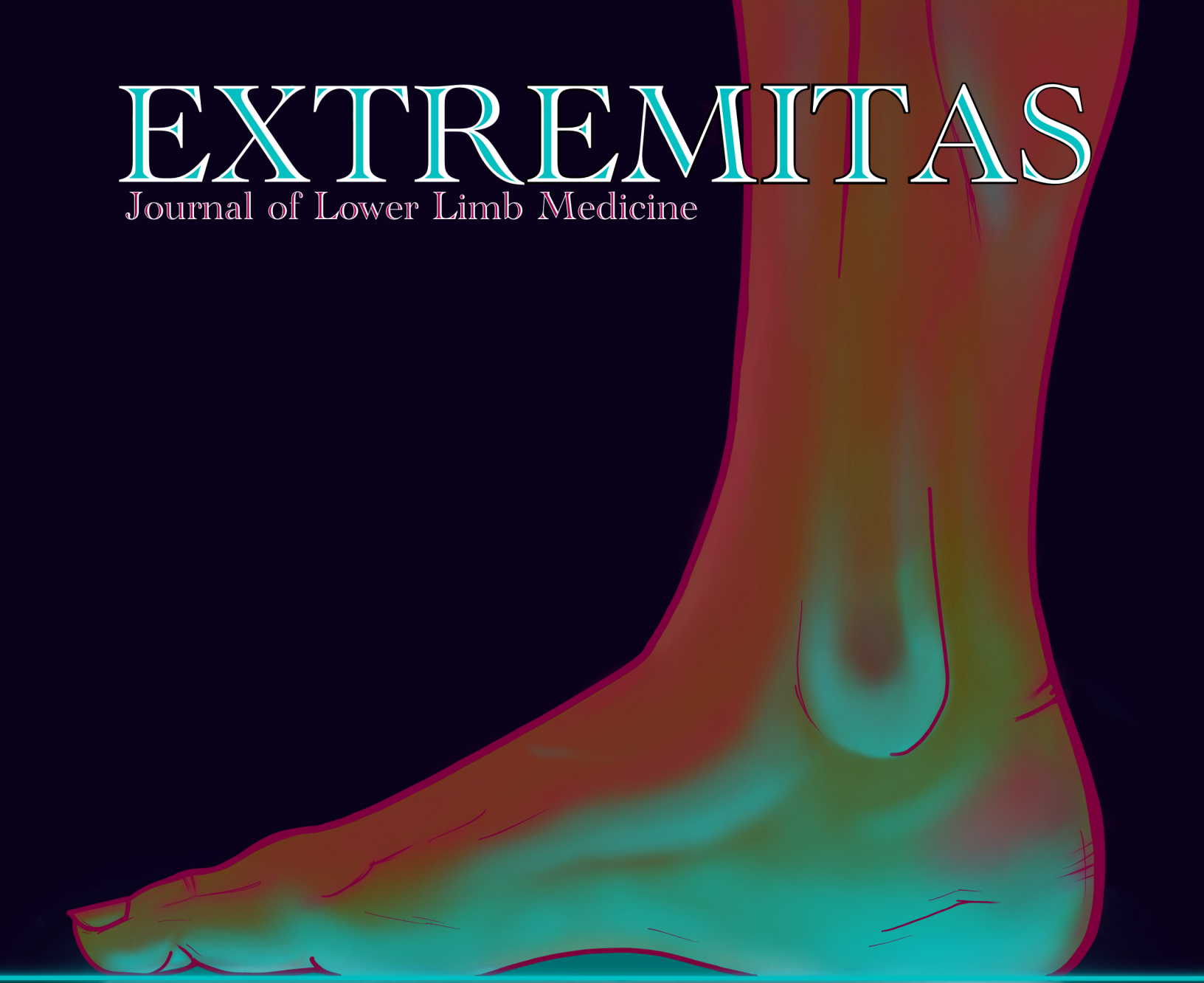
EXTREMITAS

Journal of Lower Limb Medicine



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Journal of Lower Limb Medicine

The Extremitas Editor's Choice Award

Congratulations to this year's winning authors, Airam Caldera and Dr. Joseph Park for their research titled ***Osteoid Osteoma of the Talar Neck: A Case Report!***

The winning author(s) of the scholarship were voted on by the editing staff and Dr. Shapiro for upholding the tradition of high quality research writing in Extremitas. You may read the abstract of their paper below.

Airam Caldera
DPM Candidate 2024

Dr. Joseph Park, DPM
WesternU Faculty

ABSTRACT

Objective: We report our experience in diagnosing and treating an osteoid osteoma in the talar neck. This case report illustrates the successful surgical treatment of this condition and also discusses reasons why this pathology frequently has a delayed diagnosis.

Case Report: This article describes the workup of a 22-year-old patient with a 3-year history of persistent ankle pain who underwent arthroscopic evaluation and open excision of an osteoid osteoma of the talar neck with subsequent bone grafting.

Discussion: The difficulty in diagnosing osteoid osteoma of the small bones of the feet is widely recognized. Subperiosteal osteoid osteomas are difficult to diagnose because of their unique radiographic appearance. These types of osteoid osteomas lack the periosteal response with sclerotic bone which is typically present. The clinical picture of this diagnosis can vary but usually includes no traumatic onset of pain, intermittent pain, pain that worsens at night, and pain relieved by NSAIDs or Aspirin, in an adolescent and young adult population. Advanced imaging should be considered if the pain does not subside with standard treatments.

Conclusion: This article reports our experience in the diagnosis and successful operative excision of an osteoid osteoma of the talar neck. This article serves as an educational tool for providers to help reduce the time to diagnosis for future patients.

Letter from the Editor in Chief

Dear Readers,

The *Extremitas Journal of Lower Limb Medicine* has been a presence at Western University for a decade now and has grown considerably since its start. We strive to provide students from all colleges the opportunity to engage in research and academic literature. Through this we want to cultivate an environment where students can learn from one another in order to become better healthcare professionals.

