39% versus 16%; RR 2.47, 95% CI 1.12, 5.44; $P = 0.024$; NNH 5, 95% CI 2.4, 23.1).

Additionally, Menz et al. made a distinction between “responders” and “non-responders” through the same parallel group randomized clinical trial in order to identify the specific factors associated with a positive response to the two interventions (foot orthoses and rocker-sole shoe). The study defines a responder as a subject that perceives his overall improvement at week 12 to be above a 4 (4 = moderately better) on a 15-point scale. Ultimately, 29 (62%) subjects were...
classified as responders in the orthoses group and 16 (39%) were classified as responders in the rocker-sole footwear group. In the orthoses group the following variables were unique to responders: greater baseline pain severity while walking, a higher FFI difficulty score, and more frequent use of the foot orthoses. The FFI is the Foot Function Index which is a scale to measure pain, activity level, and disability. In the rocker-sole group the following variables were unique to responders: a higher FFI stiffness score and greater radiographic severity. However, the accuracy of the variables for the foot orthoses group was 62% and the accuracy of the variables in identifying responders for the rocker-sole group was only 53%.

**DISCUSSION**

Based on the 5 articles that were reviewed, it was deemed that both foot orthoses and rocker-sole shoes were effective for reducing pain associated with first MTPJ OA between baseline and post-intervention. However, the reduction of pain caused by these two interventions is achieved through different mechanisms. Welsh et al. focused on the use of foot orthoses alone for treating first MTPJ pain. It was recognized that the pain in the first MTPJ was reduced with foot orthoses, but the changes in pain were not necessarily associated with kinematics. Participants illustrated reduction in pain at 8, 12, and 24 weeks post-intervention. The exploratory analysis did not show changes associated with dorsiflexion of the MTPJ nor altered ankle/subtalar complex eversion. Menz et al. further studied non-surgical interventions for treating first MTPJ OA by comparing prefabricated foot orthoses to rocker-sole footwear. The randomized trial focused on the effectiveness as well as analyzing the mechanism of action for each. Though Menz et al. found that both foot orthoses and rocker-sole shoes reduce pain in people with first MTPJ OA, it was discovered that foot orthoses are likely a preferred method for patients. There were more adverse events, such as new onset back pain, in participants wearing rocker-sole footwear than in those wearing foot orthoses. The study also suggests that participants in the rocker-sole footwear group were less compliant than those in the foot orthoses group due to the appearance of rocker-sole shoes, which may have been less aesthetically pleasing to participants than the foot orthoses, which are concealed inside shoes. With this in mind, though both rocker-sole and foot orthoses have similar changes in FHSQ pain scores, foot orthoses are deemed a more appropriate intervention due to improved compliance. The author does propose that perhaps rocker-sole footwear has the potential for greater effectiveness if the adherence could be surpassed. One of the possible mechanisms in which both interventions benefit pain associated with first MTPJ involves reducing peak pressure beneath the first MTPJ. Menz et al. suggests that foot orthoses achieve this by redistributing load away from the first MTPJ, while rocker-sole footwear appears to achieve this through a reduction in cadence and a reduction in sagittal plane hip motion during gait. Menz et al. also analyzed possible predictors of response for rocker-sole footwear and prefabricated foot orthoses. It was found that further studies are necessary to identify factors that would predict responses to both interventions. Those in the orthoses group had greater baseline pain, greater difficulty ambulating, and wore their intervention more often. Those in the rocker-sole group had greater baseline joint stiffness, greater radiographic OA severity, and wore their intervention less often. These classifications
were not sufficient enough to predict responses in a clinical setting. The main limitation in all of the studies was the inability to blind participants to the intervention they were receiving. The studies discussed here demonstrate effective treatment of first MTPJ OA through different mechanisms for foot orthoses and rocker-sole shoes; however, further research is needed to evaluate the mechanisms and long-term effects.

CONCLUSION

The 5 articles utilized in this qualitative systematic review of literature demonstrated that foot orthoses and rocker-sole footwear were both effective in treating pain associated with first MTPJ OA. Welsh et al. explored changes in first MTPJ pain and kinematics after use of foot orthoses and concluded that the use of foot orthoses demonstrated a significant decrease in first MTPJ pain but was not associated with the kinematics. Menz et al. was the first publication to compare foot orthoses versus rocker-sole footwear for treating first MTPJ OA. The study explores the effectiveness of rocker-sole footwear versus prefabricated foot orthoses in reducing pain associated with first MTPJ OA through a randomized trial. It was concluded that prefabricated foot orthoses and rocker-sole footwear were similarly effective in reducing pain associated with first MTPJ OA, prefabricated foot orthoses had greater adherence, and both interventions achieved a reduction in pain through varying mechanisms which requires further study. After performing a qualitative systematic review of literature using PubMed database, the 5 articles retrieved from the search and reviewed lead us to believe and ultimately conclude that prefabricated foot orthoses are a superior non-surgical intervention for treating those with first MTPJ OA due to both the effective reduction in pain at the first MTPJ and greater adherence.

AUTHORS’ CONTRIBUTIONS

Two authors contributed equally to the production of this article. All conceived the topic, performed initial literature reviews, and authored the introduction, results, discussion, and conclusion. All authors drafted, read, reviewed, and agreed upon the final manuscript.

STATEMENT OF COMPETING INTEREST

The authors declare that they have no competing interests.

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A Systematic Review of the Efficacy of Extracorporeal Shock Wave Therapy in Treatment of Morton’s Neuroma

By: Monica Kelley, BS, BA

ABSTRACT

Introduction
Morton’s neuroma is a common acquired deformity of the forefoot caused by enlargement and inflammation of the third common digital nerve. Morton’s neuroma may be caused by ischemia or accumulated trauma. Accumulated trauma is repeated pressure or force resulting from a variety of etiologies, such as improper shoe wear or underlying biomechanical issues. Morton’s neuroma is characterized by painful walking at toe-off and abnormal paresthesias in the third interspace. Conservative treatments and invasive treatments, such as steroids, orthotics, alcohol injections or neurectomies are palliative in nature and do not treat the underlying etiology of a neuroma. Extracorporeal shock wave therapy (ESWT) is the application of high intensity pulses to an affected area of injury and is currently used for plantar fasciitis and other musculoskeletal conditions. It has been proposed that ESWT may have some use in providing palliative treatment of a neuroma and also reducing the size of a neuroma. The objective of this article is to systematically review current research on the application of ESWT in conservative treatment of Morton’s neuroma.

Study design: Qualitative Systematic Review of Literature

Methods
Pub Med and Pub Med Central searches were conducted using search criteria “extracorporeal shock wave therapy AND neuroma”. Inclusion criteria included studies conducted from 2009 to 2019, as well as studies that focused on the use of ESWT in treatment of Morton’s neuroma symptoms. Exclusion criteria included articles published prior to 2009, studies focusing on treatment of ESWT for other medical conditions, studies focusing on non-ESWT treatments for Morton’s neuroma and repeat studies. There was a total yield of 9 articles.