This year's publication consists of a variety of topics written by students spanning a multitude of healthcare professions. WesternU works effortlessly to promote a multidisciplinary learning environment for its students and this journal is evidence of that goal. It is inspiring to read the quality of work our authors produce and I am truly thankful for all the authors who contributed to this year's publication.

I would like to extend a special thank you to our faculty mentor, Dr. Jarrod Shapiro. He has been an amazing presence with his guidance, wisdom, and support throughout the entire publication process. Additionally, this year's publication would not be possible without our remarkable sponsors and their support. It is through their generous donations that we can continue to publish the journal. They understand the importance of research in order to make medical advancements and I am grateful for their continued support.

Our editorial team consisted of bright individuals whose commitment and hard work helped create this year's journal. It was a pleasure to work with the team and I look forward to reading future publications. Lastly, I would like to thank my family, friends, and loved ones for supporting me as this year's Editor-in-Chief.

It is with great honor to present to you the 10th annual volume of Extremitas Journal of Lower Limb Medicine.

Sincerely,

Harsh Varshney
EDITOR IN CHIEF
DPM Candidate 2024

2022-2023 Editorial Team

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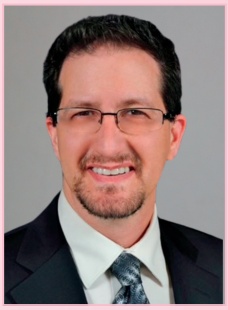

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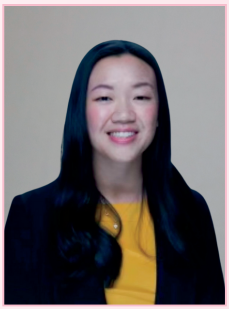

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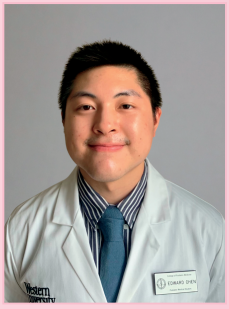

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Reflections from the Team

"I feel so grateful to have had the opportunity to work with this amazing team on this year's edition. I am proud of my teammates for putting in the hard work to create this unique and collaborative journal. Thank you to our sponsors, authors who entrusted us with their work, and Dr. Shapiro for allowing this journal to be possible every year."

Vivian Chan, DPM Candidate 2024

"Being part of Extremitas for the past few years has been an immense honor. Our authors and editors have worked tirelessly to bring forth the best content for our readers. I would like to express my heartfelt gratitude to the entire team, Dr. Shapiro, and our sponsors for their support and contributions that make this possible."

Elaine Chu, DPM Candidate 2024

"I am very thankful to have been a part of the Extremitas team this year! I learned so much about a wide range of interesting topics during the editing process. It was a pleasure to work with my fellow editors and together make a positive impact in the world of Podiatric medicine research."

Airam Caldera, DPM Candidate 2024

"I am so blessed to be a part of this team of hard workers. It was amazing to witness the growth of all the authors and team members as we worked to create this journal. I would like to thank Dr. Shapiro, the authors, and our amazing Extremitas team."

Chanelle Mariano, DPM Candidate 2024

"Having the opportunity to be a part of the extremitas team has been such a fun and rewarding experience. It allows me to work with an incredible team of classmates and authors and allows me to grow in my own research abilities. Thank you to everyone who worked so hard to make this such an incredible experience, I'm so grateful to of be helping further podiatric research."

Savannah Santiago, DPM Candidate 2024

"It is has been an honor to be part of the Extremitas team and to collaborate with everyone to make this year's edition possible. Thank you to our advisor, Dr. Shapiro, our sponsors, the editing team and authors who put together another wonderful journal."

Tia Furness, DPM Candidate 2024

"As Vince Lombardi said, "Perfection is not attainable, but if we chase perfection we can catch excellence.""

Robert Erickson, DPM Candidate 2025

"Working with such a talented group of authors on this journal has been an incredible experience, and I am honored to have been a part of it. I would like to express my gratitude and thanks to the sponsors and Dr. Shapiro for their invaluable contributions, which were key in making this project a success. Additionally, I would like to congratulate all the authors who submitted their work this year - it was a pleasure to read such impressive and thought-provoking papers. Great job, everyone!"

Tiffany Duarte, DPM Candidate 2025

"I am honored to be part of this rewarding experience as an editor working alongside my brilliant colleagues. Thank you for all those that helped make this journal possible and thank you to the authors and editors for all the diligence. I hope everyone enjoys the journal!"

Edward Chen, DPM Candidate 2025

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Surgical Interventions

Recent Advancements in Arthroscopic Anterior Talofibular Ligament Repair Procedures: A Literature Review

Marcus Alegria[+], B.S. and Megan Lucavs[+], B.A.

[+]Western University of Health Sciences

ABSTRACT

Objective: This paper will review recent advancements in ATFL repair procedures and explore the pertinence of these findings in the treatment of lateral ankle injury involving damage to the ATFL.

Methods: A literature search was performed on PubMed and the Pumerantz Library to identify articles within the last decade that have investigated different techniques for arthroscopic ATFL repair. The terms used in this search were "ATFL repair", "arthroscopic ATFL repair", and "ankle arthroscopy".

Results: Advancements in surgical technology have resulted in numerous newly proposed arthroscopic techniques adding different options that are comparable to the gold standard Broström-Gould procedure. The benefits of choosing minimally invasive arthroscopic ATFL repair vs open procedures may include decreased risk for nerve damage and quicker healing times. Techniques such as suture configuration, ATFL repair with or without additional IER repair, and number of suture anchors have been studied to determine which techniques are most optimal.

Conclusion: Arthroscopy is a relatively new field of study in foot and ankle surgery. The effectiveness of newly proposed arthroscopic ATFL repairs have been proven to be as effective as gold standard open procedures, although more challenging. Further studies involving larger cohorts need to be conducted to determine clinical significance of these techniques.