Results
9 articles were selected for systematic review. Current research found no statistically significant improvement in pain (measured on the Visual Analog Scale) of a Morton’s neuroma with ESWT after one month of treatment (95% CI: 0 to 7.1). Other research suggests that low energy ESWT with a flux density of 0.10 mJ/mm²/min treatment for at least three weeks may result in slight reduction of the diameter of a neuroma. Overall, current research was relatively inconclusive.

Discussion
Although the studies showed moderate reduction in pain with treatment of ESWT, it was not significant compared to placebo after one month of therapy. Ultrasonography indicated that the size of the neuroma pre-treatment and post-treatment did not substantially change. ESWT can therefore be considered an unreliable palliative treatment for Morton’s neuroma.
Keywords: extracorporeal shock wave therapy, treatment, neuroma, Morton’s neuroma

Level of evidence: 4
INTRODUCTION

Morton’s neuroma is an inflammation, enlargement and fibrosis of the third common digital nerve located in the pedal third intermetatarsal space. It is worthy to note that the third common digital nerve is a rather small nerve located between two large metatarsal heads and close to other ligaments in the forefoot which may make the nerve susceptible to pathology. The exact etiology of Morton’s neuroma has been debated, but there are some commonly accepted etiologies of the condition. One etiology suggests Morton’s neuroma may be due to an entrapment of the third common digital nerve between the third and fourth metatarsal heads, plantar to the deep transverse metatarsal ligament. Other etiologies of Morton’s neuroma have also been considered, such as ischemia of the third common digital nerve or compression of the nerve by enlarged intermetatarsal bursa. However, there is general agreement that neuromas are caused by some form of nerve entrapment from surrounding structures that subsequently cause inflammation of the nerve.

When considering the etiologies of Morton’s neuroma, it is worthy to take biomechanical abnormalities into consideration. Studies have shown that during late stance phase, a hypermobile first ray can cause excessive compression of the common digital nerves between the plantar foot and the overlying deep transverse metatarsal ligament. Increased compression force is a result of transfer forces from the first ray to lateral metatarsals. Patients with a neuroma may therefore also present with comorbidities of stress fractures of the lesser metatarsals as a result. These same compressive forces also increase pressure on bursa between the metatarsal heads, causing their inflammation and enlargement - further contributing to the development of a Morton’s neuroma. Any other forefoot conditions, such as degenerative joint disease or plantar plate rupture, which causes abnormal positioning of forefoot structures, are implicated in producing excessive force that compresses and inflames the common digital nerves. It is important to note that these mentioned biomechanical etiologies are the result of chronic compression and irritation of the common digital nerves, so early treatment of structural or biomechanical abnormalities is essential in hindering the development of a Morton’s neuroma.

Morton’s neuroma is most commonly seen in middle aged adults, with women being ten times more likely to present with neuromas than men. The development of a neuroma can be attributed to injury, narrow and non-supportive shoes, or repetitive trauma to the forefoot, which may occur in sports with high contact force of the foot such as tennis or long distance running. The chief complaint that patients present with is painful, burning sensation to the third interspace when walking. Patients often describe a sensation of walking on a pebble or a small sharp object. Patients may also notice that the pain is exacerbated when wearing narrow shoes or high heels, which improves when wearing wider shoes.

Differential diagnosis of a neuroma may include a plantar plate rupture, neuropathy, metatarsal stress fractures or interdigital neuritis.

Specific physical findings of a neuroma may reveal splaying of the third and fourth toes, known as the Sullivan sign. A patient may experience pain and tenderness upon palpation of the foot, proximal to the third interspace Paresthesia to the third interspace.
is confirmed by a Tinel’s test. Lateral compression of the metatarsal heads with simultaneous palpation of the plantar third interspace may produce a palpable “click”, known as Mulder’s sign.

Recent studies have found that while clinical signs are the most sensitive in diagnosing a Morton’s neuroma, ultrasound and MRI with or without contrast are also additional diagnostic tools that are used for further confirmation of a Morton’s neuroma. Such imaging modalities are essential to rule out aforementioned differential diagnoses, specifically metatarsal stress fracture. As mentioned previously, patients with transfer forces to the lateral forefoot may not only present with a Morton’s neuroma, but also stress fractures and it is therefore important to discern whether a patient exhibits both a neuroma and a stress fracture. It is also essential to detect normal attachment of the plantar plate to metatarsal heads and proximal phalanges, as plantar plate tears can cause subluxation of metatarsophalangeal joints and contribute to Morton’s neuroma. An MRI and ultrasound of a healthy patient will ideally present with an intact plantar plate, an absence of stress fractures and degenerative joint disease, and no noticeable enlargement of common digital nerves of bursa. Ultrasound of a neuroma presents as a round to ovoid lesion proximal and plantar to the third and fourth metatarsal heads. Imaging may also present with enlarged intermetatarsal bursa and the previously mentioned possible comorbidities. Regardless of the effects of ESWT, imaging should be used in diagnosis of a Morton’s neuroma. Imaging may also be useful in assessing whether a patient has resolution of clinical symptoms, but should not be substituted for other clinical tests such as the visual analog scale (VAS), Mulder’s click, gait analysis and other tests.

Initial treatment of neuromas is often conservative and includes orthotics, wide shoes, physical therapy, steroid injections or alcohol sclerosing injections. While these conservative treatments may provide pain relief to the forefoot, they primarily reduce inflammation or prevent further inflammation from occurring. The ideal goal of treatment for Morton’s neuroma would be to treat the etiology of a neuroma itself.

Neurectomy is a surgical procedure that involves complete removal of a neuroma from a patient’s foot. Although neurectomy improves symptoms, it can lead to scar tissue formation, subsequent development of a new neuroma (which is known as a “stump neuroma”) and numbness around the third interspace.

Extracorporeal shock wave therapy, or ESWT, may be used after common and accepted non-invasive treatments have failed. ESWT is a non-invasive treatment that involves applying continuous, high intensity pulsating acoustic waves to an affected area of injury. ESWT was originally used in the treatment of kidney stones and is currently being used to treat plantar fasciitis, delayed union of fractures, and various tendinopathies of the lower extremity. In recent years, there has been increasing research of using ESWT for the treatment of Morton’s neuromas. Research has suggested that ESWT can inhibit pain receptors in the forefoot and provide temporary pain relief caused by a Morton’s neuroma. In other biologic tissues, such as bones and tendons, high intensity shock waves cause disruption of cellular pathology that is not currently well understood, but results in tissue regeneration.
and healing. Therefore, it may be plausible to reason that ESWT may have a similar effect on inflamed neural tissue. The objective of this study is to systematically review the efficacy of extracorporeal shock wave therapy (ESWT) in patients with Morton’s neuroma.

**METHODS**

Studies were searched using PubMed and PubMed Central via the US National Library of Medicine. Studies were found by using the search term “extracorporeal shock wave therapy AND neuroma”. PubMed yielded 8 articles; PubMed Central yielded 33 articles. Inclusion criteria included studies done in the past 10 years from 2009 to 2019 and studies that focused on the treatment of a neuroma or Morton’s neuroma with ESWT. Exclusion criteria included articles focusing on the application of ESWT in treatment of other medical conditions, studies completed more than 10 years ago, repeat studies from another database used in the literature search, studies that focused on neuroma but did not study ESWT as treatment, case reports and instructional reviews. After application of inclusion and exclusion criteria, there was a total yield of 9 articles; 7 included from PubMed and 2 included from PubMed Central.