Introduction

The anterior talofibular ligament (ATFL) is the most common ligament that is injured in a lateral ankle sprain. It is the weakest of the three lateral collateral ligaments of the ankle, and thus the most vulnerable to injury.[1] The majority of patients with acute lateral ankle sprains are successfully treated non-surgically with 5-20% of cases leading to chronic lateral ankle instability.[2] Chronic ankle instability is diagnosed based on instability lasting more than 6 months, positive anterior drawer test of the ankle and talar tilt test. Surgical repair of the ATFL should be considered in the 20-40% of patients who fail non-surgical treatment.[2,3]

The Broström-Gould technique, proposed 42 years ago, is an open procedure that still remains the gold standard surgical ATFL repair technique to treat chronic lateral ankle instability.[2,3,4] This procedure, which involves repairing remnants of the native ATFL with reinforcement of the inferior extensor retinaculum (IER), was proposed to spare ankle degeneration caused by earlier proposed surgical techniques involving the sacrifice of local tissue to repair the ATFL.[2] Over the past decade, advancements in surgical technology have lead to the introduction of arthroscopy for the minimally invasive direct visualization of joints resulting in numerous newly introduced ATFL repair techniques.[2,3,4,5] Although the literature has reported comparable clinical outcomes with these procedures, arthroscopic procedures are viewed as more technologically challenging than open procedures like the Broström-Gould technique.[2,5]

With arthroscopic procedures being a relatively new field of surgical advancement in repairing the ATFL there is little research determining a standard procedure. This study will discuss numerous studies conducted over the past decade identifying new techniques. The purpose of this systematic review is to review the literature published within the last decade and provide an overview of arthroscopic techniques used to surgically repair the ATFL to correct lateral ankle instability and compare the efficacy of these strategies.

Methods

A PubMed search was conducted to identify relevant recent literature from 2012-2022 that discussed the efficacy of newly discussed arthroscopic ATFL repair procedures. Keywords, such as "ATFL repair", "arthroscopic ATFL repair", and "ankle arthroscopy" were used to narrow down these literature searches. Articles that were older than 10 years old were excluded in this study to focus on current advancements. Studies that underscored known techniques to repair the ATFL were also included.

Results

The majority of articles found discussed successful outcomes of arthroscopic ATFL repair techniques. In a 2018 systemic review, Guelfi et al

looked at total ankles treated with open Broström-Gould technique vs. total ankles treated by arthroscopic ATFL repair techniques from 1972-2015. Researchers looked at 721 total cases surgically treating chronic lateral ankle instability involving ATFL repair. 505 cases across 13 studies used the Broström-Gould technique while 216 cases across 6 studies used arthroscopic surgical procedures. This study reported a mean postoperative AOFAS score of 90.1% and patient satisfaction rate of 91.7% across 11 studies treated with open Broström-Gould procedure, and a mean postoperative AOFAS score of 92.48% and patient satisfaction rate of 96.4% across 5 studies treated with arthroscopic techniques. 40 out of the 505 Broström-Gould cases reported complications while 33 of the 216 arthroscopic cases reported complications.[2]

Araujo Nunes G et al reported a retrospective case series involving 18 patients that underwent all-inside arthroscopic ATFL repair with a mean follow up period of 12 months. In this study, knotless sutures were used to repair the native ATFL to correct chronic lateral ankle insufficiency. The AOFAS indicated an improvement from 69.6 points preoperatively to 98.1 points postoperatively. All patients were able to return to sports without limitations. Researchers reported a complication involving neurapraxia of the superficial fibular nerve in 1 out of 18 cases. Favorable clinical outcomes of arthroscopic ATFL procedures from originator centers have been comparable with that in non-originator centers.[5]

In a 2022 multicenter retrospective study, Zhi, X et al compared arthroscopic ATFL repair using an absorbable suture anchor vs knotless suture anchor across 185 cases. Group A (107 patients) underwent one absorbable suture anchor repair while Group B (78 patients) underwent one knotless suture anchor repair. At 18 months of follow up, Groups A and B showed postoperative Karlsson-Peterson score of 93.5 ± 5.3 vs. 92.4 ± 6.3, VAS score of 0.5 ± 0.7 vs. 0.9 ± 1.0, and CAIT score of 93.1 ± 6.6 vs. 93.1 ± 6.5, respectively. Knot irritation was only seen in Group A in 10 out of the 107 patients while anchor loosening was seen in 6 out of the 78 patients in Group B.[3]

Willegger, M et al performed a cadaver study involving 12 fresh-frozen human lower leg specimens to evaluate the biomechanical stability of tape augmentation for ATFL repair compared to native ATFL repair. Biomechanical stability of the repaired ligaments were tested by internal rotation of the tibia on an inverted hindfoot and by looking at angle and torque at failure with each group. The angle of failure in the native ATFL repair group was 33 ± 10° vs 46 ± 16° for the tape augmentation group. The amount of torque at failure for the native ATFL group was 8.3 ± 4.5 Nm vs 11.2 ± 7.1 Nm for the tape augmentation group. Researchers indicated tape augmentation for ATFL repair showed comparable biomechanical stability with native ATFL repair.[6]

A prospective cohort study was performed by Li, Hong et al that compared the function and activity level outcomes of patients who underwent an arthroscopic ATFL repair with two suture anchors compared to one suture anchor. 51 patients with chronic lateral ankle instability were included in this study with 20 patients receiving one-suture anchors and 31 patients receiving two-suture anchors. Two years was the minimum follow up. This study revealed that two-suture anchors provided better functional outcomes with a significantly higher percentage of participation in sports (68%) than with the one-suture anchor group (30%). The one-suture anchor and two-suture anchor groups revealed a AOFAS score (90.9 ±9 vs 91 ±10), Karlsson score (80 ±14 vs 88 ±12), and Tegner activity score (4 ±1 vs 5 ±1).[7]