**RESULTS**

A systematic review by Matthews et al. examined the efficacy of non-surgical interventions for Morton’s neuroma. One article assessed in the Matthews systematic review (Seok et al) was included in this current systematic review, as the article by Seok et al studied the efficacy of ESWT in treatment of Morton neuromas. All articles that Matthews et al included in their systematic review were quantified by using the visual analog scale (VAS) on a scale of 0 – 100 using the data from each original study. In order to remove potential bias in studies, three independent reviewers evaluated each study and rated the studies based on a quality index. The index took inter-rater reliability, reproducibility, and study design type into consideration. After assessment of ESWT-specific studies, Matthews et al concluded that there is no significant reduction in pain after one month of treatment with ESWT (MD: -5.9, 95% CI: -21.9 to 10.1). The systematic review also found that there is no statistically significant improvement in terms of the VAS of a Morton’s neuroma with ESWT after one month of treatment (95% CI: 0 to 7.1). The systematic review by Matthews et al suggests that ESWT is not effective in
treating Morton’s neuroma or in reducing pain.

In Matthews systematic review, a study conducted by Seok et al. was included, which focused on the use of ESWT as treatment for Morton’s neuroma. The study by Seok used the visual analog scale (VAS), American Orthopaedic Foot and Ankle Society lesser toes (AOFAS) scores, and Johnson satisfaction tests to measure pain relief in patient’s with Morton’s neuroma. The Johnson satisfaction test is measurement of neuroma diameter each week of the study. The study found decreased VAS scores and improvement of AOFAS scores, indicative of improvement in pain, but an insignificant decrease in the diameter of neuromas using the Johnson satisfaction test. The original study conducted by Seok et. al was inconclusive and suggested the possibility of reduction in pain with Morton’s neuroma. Overall, the study alludes that increasing treatment duration for more than one month may result in significant reduction of the diameter of the neuroma with ESWT.

Jung et al performed a randomized controlled trial study which focused on the efficacy of ESWT on stump neuroma. Although stump neuroma has a different etiology than Morton’s neuroma, the study evaluated reduction of various types of neuroma sizes with ESWT, and may be useful in inferring how Morton’s neuroma would respond to ESWT. The study consisted of 15 patients who were treated with ESWT once per week for a duration of three weeks. Neuroma diameter was measured weekly using ultrasonography and was used to verify effectiveness of ESWT in neuroma treatment. Jung et. al used the McGill pain questionnaire and VAS to quantify pain. It was found that patients experienced reduction in pain after treatment (38.8+/- 9.0 to 11.3 +/- 3.1). However, similarly to the Seok et. al study, there was no significant change in neuroma size.

Fridman et al conducted a placebo-controlled double blinded study to assess the efficacy of ESWT in treating neuromas. Patients included in the study had a visual analog scale pain score of 4 or greater prior to ESWT and had a neuroma for at least 8 months. Five milliliters of bupivacaine hydrochloride and ESWT of 21,000 pulses at 21 kV was given under sedation once a week for 12 weeks. The placebo group was also given sedation and 5 mL of bupivacaine hydrochloride was injected at the site of the neuroma; however the placebo patients did not receive ESWT. The study found that the 13 patients treated showed significant pain reduction, with 69% of patients reporting a visual analog score of 3 or less after 12 weeks of treatment. However the results of the study may not be as promising due to the small sample size. A literature review by Jain et al noted that the Fridman et al study did not extrapolate the results of the small sample size to a larger population, and also emphasized that use of the visual analog scale in reporting pain can be subjective.
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<td>No significant reduction in pain after 1 months of therapy</td>
<td>MD: -5.9, (95% CI: -21.9 to 10.1).</td>
<td>No significant improvement after 1 month of therapy</td>
<td>95% CI: 0 – 7.1.</td>
</tr>
<tr>
<td>Seok et al</td>
<td>Significant reduction in pain after 1 month of therapy</td>
<td>MD: -28.3, (95% CI -37.8 to 18.8)</td>
<td>No significant improvement after 1 month of therapy</td>
<td>95% CI: 0% (0 – 22)</td>
</tr>
<tr>
<td>Jung et al</td>
<td>Significant reduction in pain after 3 weeks of therapy</td>
<td>95% CI: 38.8± 9.0 to 11.3± 3.1</td>
<td>No significant improvement after 1 month of therapy</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>Fridman et al</td>
<td>Significant reduction in pain after 12 weeks of therapy</td>
<td>95% CI: 2.46 (p &lt; 0.0001)</td>
<td>Significant improvement after 12 weeks of therapy</td>
<td>Patients: (P &lt; 0.0001) Control: (p &lt; 0.1218)</td>
</tr>
</tbody>
</table>

Table 1. Summary of literature review outcomes

**DISCUSSION**

The literature review of treatment of Morton’s neuroma with ESWT is unique in that it appears to reduce pain in patients but does not affect the neuroma size itself. The extrapolation of data from Mathews et al suggests that there may be lack of significant reduction in pain after 1 month of therapy.5 Despite the findings by Seok et al and Jung et al of pain reduction with use of ESWT, it is noteworthy that control patients (who received transcutaneous electrical nerve stimulation and pharmacologic treatment) experienced a reduction in pain as well.5 This could be a likely outcome due to ESWT transmitting acoustic pulses which provide an overall temporary reduction in sensation from the neuroma as well as other unaffected nerves in the area of the neuroma. Fridman et al is the only study that had relatively different reports in pain reduction among patients and controls. However, the small sample size and limited use of statistical analysis in the study makes it difficult to assess whether the findings are applicable to a larger population.4

The use of ultrasonography is significant because it was important to confirm the reduction of neuromas size, which directly correlates with treatment of the underlying condition. Although the studies had a short duration, lasting from 3-12 weeks, follow up studies of longer treatment with ESWT would have been useful to determine slight reduction in neuroma size with ESWT. Although acoustic pulses from ESWT are useful in reducing inflammation in other tissues, such as plantar fascia, the studies confirmed that neuroma size, fibrosis and inflammation cannot be effectively treated with ESWT.4

**CONCLUSION**

ESWT can be used as a temporary pain relief of symptoms, similar to treatments
such as corticosteroid injections. ESWT is not a preferential non-invasive treatment for Morton’s neuroma, as the compliance rate can be low due to patients requiring a weekly treatments for at least 12 weeks.\textsuperscript{4} The reviewed literature suggests that ESWT is not effective in reducing the size of a neuroma or preventing the progression of neuroma development.\textsuperscript{4,5,6} Although neurectomies are associated with possible complications, they may be the most reliable current option in treating a Morton’s neuroma.

**STATEMENT OF COMPETING INTERESTS**

The authors declare that they have no competing interests.

**REFERENCES**

6. Hulstaert T., Shahabpour M., Provyn S. Forefoot pain the lesser toes: anatomical

Foot and Ankle Synovial Chondromatosis: A Literature Review

By: Yolisept C. Bencosme, MBS, BA; Stephan L. Joseph, MPH

ABSTRACT

Introduction

Synovial Chondromatosis (SC) is a benign and rare condition of unknown etiology that is most commonly seen in large joints such as the shoulder, hip and knee. Despite the subdivisions of primary and secondary chondromatosis, it is thought to be the result of both metaplasia and hyperplasia of chondrocytes. The process is described as occurring in three phases that begin either spontaneously, as in primary chondromatosis, or following degenerative conditions, as in secondary chondromatosis. This condition is more common in men than in women and is seen more often in middle aged patients; however, there are case reports describing the pathology in much younger patients, involving individuals of prepubescent age. The purpose of this literature review is to describe chondromatosis in joints of the lower extremity, with special attention to the foot and ankle. Additionally, the discussion will present the most current intervention for treatment and address the need for further research on this subject.

Study Design: Qualitative systematic review of literature

Methods

An English language literature search was conducted on the PubMed database. Articles related to knee, foot and ankle synovial chondromatosis were found using the search terms: (“chondromatosis, synovial”[MeSH Terms] OR (“chondromatosis”[All Fields] AND "synovial”[All Fields]) OR "synovial chondromatosis”[All Fields] OR (“synovial”[All Fields] AND "chondromatosis”[All Fields])) AND (“loattrfree full text”[sh] AND (“2000/01/01”[PDAT]: “2019/12/31”[PDAT])). The inclusion criteria included foot and ankle synovial chondromatosis, in both male and female subjects, between the years 2000-2019. The exclusion criteria; were “hip chondromatosis, patients younger than 20 years old, case reports/series in which both benign and malignant tumors were evaluated.

Results

205 articles were found with the initial search inquiry. When the inclusion and exclusion criteria were applied, a total of 20 case reports were found to be relevant to the topic. This included 16 male case reports and 5 female case reports.

Conclusion

While many case reports share key features that allow for the delineation between primary and secondary SC, predisposing factors cannot be fully defined. In carrying out this literature review, patterns between history or trauma/injury and SC prevalence were analyzed. At this time a causal connection between trauma and SC cannot be proposed as trauma preceding the onset of SC was variable among the case reports reviewed. In every case, histological examination confirmed the diagnoses of SC and evidence of benign neoplastic changes. Milgram classified SC as occurring in three stages, but this review suggests the classification is variable.

Level of evidence: 4
INTRODUCTION

Synovial chondromatosis (SC) is a rare arthropathy of unknown etiology. Although most often affecting larger joints such as the hip, knee and shoulder, SC has been found to affect the joints of the foot and ankle, as well as the temporomandibular joint. This is a condition in which benign cartilaginous nodules infiltrate the synovium following what’s thought to be a benign neoplastic process. The underlying mechanism of this pathological process is not well understood, however research suggests SC may occur as either a primary or secondary form. In either case, metaplastic and hyperplastic processes of chondrocytes are thought to play a role in the formation of cartilaginous nodules. The nodules have been found as free floating intra-articular bodies as well as coalesced cartilaginous masses in the affected joints. As such, the development of SC is characterized as a gradually progressive pathological process that usually affects monoarticular and unilaterally.

Primary SC is considered the rarer form because it is thought to ensue spontaneously in three phases without underlying comorbidities and without a traumatic stimulus. It is also generally thought to be more progressive, more likely to recur, and may lead to severe degenerative conditions. During the initial phase of primary SC metaplastic changes in chondrocytes precipitate the formation of cartilaginous nodules that remain attached to the synovial lining of the affected joint. The translational phase is marked by the detachment of the nodules as free-floating bodies within the synovial fluid. During the inactive phase, the nodules calcify and may coalesce to form large masses of cartilage or remain as multiple free floating bodies in the affected joint. The nodules remain benign entities and rarely precipitate malignancy.

Secondary SC is thought to succeed trauma as well as degenerative conditions such as osteoarthritis and rheumatoid arthritis. In the latter, preexisting conditions may “mask” SC as the culprit of a patient’s new onset of pain or progressive discomfort which makes it difficult to diagnose; most patients have a lengthy clinical history before an accurate diagnosis is made. The former has been considered to incite the development of SC in up to 50% of reported case reports, especially among physically active patients. However, in either case the exact trigger for metaplastic changes in chondrocytes remains unknown and controversial.

Case reports suggest males are twice as likely to be affected, with a mean age of 47.7 years. SC of the knee accounts for more than 50% of the reported case reports and the exact prevalence of SC in the foot and ankle are unknown and thought of as rare occurrences. However, there have been previous reports of primary SC found in the subtalar, naviculocuneiform, calcaneocuboid and metatarsophalangeal joints.

Clinical presentation
The presentation of SC is often gradual and asymptomatic. Patients often offer a vague history of several years of joint pain and swelling, that may or may not include history of trauma. Milgram (1977) characterized symptoms of SC dependent on the phase of the disease. Phase 1 he characterized as swelling, phase 2 he characterized as pain and swelling, and phase 3 he characterized as pain, swelling and limited range of motion. However, the classification of symptoms is variable as the triad of pain, swelling, and decreased range of motion is not present in every case of SC.
Synovial chondromatosis of the foot and ankle is exceedingly rare. Most case reports involve adult patients, but there are reports that discuss the pathology in children. SC of the ankle is more common than SC of distal joints of the foot; SC of the talonavicular and Lisfranc joints are rarer still, with two such reports, respectively, to date. In almost all case reports used for this literature review patients complained of progressively worsening pain, with mild swelling. In some case reports there was no history of trauma, while in others history of trauma seemed either to precipitate or worsen the pain and swelling thus motivating the patient to seek medical attention. Some patients experienced limited range of motion, while others remained with bilateral, symmetrical range of motion.

METHODS

The search phrase “Synovial Chondromatosis” was used using Science Direct for articles published in the Journal of Foot and Ankle Surgery that resulted in a total of 23 articles. The inclusion criteria included foot and ankle synovial chondromatosis, in both male and female subjects, between the years 2000-2019. The exclusion criteria; were “hip chondromatosis, patients younger than 20 years old, case reports/series in which both benign and malignant tumors were evaluated. A total of 5 articles were selected.