Lee S.H. et al investigated the efficacy of additional inferior extensor retinaculum (IER) repair after arthroscopic repair of the ATFL. This study followed 82 patients undergoing arthroscopic ATFL repair for treatment of chronic lateral ankle instability. The mean follow up was 32.6 months. Two groups were identified; Group A had 37 patients who underwent arthroscopic ATFL repair without additional IER repair and Group R had 45 patients who underwent arthroscopic ATFL repair with additional IER repair. This study concluded that there was no significant difference in AOFAS, FAOS, and Karlsson scores or in radiographic findings between Groups A and R indicating no difference between outcomes in patients who had an isolated ATFL repair vs ATFL repair with an additional IER repair. Additionally, 3 out of the 45 patients in Group R developed peroneal nerve injury associated with the knot which was not observed in Group A.[8]

Suture configuration used in arthroscopically repairing the ATFL is discussed by Feng S-M et al and Qin J et al. The former study is a retrospective cohort study including 71 patients undergoing arthroscopic ATFL repair to treat chronic lateral ankle instability which investigated the functional outcomes between loop suture compared to that of free-edge suture configuration. The researchers determined that both configurations provided comparable postoperative outcomes with similar AOFAS, KAFA, AJPS, and rate of return to sports, but the loop suture configuration achieved better anterior talar translation (3.22 mm vs 3.60 mm), although it demands a longer procedure time.[9]

Qin J et al performed a retrospective cohort study that investigated the efficacy of the lasso-loop stitch technique for arthroscopic ATFL repair. This study involved 43 cases with a mean follow up period of 28.23 ±3.64 months. The researchers found that fully intra-articular lasso-loop stitch technique for ATFL repair is reliable and safe indicated by Karlsson-Peterson, CAIT, and VAS scores of 90.26 ±6.58, 88.56 ±7.21, and 0.79 ±1.06, respectively. Additionally, no nerve injuries were observed in this study.[4]

Discussion

Arthroscopic techniques had similar efficacy to the excellent results produced with the gold standard Broström-Gould technique.[2] All the recent advancements in arthroscopic ATFL repairs discussed in this study have gained popularity due to the minimal invasiveness and comparable outcomes. Many of the studies discussed have emphasized the need to conduct more trials with increased subject numbers and increase the length of months being followed up in order to determine long term success of these procedures.

The retrospective study of Araujo Nunes G et al found that all-inside arthroscopic ATFL repair technique achieved good clinical results and had a low complication rate. A longer term follow up should be assessed further and more trials should be conducted to confirm these benefits.[5]

A major theme seen across three articles was determining outcomes based on suture configuration and number of suture anchors. Zhi, X et al found that absorbable suture anchor repair still achieved similar outcomes to that of knotless anchor repair techniques. The ankle stability scores also increased significantly in both groups. The knotless anchor has a higher risk of loosening, deviating direction, or breaking while the absorbable anchor still has a chance of knot irritation. This study did have several limitations due to the study not being randomized, being a three-medical center study with regional difference of performance possibly affecting the outcome, and having a short follow up time.[3]

The prospective study done by Li, Hong et al concluded that a two anchor repair of the lateral ankle ligament was able to produce better functional outcome than with the one anchor repair arthroscopy. This study also found that rate of return to sport was higher for the two anchor repair, concluding rate of return is related to a firm repair of the ATFL using suture anchors. This study did involve concomitant injuries in the cohorts so it is unclear if these injuries affected the results of this study.[7] Further investigation into using two absorbable suture anchors vs two knotless suture anchors could be warranted given the better functional outcomes with two suture anchors.

An additional study done by Feng S-M et al noted that an arthroscopic ATFL repair in loop suture configuration offers no short-term postoperative advantages. Though they did have better anterior talar translation compared to the free edge suture, the difference still seems clinically insignificant.[9] Another study discussing the lasso-loop stitch techniques done by Qin J et al concluded that this technique was shown to be reliable and safe, but that future clinical trials are still needed to confirm clinical outcomes with a long term follow up.[4]

Instead of looking at altering suture techniques, Willegger, M et al assessed tape augmentation repair and determined that tape augmented repair vs. native ATFL repair had comparable torque and angle at failure during the biomechanical testing. They did find that the mode of failures were different, as talar anchor pull-out most commonly occurred during the augmented repair and ligament rupture in mid-substance was most frequently seen in the native ATFL repair. It was also discussed that tape augmentation was able to enhance stability in ATFL reconstructions and could allow for an accelerated rehab. Some limitations to this study are that there were only 12 tested specimens and the fact that in vivo conditions had to be mimicked in the laboratory which might not represent in vivo stresses on the ATFL.[6]

The efficacy of inferior extensor retinaculum repair was assessed in the study performed by Lee S.H. et al. The investigators noted that surgical treatment of the CAI by arthroscopic isolated ATFL repair or arthroscopic ATFL repair with IER augmentation had similar postoperative outcomes during the 2 years of follow up. It is unclear if this single centered study involving 82 patients is sufficient to conclude the necessity of additional IER repair with ATFL arthroscopic repair. More research into this is needed involving multi-centered studies with multiple surgeons.[8]

Conclusion

Broström-Gould technique remains the gold standard method to repair the ATFL to treat chronic lateral ankle instability. Recently proposed arthroscopic ATFL repairs have gained popularity due to quicker healing times, minimal invasiveness, and decreased risk for nerve injury that can be associated with open repairs. Due to this, there have been many advancements in arthroscopic ATFL repairs in order to determine the technique with the most efficacy. Further studies are still needed to conclude which technique will provide the most optimal surgical outcome.