A PubMed search was conducted using the search phrase: ("chondromatosis, synovial"[MeSH Terms] OR ("chondromatosis"[All Fields] AND "synovial"[All Fields]) OR "synovial chondromatosis"[All Fields] OR ("synovial"[All Fields] AND "chondromatosis"[All Fields])) AND ("loattrfree full text"[sb] AND ("2000/01/01"[PDAT]: "2019/12/31"[PDAT])). The search resulted in 182 articles. The inclusion criteria included foot and ankle synovial chondromatosis, in both male and female subjects, between the years 2000-2019. The exclusion criteria; were “hip chondromatosis, patients younger than 20 years old, case reports/series in which both benign and malignant tumors were evaluated. A total of 16 articles were selected. Between the two search engines a total of 21 articles were selected.
RESULTS

Knee Joint
SC is a rare condition most often affecting large joints. When it occurs in the lower extremities, the knee accounts for more than 50% of case reports. The disease is typically intracapsular, but it may occur extracapsular, albeit rarely. Mackenzie et al (2010) reported an exceedingly rare case in which a 49-year-old male presented with both intra- and extra- capsular SC. The patient described 6 months worth of pain and swelling, exacerbated with weight bearing and ambulation. The physical exam revealed full range of motion with knee extension, but limited range of motion with knee flexion. His clinical history was unremarkable, he denied history of injury or trauma, and denied personal and known familial inflammatory diseases. The history and findings led to the diagnosis of primary SC which coincides with the current characterizations of primary SC. While the exact etiology causing the condition is unknown, and while taking into account the presence of intra- and extra- capsular calcified nodules, the authors postulated that either intra-articular SC penetrated the popliteal bursa giving rise to extra-capsular nodules, or bursal chondromatosis infiltrated the knee joint leading to intra-capsular SC. Cartilage cells were absent inside the synovial membrane thus suggesting metaplastic changes of the synovial cells into chondrocytes and hyperplasia thereafter. These findings further strengthen the theory that metaplasia and hyperplasia
play significant roles in SC formation. This is the only case, to date, in which both intra- and extra- capsular SC coexisted in the same joint and therefore warranted special mention.\(^7\).

In the case reports reviewed, most patients with SC affecting the knee sought medical attention after months or years of gradually progressive knee pain and swelling. In all case reports patients experienced decreased range of motion in either knee extension or knee flexion, or both, and in all cases full range of motion was regained after treatment. Interestingly enough, most case were devoid of a history of trauma or injury that might have precipitated the disease — this by definition rules out secondary SC and suggests primary SC as the diagnoses. Additionally, most case were devoid of pre-existing inflammatory conditions as well as familial history of inflammatory disease.

Another commonality of the physical examination revealed wasting of the quadriceps muscles. Osteoarthritic changes were mostly attributed to SC and noted as a possible postoperatively adverse effect.\(^2,4,15,\)\(^1\) It should be noted that most patients described a “locking” sensation. This is a common symptom found in other conditions such as meniscus damage, Osteoarthritis (OA), osteochondritis dessecans, osteochondral fractures, synovial cyst, etc.\(^8\) which makes it difficult to rule out other conditions based on clinical presentation alone. Therefore, radiographic imaging and MRI modalities, as well as laboratory studies, were used to make the diagnosis of SC. Grace et al (2018) laboratory results included rheumatoid factor (among others) to rule out Rheumatoid Arthritis (RA).

Positive weekly results prompted an RA referral which the patient complied with seven months after the fact. The rheumatologist, however, was unconcerned with the positive weekly results and ultimately ruled out RA as a possible diagnosis after his/her assessment. This case illustrates how closely the clinical presentation of SC can mimic that of inflammatory conditions and potential misdiagnoses.

**Ankle Joint**

SC of the foot and ankle are rare occurrences, with the ankle accounting for the majority of the case reports and the distal joints involved in seldom case reports. Kim, J.B., Song et al (2016) reported a case in which a 45-year-old female with persistent foot pain and swelling sought medical attention after noting her condition was becoming progressively worse over the two months prior to her visit. She denied a history of injury or trauma and her medical history was unremarkable. Ambulation and footwear exacerbated her pain, but she denied any locking or clicking sensations. Physical examination revealed only focal swelling without erythema over the anterolateral ankle and a non tender 4x3cm soft tissue mass. A non tender 1x2cm mass was also found around the anterior to medial malleolar aspect of the foot. Both masses were described as firm and immobile. The patient had symmetrical normal alignment of the hindfoot, midfoot, and forefoot.\(^5\) Plain radiographic imaging and MRI modalities revealed a cystic mass extending from the talonavicular joint to the sinus tarsi, but no loose bodies were evident at this time. The surgeons decided to excise the mass using a lateral approach centered over the mass\(^5\) and indeed found multiple loose bodies and a hypertrophied synovium. These findings, alongside the patient’s clinical presentation, and lack of medical history, suggested primary SC. The diagnosis was confirmed histologically and malignancy was ruled out.
A year later, the patient was asymptomatic and without recurrence;\(^5\) she returned to her normal physical activities. The SC occurred in the talonavicular joint while the ankle and hindfoot remained asymptomatic. There is only one other reported case in which SC occurred in the talonavicular joint, but unlike the one presented here, both the ankle and hindfoot were symptomatic.\(^5\) To date, the case presented here is the only one of its kind. It’s important to note this patient sought medical attention during phase II \(^5\) of the disease and loose bodies were encountered only after the surgeons decided to remove the mass. It is unclear if the cystic mass preceded the formation of loose bodies or if the mass was the result of the condition. However, primary SC suggests spontaneity rather than the result of a preexisting condition and therefore it’s plausible the cystic mass occurred after the formation of cartilaginous bodies following a hypertrophied synovium.

Fujita et al (2006) reported a unique case of SC in the Lisfranc joint. A 69-year-old female presented with a ten year history of left foot pain. She sought medical attention four years after a vase fell on her foot which further exasperated her discomfort and since then her pain worsened with ambulation and prolonged standing.\(^3\) Physical examination revealed a hard mass over the dorsal aspect of the intermetatarsal space of the fourth and fifth metatarsal bones.\(^3\) The mass was firm and non-tender and the skin was neither warm to touch nor erythematous. Radiographic imaging revealed calcified nodules around the proximal third of the fourth and fifth metatarsal bones and the cubometatarsal joint.\(^3\) A CT revealed multiple nodules in the plantar and dorsal aspects of the left foot, coinciding with the patient’s complaint of pain during prolonged standing and walking. The CT also demonstrated an intra-articular calcified focus\(^3\) of the Lisfranc joint. These findings led to the diagnosis of SC and surgical treatment. During a follow-up visit the patient was able to walk without pain, and imaging confirmed the absence of osteoarthritic changes of the Lisfranc joint.\(^3\) The authors did not specify whether the diagnosis was of primary or secondary SC. However, given the patient’s clinical presentation, and the lack of preexisting inflammatory disease, it’s plausible the diagnosis was primary SC likely aggravated by the injury. The lack of recurrence postoperatively, and lack of degeneration of the Lisfranc joint is important to note because, as previously mentioned, primary SC is thought to lead to degenerative disease and recurrence. In accordance with Fujita et al, a longer follow-up period is necessary\(^3\) to fully evaluate postoperative success and “cure” of SC.

If SC of the foot and ankle are rare, tenosynovial chondromatosis is exceedingly rare. It has been thought of as an extra-articular counterpart of SC which more often occurs intra-articularly.\(^6\) Lui, T.H. et al (2015) presented three case reports of SC of the flexor hallucis longus (FHL), each treated by tendoscopy. The key difference among the three patients were their respective medical histories. Patient one (49-year-old female) denied any history of trauma. Patient two (58-year-old male) complained of the onset of pain status post a fall. Patient three (61-year-old male) reported a history of repeated inversion ankle sprains.

Patient one complained of a spontaneous onset of pain and swelling of six-month duration. The pain was mechanical in nature.\(^6\) Physical exam revealed full range of motion and mild swelling overlying the FHL
region. The skin was warm to touch. Radiographic imaging and MRI revealed an intact tendon and multiple dense foci along the tendon sheath along with a 4x8mm osteochondral lesion in the medial talar dome. A tendoscopy was performed and loose bodies were removed. Histological examination confirmed SC.

Patient two experienced worsening pain upon ambulation for five years following trauma. Plain film did not reveal abnormalities. However, MRI imaging revealed a 12x10x28mm ganglion alongside ≥ 4mm osteocartilagenous nodules. The FHL remained intact. A tendoscopy was performed and multiple nodules along the sheath were removed. A 29-month follow-up revealed no evidence of recurrence.

Patient three was a former soccer player with a history of repeated ankle sprains. He presented complaining of ankle pain with walking and squatting lasting a year. During a physical exam the ankle was not tender to palpation but the pain was reproducible with passive dorsiflexion. Radiographic images revealed osteoarthritic changes and ossified bodies at the posterior ankle. MRI revealed loose bodies along the tendon sheath and under the sustentaculum tali. The FHL itself remained intact. At a 23-month follow-up the patient was asymptomatic with no evidence of recurrence.

Each of these case reports are unique in their reproducibility of pain, tenderness, and most notably the onset. However, they share a key feature, an intact FHL tendon despite loose cartilaginous bodies found along side the tendon sheath. Range of motion was preserved in each of the cases and full activity without recurrence of disease was observed during follow-up visits. Considering the rarity of these case reports, and tendinous involvement, it is unclear if the onset of the patient’s conditions, along with their respective medical histories, are enough to classify the case as primary or secondary SC. As such, Lui T.H et al. described tenosynovial osteochondromatosis as a counterpart to SC.

To date, there have only been five reported cases of SC involving the FHL — including the case reported by Lui, T.H. et al— and only one involved the triad of the FHL, FDL, and tarsal tunnel. The case used for this literature review (the only such case to date) described extensive involvement of the FHL, FDL, PT, and tarsal tunnel. Shearer, H et al (2017) reported a case of a twenty-six-year-old male that complained of chronic and persistent bilateral ankle pain. The pain was exasperated with physical activity and the patient described locking sensations. Physical examination demonstrated decreased range of motion with active dorsiflexion until the patient manually self-mobilized, and decreased range of motion with plantarflexion. Alignment was normal. The ankle was devoid of edema and erythema. The patient was initially diagnosed with bilateral synovial hypertrophy and ligamentous laxity, however radiographic imaging revealed multiple calcified free-floating nodules. The ankle mortise and subtalar joint spaces were maintained, but mild degenerative joint disease was evident; the diagnoses was changed to primary SC. The patient later returned for another visit, status post an inversion left ankle sprain, and imaging revealed several free-floating cartilaginous bodies. Conservative treatment failed and the patient was referred to an orthopedic surgeon.

The aforementioned case reports warranted special mention because of their rarity. The
the following table presents all of the case reports used for this literature review. While SC of the foot and ankle are generally rare, the following case reports are ‘more common” relative to those presented above.

<table>
<thead>
<tr>
<th>Author</th>
<th>Location of Synovial Chondromatosis</th>
<th>Case</th>
<th>Previous Trauma Prior to Chief Complaint</th>
<th>Diagnostic Imaging</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dorsal et al. (2007)</td>
<td>• Left ankle</td>
<td>• 22 year-old</td>
<td>• No</td>
<td>• X-ray • MRI</td>
<td>Arthroscopy • Standard anterolateral approach under manual traction and manipulation • Hypertrophic synovium on anterior aspect of the lateral malleolus, was excised • Bone spur on the anterior aspect of the distal, tibial, articular surface was excised • Loose bodies were excised • After compressive dressing, early active motion of the ankle joint was started</td>
<td>• Immediately post-op, patient was allowed to bear weight • No immobilization administrated under accelerated physiotherapy • Pain free</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Author</th>
<th>Location of Synovial Chondromatosis</th>
<th>Case</th>
<th>Previous Trauma Prior to Chief Complaint</th>
<th>Diagnostic Imaging</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filho et al. (2011)</td>
<td>• Left knee • Osteoblastic infrapatellar mass</td>
<td>• 40 year-old</td>
<td>• N/A</td>
<td>• X-ray • MRI</td>
<td>Surgical: total excision of the mass • A splint on the malleolar thigh for analgesia for one week • After splint was removed released for physiotherapy</td>
<td>• 2 months, ROM returned to normal • Anatomo-pathological examination confirmed synovial chondromatosis</td>
</tr>
<tr>
<td>Fujita et al. (2006)</td>
<td>Left foot</td>
<td>Multiple calcified masses around the cubometatarsal joint and proximal 3rd of the 4th and 5th metatarsal bones</td>
<td>69 year-old</td>
<td>Left foot pain and discomfort</td>
<td>Yes</td>
<td>X-ray, CT, MRI</td>
</tr>
<tr>
<td>Grace et al. (2018)</td>
<td>Left Knee</td>
<td>Bakers Cyst</td>
<td>34 year-old Male</td>
<td>Anterior left knee pain and swelling of insidious onset</td>
<td>Veteran</td>
<td>No</td>
</tr>
</tbody>
</table>