References

1. Le T, Liu H, Jenkins SM, et al. Single Knotless Suture Anchor Repair of Anterior Talofibular Ligament Following Distal Fibula Nonunion Excision. *Arthroscopy Techniques*. 2022;11(3):e449-e455.
2. Guelfi M, Zamperetti M, Pantalone A, Usuelli FG, Salini V, Martin Oliva X. Open and arthroscopic lateral ligament repair for treatment of chronic ankle instability: A systematic review. *Foot and Ankle Surgery*. 2018;24(1):11-18.
3. Zhi, X. *et al.* (2022) 'Absorbable suture anchor and knotless anchor techniques produced similar outcomes in arthroscopic anterior talofibular ligament repair', *Knee Surgery, Sports Traumatology, Arthroscopy*, 30(6), pp. 2158–2165.
4. Qin J, Fu Q, Zhou Q, et al. Fully Intra-articular Lasso-Loop Stitch Technique for Arthroscopic Anterior Talofibular Ligament Repair. *Foot & Ankle International*. 2022;43(3):439-447.
5. Araujo Nunes G, Ferreira GF, Caetano RM, Mann TS, Guelfi M. All-inside arthroscopic repair of the anterior talofibular ligament: a case series. *International Orthopaedics*. January 2022.
6. Willegger, M. *et al.* (2016) 'Biomechanical stability of tape augmentation for anterior talofibular ligament (ATFL) repair compared to the native ATFL', *Knee Surgery Sports Traumatology Arthroscopy*, 24(4), pp. 1015–1021.
7. Li, Hong *et al.* (2020) 'Anterior talofibular ligament (ATFL) repair using two suture anchors produced better functional outcomes than using one suture anchor for the treatment of chronic lateral ankle instability', *Knee Surgery Sports Traumatology Arthroscopy*, 28(1), pp. 221–226.
8. Lee, S.H., Cho, H.G. and Yang, J.H. (2021) 'Additional Inferior Extensor Retinaculum Augmentation After All-Inside Arthroscopic Anterior Talofibular Ligament Repair for Chronic Ankle Instability Is Not Necessary', American Journal of Sports Medicine, 49(7), pp. 1721–1731.
9. Feng S-M, Shao C-Q, Sun Q-Q, Oliva F, Maffulli N. Functional outcomes of all-inside arthroscopic anterior talofibular ligament repair with loop suture versus free-edge suture. *Journal of Orthopaedic Surgery & Research*. 2022;17(1):1-9.

The Modified Valenti Resection Procedure: Interpreting Surgical Efficacy for Hallux Limitus/Rigidus

Daniel Ahdoot[+], B.S. and Sean Lee[+], M.S., B.A.

[+]Western University of Health Sciences

ABSTRACT

Objective: Evaluating the efficacy of the modified Valenti Resection Procedure in treating hallux limitus and rigidus, and determining if populations requiring excessive repetitive loading to the hallux may benefit more from the procedure.

Methods: Relevant literature was found using databases such as PubMed, Embase, Google Scholar, and the Western University Pumerantz Library database. Literature published from 2000-present was used, and papers written before 2000 were excluded. Key terms such as "modified", "Valenti", "resection", "hallux limitus", and "hallux rigidus" were used.

Results: The Valenti procedure provides satisfactory balance between mobility and stability, and is highly effective and safe in treating all grades of hallux limitus/rigidus, especially in running and jumping athletes. While the procedure allows for an early recovery with fewer complications, and has a low incidence of the requirement of a revision surgery, a common complication seen is transient sesamoiditis.

Conclusion: The modified Valenti procedure is a safe and efficacious option for treating mild to severe hallux limitus and rigidus. Certain populations that require 1st MTPJ mobility may benefit the most from this procedure. The most common complication from the procedure was sesamoiditis.

Introduction

The 1st metatarsophalangeal joint (MTPJ) plays an important role in gait, particularly in dorsiflexion in the terminal and pre-swing phases to ensure smooth weight transfer over the foot.[1] Hallux limitus and rigidus are both pathologies of the 1st MTPJ involving limitations in range of motion (ROM) of the joint. Hallux limitus is characterized by restriction in ROM in the sagittal plane, while hallux rigidus is a more severe pathology described as complete absence of sagittal plane motion with pathologic cartilage and joint fusion.[2] Both of these conditions can increase peak pressure and maximal forces on the hallux, leading to joint dysfunction and pain.

Conservative measures in treating hallux rigidus have shown to be effective in relieving pain and improving 1st MTPJ ROM in about 50% of patients.[3] For patients in which non-operative measures do not resolve the symptoms, numerous surgical procedures have been developed to treat hallux limitus and rigidus, each with their respective advantages and disadvantages. An example is the cheilectomy, which involves resection of dorsal osteophytes, the lateral and medial margins of the 1st metatarsal, and the dorsal lip of the proximal phalanx.[4] While cheilectomy allows for early joint ROM and rapid alleviation of symptoms, disadvantages include not addressing the root cause of the condition, potentially leading to recurrence of symptoms, and potential joint destruction (arthrodesis). For severe cases of hallux rigidus, arthrodesis has been established as the gold standard, but severely sacrifices mobility of the joint.[3]

Modifications of traditional surgeries for hallux limitus/rigidus have been proposed in literature, aimed at improving outcomes while maintaining the principles of the original surgeries. For instance, the Cheilectomy with Double-V osteotomy was explored to remedy excessive shortening of the proximal phalanx frequently present in other procedures, and was found to have significant improvement in pain relief, functionality, and alignment of the joint.[5]

The Valenti procedure was introduced in 1987 with the intention of improving 1st MTPJ ROM by resecting the dorsal half of the metatarsal head and proximal phalanx in a sagittal 'V' fashion, preserving the plantar structures.[6] Previous literature exploring the efficacy of the Valenti procedure found that it was beneficial compared to other hallux limitus/rigidus procedures by allowing immediate weight bearing, less rehab time, and quicker return to play for sports and return to daily activities.[7] The procedure also allows for more recovery of dorsiflexion in the hallux without excessive shortening compared to other procedures for hallux limitus such as the Keller arthroplasty, helping preserve ROM after the operation.[8] The procedure has since been modified to improve joint stability by resecting less of the metatarsal head and proximal phalanx.