- Base of 4th Metatarsal bone was then subluxed dorsally and 5th metatarsal bone was dislocated laterally to expose the intermetatarsal space and plantar aspect of the Lisfranc joint.
- Which then the masses from plantar aspect were removed.
<table>
<thead>
<tr>
<th>Study</th>
<th>Location</th>
<th>Age</th>
<th>Sex</th>
<th>Symptoms</th>
<th>Imaging</th>
<th>Surgical Intervention</th>
<th>Follow-up</th>
<th>Other Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim et al. (2016)</td>
<td>Ankle, Anterolateral ankle and anterior to the medial malleol</td>
<td>45 y.o</td>
<td>Female</td>
<td>Persistent foot pain, swelling, and discomfort</td>
<td>X-ray, MRI</td>
<td>Surgical intervention, Excision of masses was carried out</td>
<td>12 month follow-up</td>
<td>Patient pain free and had no restrictions in activity or shoe wear, No recurrence of lesions</td>
</tr>
<tr>
<td>Lui et al. (2015)</td>
<td>Left ankle, Between posterior talar process and FHL tendon</td>
<td>49 y.o</td>
<td>Female</td>
<td>Spontaneous onset of left ankle pain and swelling for 6 months, History of hypertension and psoriasis</td>
<td>X-ray, MRI</td>
<td>Arthroscopy, FHL Tendonscopy, Posterior Subtalar Arthroscopy, Removal of loose bodies and synovectomy were performed</td>
<td>Preoperative signs and symptoms were resolved, No neurological complication, No recurrence was found at 19 months post-op</td>
<td></td>
</tr>
<tr>
<td>Mackenzie et al. (2010)</td>
<td>Right Knee, Intra- and extra-articular disease</td>
<td>49 y.o</td>
<td>Male</td>
<td>6 month history of progressively worsening right knee pain and swelling</td>
<td>X-ray, MRI</td>
<td>Arthroscopy, Synovectomy with debridement and excision, Open exploration of popliteal fossa</td>
<td>Recovered full ROM, Residual medial joint line tenderness due osteoarthritis</td>
<td></td>
</tr>
<tr>
<td>Reference</td>
<td>Location</td>
<td>Diagnosis</td>
<td>Age</td>
<td>Gender</td>
<td>Procedure</td>
<td>Results</td>
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<tr>
<td>Majima et al. (2009)</td>
<td>Left Knee, Synovium of ACL</td>
<td>36 year-old Male, Knee pain, Damage to meniscus</td>
<td>Yes</td>
<td>MRI</td>
<td>Arthroscopy, Removal of synovium</td>
<td>Pain dramatically decreased, Full weight bearing started at postoperative (post-op) day one, MRI, the ACL presented normal signal intensity and no thickening of other synovia, 4 years after surgery, no pain</td>
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<tr>
<td>O’Connel et al. (2017)</td>
<td>Right knee, Hoffa’s Fat pad</td>
<td>33 year-old Male, 6 month history of worsening knee pain</td>
<td>No</td>
<td>X-ray, CT, MRI</td>
<td>Excision biopsy of lesion under general anesthetic, Lesion completely excised</td>
<td>Uncomplicated and rapid recovery, 2 weeks, his would healed, 6 weeks knee was pain free, Histological findings showed lobulated, predominantly cartilaginous tissue with foci of ossification and vascular proliferation consistent with solitary synovial osteochondroma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ozmeric et al. (2014)</td>
<td>Right ankle, Anterior ankle joint, Anterior impingement syndrome</td>
<td>28 year-old Male, Progressive pain with reduced ROM for a 1 year</td>
<td>No</td>
<td>X-ray, MRI</td>
<td>Arthroscopy, Ankle joint entered via anteromedial and anterolateral arthroscopic portals during spinal anesthesia and tourniquet application, Arthroscopic partial synovectomy and excision of loose bodies</td>
<td>11th month post-op, patients dorsiflexion and plantar flexion were 25° and 30°, No complications were diagnosed in the follow period with no recurrence on diagnostic imaging</td>
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</tr>
<tr>
<td>Ozyurk et al. (2013)</td>
<td>• Left ankle subcentimeter structures in anterior aspect of tibiotalar joint</td>
<td>• 35 year-old male with 18 month history of chronic left ankle pain and swelling</td>
<td>• N/A</td>
<td>• X-ray</td>
<td>• MRI</td>
<td>• Open excision of the osteochondromatous lesions within the joint</td>
<td>• N/A</td>
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<tr>
<td>Pinter et al. (2019)</td>
<td>• Right ankle mass involving the tendon sheaths of FHL, FDL, and PT tendons with extension through the planar tarsal region</td>
<td>• 48 year-old male with 6 to 8 weeks of plantar heel pain and slowly enlarging mass for the past 6 years</td>
<td>• N/A</td>
<td>• X-ray</td>
<td>• MRI</td>
<td>• Initial opted for conservative treatment with a boot, NSAIDS, and physical therapy. 10 week follow, patient then underwent surgical excision of the tumor. Tarsal tunnel release and gastrocnemius recession were also performed</td>
<td>Post-op uncomplicated 8 week post pain and tarsal tunnel symptoms had completely resolved</td>
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<td>Saxena et al. (2017)</td>
<td>Case 1</td>
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<tr>
<td></td>
<td>Right ankle</td>
<td>37 year-old</td>
<td>Yes</td>
<td>X-ray</td>
<td>Arthroscopy</td>
<td>Arthroscopy</td>
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<td></td>
<td></td>
<td>Male</td>
<td>MRI</td>
<td>23 loose bodies removed</td>
<td>23 loose bodies removed</td>
<td>23 loose bodies removed</td>
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<td></td>
<td></td>
<td>Persistent pain in right ankle</td>
<td>MRI</td>
<td>Arthroscopic ankle synovectomy was performed anteriorly, and joint lavage was performed with 3% hydrogen peroxide</td>
<td>Arthroscopic ankle synovectomy was performed anteriorly, and joint lavage was performed with 3% hydrogen peroxide</td>
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<td></td>
<td></td>
<td>Several years of ankle sprains</td>
<td>CT</td>
<td>Case 1</td>
<td>Case 1</td>
<td>Case 1</td>
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<td></td>
<td>3% hydrogen peroxide</td>
<td>Case 1</td>
<td>Case 1</td>
<td>Case 1</td>
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<td></td>
<td></td>
<td></td>
<td>Limitations with all daily activities</td>
<td>Case 1</td>
<td>Case 1</td>
<td>Case 1</td>
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<td>Last follow up- at &gt; 12 years after the index surgery has mild symptoms with no recurrence and minimal arthrosis</td>
<td>Case 1</td>
<td>Case 1</td>
<td>Case 1</td>
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<tr>
<td>Saxena et al. (2017)</td>
<td>Case 2</td>
<td>Case 2</td>
<td>Case 2</td>
<td>Case 2</td>
<td>Case 2</td>
<td>Case 2</td>
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<tr>
<td></td>
<td>Right ankle</td>
<td>Right ankle</td>
<td>Yes</td>
<td>X-ray</td>
<td>Arthroscopy</td>
<td>Arthroscopy</td>
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<td></td>
<td>Anterior and posterior aspect of ankle joint</td>
<td>pain</td>
<td>CT</td>
<td>126 loose bodies removed</td>
<td>126 loose bodies removed</td>
<td>126 loose bodies removed</td>
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<td></td>
<td></td>
<td>Multiple right ankle sprains</td>
<td>126 loose bodies removed</td>
<td>Synovectomy was performed, and irrigation as performed with 3% hydrogen peroxide</td>
<td>Synovectomy was performed, and irrigation as performed with 3% hydrogen peroxide</td>
<td>Synovectomy was performed, and irrigation as performed with 3% hydrogen peroxide</td>
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<td>Synovectomy was performed, and irrigation as performed with 3% hydrogen peroxide</td>
<td>Case 2</td>
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<td></td>
<td></td>
<td>2 year follow up, no pain and no limitations</td>
<td>Case 2</td>
<td>Case 2</td>
<td>Case 2</td>
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</tbody>
</table>

Case 1
- Right ankle
- 37 year-old
- Male
- Persistent pain in right ankle
- Several years of ankle sprains

Case 2
- Right ankle
- 43 year-old
- Male
- Right ankle pain
- Multiple right ankle sprains

Case 1
- X-ray
- MRI
- 23 loose bodies removed
- Arthroscopic ankle synovectomy was performed anteriorly, and joint lavage was performed with 3% hydrogen peroxide

Case 2
- Arthrotomy
- Open approach was taken: anteromedial, anterolateral, and posterolateral
- 126 loose bodies removed
- Synovectomy was performed, and irrigation as performed with 3% hydrogen peroxide

Case 1
- Ankle was otherwise stable
- Returned to physical activities within 5 months without pain or limitations
- 10 years post-op some mild ankle pain. MRI showed anterior distal tibial exostosis and a posterior cartilaginous loose body
- Limitations with all daily activities
- Last follow up- at > 12 years after the index surgery has mild symptoms with no recurrence and minimal arthrosis