The aim of this review is to evaluate surgical outcomes of the modified Valenti resection

procedure, and determine if populations requiring excessive repetitive loading to the hallux and quicker return to activity (i.e. athletes) may benefit more from the Valenti procedure as opposed to other surgeries for hallux limitus/rigidus.

Methods

In order to obtain data on surgical efficacy of the modified Valenti procedure, relevant literature was found using PubMed, Embase, Web of Science, Google Scholar, the Cochrane Library, and the Western University Pumerantz Library database. Using keywords such as "modified", "Valenti", "procedure", "surgical", "resection", "efficacy", "hallux limitus", and "hallux rigidus", as well as boolean searches such as (modified AND Valenti) AND (hallux AND limitus OR rigidus), provided the most pertinent literature. Literature published from 2000-present was used, as the Valenti procedure was established in 1987. Information from chosen articles was then evaluated in order to determine improvements in 1st MTPJ ROM, return to daily living activities, and post-surgical complications.

Results

In a systematic review by Colò et al.[9],148 different articles pertaining to the Valenti procedure were collected. Of these 148 articles, eight were selected to be used in the systematic review, as they contained the most comprehensive information regarding indications, management, and clinical outcomes of the Valenti procedure. Amongst the combined 347 patients (138 females, 185 males) in the 8 articles, it was found that the mean follow-up after a Valenti procedure was 6±7.1(range 0.2-17.5) years. The average age of patients at the time of surgery was 52.5±6.4 (range 13-75) years. It was also found that the most common complication following a Valenti procedure was transient sesamoiditis, which occurred in 21 (7.4%) of patients. The second most common complication was metatarsus elevatus, seen in 15 patients (5.3%). The systematic review did not find significant differences in clinical outcomes when comparing original versus modified techniques. With these findings, Coló et al. came to the conclusion that the Valenti procedure does in fact allow an early recovery with fewer complications when compared to fusion, interposition arthroplasties or osteotomies. However, the procedure does not necessarily prevent the need for future procedures such as implants or fusion.[9]

Harisboure et al.[10] conducted a retrospective analysis and observed 32 patients from a group of 41 cases. All of these patients had received treatment for hallux rigidus using the Valenti procedure between November 1999 and July 2004. These patients were found to have a mean age of fifty-seven years at the time of the operation. 41% of patients additionally presented with a static disorder of the foot, and one or multiple additional procedures were done at the time of the Valenti procedure, in 24% of the cases. Using the AOFAS score, patients were assessed on walking distance, gait, the tip-toe test, and patient satisfaction. Twenty-four patients of the original thirty-two (thirty-two cases) were reviewed and assessed with an average follow-up of 5.5 years. A complication observed in two of the cases was reflex sympathetic dystrophy.[10]

The mean final AOFAS score was found to be 81 out of 100, a significant increase from the average preoperative score of 47 out of 100. Additionally, 94% of cases reported occasional or no pain at all, and 91% of cases reported absent or moderate discomfort while wearing shoes following the Valenti procedure. Joint range of motion of patients also increased to greater than 30º in 72% of cases. The final result demonstrated an average of 30% subluxation of the first phalanx base, however no clinical consequences presented. While the Valenti procedure may put patients at possible risk for metatarsophalangeal joint destabilization if the resection is overzealous, there will be no impairment of the final functional outcome of the joint. Due to these findings, Harisboure et al., stated that the Valenti procedure provides a satisfactory balance between mobility and stability and has a low complication rate, leading to positive outcomes for all hallux rigidus grades.[10]

In a systematic review, Roukis assessed the necessity for surgical revision following isolated Valenti arthroplasties for hallux rigidus. Starting with 14 possible studies, Roukis narrowed the resources used to three different studies composed of forty-four isolated Valenti procedures with a mean follow-up of ≥12 months' duration. Two (4.6%) of the cases underwent surgical revision via a Keller resection arthroplasty (n=1), and one plantarflexory base osteotomy (n=1). Although none of the studies provided sufficient evidence regarding complications involved in specific grades of hallux rigidus in patients with an isolated Valenti arthroplasty, certain complications were seen in a large number of cases. From the three studies used, transient sesamoiditis was present in 20/33 (60.6%) feet from two studies, first metatarsophalangeal joint pain was seen in 2.8 (25%) feet from a single study, and recurrent

deformity such as "dorsal bunion" development was seen in five eighths (62.5%) of feet from one study. This showed that amongst the three studies, the likelihood of complications from a Valenti arthroplasty that necessitates surgical revision was consistent. In conclusion, Roukis found that the Valenti arthroplasty has a low overall incidence (4.6%) of the requirement of a revision surgery, making it a strong surgical option to treat hallux rigidus.[11]

In an analysis, Saxena et al.[12] gathered the results of 100 modified Valenti procedures performed on running and jumping athletes suffering from hallux limitus/rigidus. The average age of patients involved in the study was 49.2±10.1 years (range 13 to 71), the average follow-up time was found to be 80.5±45.4 months (range 11.5 to 209.6 months. In terms of complications, six (6%) of the patients required corticosteroid injections at ≥ 6 months following the procedure due to symptoms of sesamoiditis. However, no complications such as a cock-up toe deformity, infection, or lateral foot complaints were noted. Of the 100 procedures, eighty-nine of them found the exact time it takes for athletes to return to activity (RTA) was 9.2±4.3 weeks, while the other 11 cases had an unclear exact RTA, but verified that they eventually did return to activity.[12]

Runners, which comprised the largest cohort, had an RTA of 8.8±4.0 weeks, while dancers had an RTA of 8.5±2.5 weeks, and soccer players had an RTA as a group of 16.5±7.7 weeks. This shows that the only significant difference in RTA was between runners and soccer players. Saxena et al. gathered that a grade 2 hallux rigidus had the lengthiest RTA, and a grade 4 had the shortest RTA, however, the difference in RTA between the various grades of hallux rigidus showed no significant difference.

While Saxena et al. were unable to find articles with which they could juxtapose RTAs, patient-reported outcomes were compared using research by Aynardi et al. Patient progress following interpositional arthroplasties with partial joint resections on 169 patients with hallux limitus/rigidus was tracked. 17.3% of these patients complained of second or third MPJ pain following the procedure. However, none of the patients in the Saxena et al. article presented with this complaint, and furthermore, a much smaller 6% of their sample size reported a different complaint of sesamoiditis.[12]

Discussion

Based on the literature reviewed, the modified Valenti procedure appears to be an appropriate alternative in treating hallux rigidus and limitus. Desired outcomes of the surgery such as improved ROM of the 1st MTPJ and reduced pain were achieved using the procedure, and clinical outcomes were similar to other procedures for hallux limitus/rigidus.[7,9] These benefits may make the procedure an appropriate alternative for populations that put excessive stress on the 1st MTPJ, such as athletic populations.[11] Saxena et al. concluded that the modified Valenti procedure is an efficacious and safe method to treat hallux limitus/rigidus in running and jumping athletes when compared to other similar procedures, as 94% of patients in this analysis returned to their desired level of activity with fewer complications.[12] However, the nature of the sport should be a consideration, as soccer players had a longer RTA than runners; soccer is a sport that requires more cutting and sudden movements, which may explain the longer RTA. The grading of hallux rigidus should also be considered, as more severe deformities had a longer RTA.[12]

Mixed results were found regarding the need for revisional surgery following a Valenti procedure. Colò et al. reported that the Valenti procedure does not necessarily avoid the requirement for future operations.[9] In contrast,, Roukis came to the conclusion that the Valenti arthroplasty has a consistently low overall incidence (4.6%) of the need for a revision surgery.[11] This discrepancy may be due to the difference in sample size used by Colò et al. compared to Roukis. While Harisboure et al. and Saxena et al. do not explicitly mention the need for revisional surgery following a Valenti procedure, they both state that the procedure has a low to no complication rate and that no significant complaints or clinical consequences were reported.[10,12.] Future research observing the requirement for revisional surgery following a Valenti arthroplasty will be beneficial for the long-term care plan of patients and their overall satisfaction. More prospective cohort studies could best be to help gather valuable data on the topic.

One common theme in complications from the procedure was sesamoiditis.[9,11] The literature, however, was inconsistent in identifying the prevalence of sesamoiditis following the modified Valenti procedure, with Colo et al. reporting 7.4% of patients and Roukis reporting 60.6% in a smaller sample. This discrepancy can be attributed partly to

sample size, but Colo et al. asserted that sesamoiditis was still the most common complication from the modified Valenti procedure, even with the low percentage. This suggests that although the modified Valenti procedure offers improved mobility as a benefit, caution must still be taken to not introduce iatrogenic 1st MTPJ hypermobility that could potentially lead to sesamoiditis. This is consistent with Harisboure's assertion that overzealous resection can lead to 1st MTPJ destabilization.[10] Future research looking at the biomechanical factors that can lead to sesamoiditis in patients undergoing the modified Valenti procedure would be beneficial in refining the procedure to help prevent this complication.

The most prevalent limitation in the literature was sample size. Most papers mentioned the challenge of finding enough patients that fit the criteria to not only undergo the Valenti procedure, but also continue with follow-up after the procedure. As more literature observing the efficacy of the Valenti procedure becomes available, broader conclusions and more standardized protocols for care following the procedure can be developed. Although other papers mentioned the benefits of the Valenti procedure in populations requiring early weight-bearing, there is only one paper that specifically targeted athletes with hallux limitus/rigidus.[12] As this was a very recently published paper, future studies that not only included athletes but also occupations that would benefit from lower recovery time and early weight-bearing would
help in providing compelling data in support of the modified Valenti procedure.

Conclusion

The modified Valenti procedure is a safe and efficacious option for treating hallux limitus and rigidus. Populations that require 1st MTPJ mobility quickly following surgery, such as athletes, may benefit the most from this procedure. The most common complication from the procedure was sesamoiditis.

References

1. Nawoczenski D, Baumhauer J, Umberger B. Relationship between clinical measurements and motion of the first metatarsophalangeal joint during gait. *J Bone Joint Surg Am.* 1999;81A:370–6.
2. Zammit GV, Menz HB, Munteanu SE, et al. Plantar pressure distribution in older people with osteoarthritis of the first metatarsophalangeal joint (hallux limitus/rigidus). *J. Orthop. Res.* 26:1665-1669.
3. Anderson MR, Ho BS, Baumhauer JF. Current Concepts Review: Hallux Rigidus. *American Orthopedic Foot & Ankle Society.* 2018;3(2):1-11.
4. Geldwert JJ, Rock GD, McGrath M et al. Cheilectomy: still a useful technique for grade I and grade II hallux limitus/rigidus. *J Foot Surg.* 1992;31(2):154-159.
5. Valero J, Moreno M, Gallart J. et al. A new surgical procedure for hallux limitus treatment: Double-V osteotomy on the base of the proximal phalanx of the hallux. *Medicine*. 2017;96:39.
6. Grady J, Smith A, Boumendjel Y et al. Hallux rigidus: the Valenti arthroplasty. *International Advances in Foot and Ankle Surgery.* 2012;37-43.
7. Kurtz DH, Harrill JC, Kaczander BI et al. The Valenti procedure for hallux limitus: A long-term follow-up and analysis. *The Journal of Foot and Ankle Surgery.* 1999;38(2):123-130.
8. Maffulli N,Papalia R, Palumbo A et al. Quantitative review of operative management of hallux rigidus. *British Medical Bulletin*. 2011;98(1):75–98.
9. Colò G, Samaila EM, Magnan B, Felli L. Valenti resection arthroplasty for hallux rigidus: A systematic review. *Foot and Ankle Surgery.* 2020;26:838-844.
10. Harisboure A, Joveniaux P, Madi K, Dehoux E. The Valenti technique in the treatment of hallux rigidus. *Orthopaedics & Traumatology: Surgery & Research.* 2009;95:202-209.
11. Roukis TS. The Need for Surgical Revision after Isolated Valenti Arthroplasty for Hallux Rigidus: A Systematic Review. *Foot and Ankle Surgery.* 2010;49:, 294-297.
12. Saxena A, Valerio DL, Behan SA, et al. Modified Valenti Arthroplasty in Running and Jumping Athletes With Hallux Limitus/Rigidus: Analysis of One Hundred Procedures. *Foot & Ankle Surgery.* 2019;58;609-616.