Case 2
- Able to return to normal activities and increase his running and hiking 4 months after removal of loosing bodies
- 2 year follow up, no pain and no limitations
| Scholl et al. (2010) | • Right ankle  
• Mobile nodule on anteromedial aspect of the right ankle | • 58 year-old  
• Female  
• Sudden onset of pain in posterior aspect of right heel  
• Uterine carcinoma (remission)  
• Sarcoidosis with ocular manifestations  
Positive for right kidney disease, gout, hypertension, sciatica and osteoarthritis | No | • X-ray  
• MRI | • Surgical intervention  
• Longitudinal incision was made over the anteromedial aspect of the ankle  
• Masses were removed  
Partial synovectomy was performed at the anterior ankle secondary to synovial hypertrophy | Posterior ankle pain resolved at 3 weeks post-op, and the patient remained symptom-free, without recurrences |
|---|---|---|---|---|---|---|
| Sedeek et al. (2015) | • Left ankle  
• Anterior aspect of ankle joint  
• Anterior positive impingement syndrome | • 21 year-old  
• Male  
• 18 month history of pain in left ankle | No | • X-ray  
• MRI | • Arthroscopy, surgical excision of the intraarticular bodies  
• Joint irrigated with abundant amount of normal saline  
• No synovectomy was performed | Partial weight bearing 2 weeks post-op  
• 1-year follow up, no pain with full ROM |
| Serbest et al. (2015) | • Right Knee  
• Anterior knee joint | • 72 year-old  
• Male  
• Swellings and pain at knee joint for nearly last 20 years | N/A | • X-ray  
• MRI | • Surgical intervention  
• Spinal anesthesia, tourniquet placed to right lower extremity  
• Knee was entered by anterior longitudinal incision  
• Medial parapatellar incision  
• Mass was excised with 3 | Active and passive exercises were started at an early period after surgery.  
• No recurrence at last visit  
• Knee movements were at full ROM compared to other knee  
• No pain |
<table>
<thead>
<tr>
<th>Case</th>
<th>Location</th>
<th>Age</th>
<th>Sex</th>
<th>History</th>
<th>Imaging</th>
<th>Management</th>
<th>Outcome</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shah et al. (2016)</td>
<td>Right Knee, Bakers Cyst</td>
<td>43 year-old</td>
<td>Male</td>
<td>1 year history of pain, swelling and restriction of right knee joint</td>
<td>No</td>
<td>X-ray, MRI</td>
<td>Surgical management, Synovium and loose bodies from cyst sent for histopathological examination</td>
<td>Histological findings also confirmed synovial chondromatosis with papillary hyperplasia of the synovium, Post-op patient was instructed in knee mobilization and strengthening exercises, Follow up at 1, 3, 6 months post-op, ROM was 0-130 degree of flexion without pain at 3 months post-op, No Recurrence 1 year after surgery</td>
</tr>
<tr>
<td>Shearer et al. (2017)</td>
<td>Bilateral Ankle, Calcification in both ankle joints and right and left flexor hallucis longus tendon sheaths</td>
<td>26 year-old</td>
<td>Male</td>
<td>Chronic pain, Multiple ankle sprains over the years</td>
<td>Yes</td>
<td>X-ray, MRI</td>
<td>Cryotherapy, ultrasound, and soft tissue work to fibularis muscles, Manual mobilizations of the ankle mortise joint</td>
<td>Asymptomatic with minor residual swelling and some periodic episodes of locking, Referred to orthopedic surgeon, who concluded surgery would be too invasive, Advised to continue with daily activities</td>
</tr>
</tbody>
</table>
Singh et al. (2014)  
Left Knee Extending to Baker’s Cyst  
32 year-old Female  
7 month history on insidious onset of pain, stiffness, and swelling  
No X-ray MRI  
Open anterior and posterior synovectomy of the knee in a one step procedure  
PT was kept in lateral position with tourniquet kept around the proximal thigh  
Knee joint exposed through a 12 cm median skin incision and medial parapatellar capsulotomy  
Anterior pathological synovial tissue and loose bodies were removed  
Posteriorly an “S” shaped incision in the popliteal fossa exposed the knee joint.  
Remaining synovium, loose bodies and Baker’s cyst were excised and sent for histopathological examination  
Histological findings also confirmed diagnosis of primary synovial chondromatosis  
Full weight bearing a day after post-op with the assistance of crutches  
Physiotherapy session focusing on reinforcement of quadriceps and hamstring muscles and active ROM of exercises  
Recovered and regained a full ROM equal to the other knee
In almost all of the case reports in which patients suffered SC of the knee, the diagnoses was primary SC. This is interesting because current literature suggests it is the rarer form as compared with secondary SC occurring usually after trauma/injury and following degenerative changes. It was also interesting to note that while most patient’s symptoms were not unique to SC alone, clinical modalities used ruled out conditions such as meniscal tear, RA, and other inflammatory conditions; most case reports only alluded to degenerative changes after the onset of SC symptoms or postoperatively. This strengthens the hypothesis that SC may in fact lead to degenerative changes rather than be secondary to such inflammatory diseases. Logic would follow then, that such findings rebuke the idea that SC “masks” underlying diseases since the degenerative changes would follow and not precede the condition of SC, which would suggest SC came first. However extensive research is
needed to fully explore this idea and prove this hypothesis. In all case reports (knee and ankle alike) the treatment of choice was arthroscopic surgery — whether the surgical approach decided upon was lateral or anterior (in ankle SC) was case dependent and subject to the surgeon’s preference. The cartilaginous nodules or coalesced masses were removed in all cases and a synovectomy was performed only in those where the synovial lining was extensively involved or in cases where the surgeon’s preferred surgical approach warranted it. Patients all regained full range of motion and were able to return to their normal physical activities. In some, but not all cases, there was a recurrence of calcified nodules followed by gradual discomfort and clinical symptoms. The inciting factors for the recurrence are unknown however, it should be noted that there are 33 reports (none of which were studied for this literature review) in which recurrence led to malignant transformation.7

CONCLUSION

Although many case reports share key features that allow for the delineation between primary and secondary SC, predisposing factors cannot be fully defined. Some case reports briefly described a patient’s level of physical activity, while others had no mention of it. Therefore, physical activity cannot be used to describe the etiology of gradual metaplastic transformation; nor can it be used to define metaplastic changes in response to physical or mechanical stressors. Only one case mentioned a potential chromosomal link, however extensive research is needed to afford a discussion about potential chromosomal abnormalities associated with SC. Among the case reports reviewed, SC seemed to be more prevalent among middle aged individuals. This coincides with current published literature. Still, however without extensive research to compare and contrast in depth medical histories among patients with SC, preferred age for the onset of SC cannot be fully explained. At this time a causal connection between trauma and SC cannot be made; trauma preceding the onset of SC was variable among the case reports reviewed. In every case, histological examination confirmed the diagnoses of SC and evidence of benign neoplastic changes. Milgram classified SC as occurring in three stages, but this review suggests the classification is variable. Much research is needed to address the variability among clinical presentation and potential reclassification of phases one through three. As it stands, Milgram’s 1977 description of the clinical progression of SC is the accepted guideline.

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