The Reverse Peroneus Brevis Muscle Flap for Reconstructive Surgery of the Lower Extremity: A Review

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ABSTRACT

Objective: The purpose of this literature review is to report the most recent literature on the outcomes of the reverse peroneus brevis muscle flap for reconstructive surgery of the lower extremity.

Methods: A search was performed using PubMed and WesternU's Pumerantz Library search engines to find the relevant literature over the past two decades. Keywords such as "reverse peroneus brevis muscle flap", "distal peroneus brevis muscle flap", and "lower extremity reconstruction" were used.

Results: The studies included in this review followed patients that underwent a reverse peroneus brevis muscle flap for various indications. These studies reported low rates of complications, where most complications included distal flap necrosis that healed uneventfully that required no further surgical intervention.

Conclusion: The peroneus brevis muscle flap can be a reliable choice for distal lower extremity reconstructive procedures and should be considered when choosing a procedure for trauma, ulcers, and osteomyelitis.

Introduction

Trauma, diabetes, peripheral vascular disease, and cancer all pose a threat for lower extremity limb loss.[1] This necessitates limb salvage techniques to preserve the lower extremity and maintain the patient's ability to ambulate. Soft tissue defects in the distal one-third of the leg have often been deemed as a challenging anatomical area in terms of reconstructive surgery due to the limited amount of available tissue coverage.[2] Healing after surgery is also complicated with comorbidities such as diabetes and peripheral vascular disease. As such, many local, regional, and free flap techniques have been proposed to address this difficult region of the lower extremity[2]. Microvascular free-flap techniques are commonly expensive and complicated, thus, the search for a reliable local flap has become very crucial in limb salvage.[3]

One local flap technique is the reverse peroneus brevis technique, also known as the distal peroneus brevis muscle flap.. The use of the peroneus brevis muscle as a flap was first described in 1977 by Methes and Nahai.[4] In 2001, Eren et al described a new distally based peroneus brevis flap to cover the area about the ankle while preserving its blood supply. This article aims to provide a current literature review on the outcomes of the reverse peroneus brevis muscle flap in reconstructive surgery.

Methods

A methodical literature review was performed, employing PubMed and WesternU's Pumerantz Library search engines, focusing on keywords such as "reverse peroneus brevis muscle flap" and "distal peroneus brevis flap." Results were then collected and additional articles were acquired using minimal variations of the keyword searches. Articles were then compiled and analyzed by the authors. Articles which reported on the outcomes of the peroneus brevis muscle flap for defects in the lower extremity were included and articles that were not reported in the English language were excluded from this review. A total of 4 articles were included in this review.

A summary of the findings are reported in the following sections, followed by a review on the surgical outcomes of the reverse peroneus brevis muscle flap for distal lower extremity reconstructive surgery.

Results

A case series performed by Bach et al, follows 15 patients following a reverse peroneus brevis flap procedure. Of these 15 patients, 5 were female and 10 were male, ranging between the ages of 29-81 years old. The defects necessitating the procedure were caused by debridement of the calcaneus following chronic osteomyelitis (n = 3),

debridement of distal fibula following chronic osteomyelitis (n = 2), excision of melanoma at the heel (n = 1), posttraumatic defects of lateral and medial malleolus (n = 2), posttraumatic defects of the Achilles tendon (n = 6), and chronic diabetic ulcer of the heel (n = 1). The defects ranged from 6 to 60 cm^2 in size and the total surgery time ranged from 68 to 134 minutes from opening to closure. Of the 15 patients included in this study, only 1 patient's flap necrosed at the distal portion of the flap, requiring further surgery and graft placement. 1 patient developed a hematoma that required evacuation of the hematoma. 2 other patients displayed delayed wound healing, however it was managed with daily dressing changes. All other patients displayed flap stability and good contour. No other patients were reported to need further reconstructive surgery. There were also no reported cases of recurrent osteomyelitis and tumors noted.

Abd-Al-Moktader et al reports on 42 patients following a reverse peroneus brevis flap. Of these patients, 30 were male and 12 were female. The defects prior to the procedure included sustained injuries in road traffic accidents with major lower leg and ankle defects (n=20), chronic ulcer and unstable scars (n=12), and post diabetic wound loss of skin over the Achilles tendon area (n=10). The outcomes of this procedure reported partial flap loss in 2 patients. Of these 2 patients, 1 healed with dressing changes. The other patient, who was an active smoker, was reported to lose the distal portion of the muscle. However, no patients were reported to necessitate further reconstructive surgery.

In a clinical series performed by Ensat et al, 10 patients underwent a reverse peroneus brevis flap procedure. Of these 10 patients, 7 were male and 3 were female. The pre-operative defects included trauma (n=8), infection (n=1), and pressure sore (n=1). The average measurements of the defect were reported to be 3.5 x 7.3 cm. The localized areas included the lateral malleolus (n=7), lateral calcaneus (n=2), and the achilles tendon (n=1). Of the 10 patients, only 1 patient had a distal tip necrosis of the flap requiring a skin graft. The other 9 patients experienced 100% flap survival with no further complications. Further healing of the flaps were uneventful and stable. All donor sites were able to heal primarily with a linear scar and no functional impairment was reported.

In a study by Nguyen and Collazo, 17 patients with Type 2 Diabetes Mellitus underwent a distally based peroneus brevis muscle flap. These patients were recommended for a below the knee amputation because of non-healing heel ulcerations at the heel and peripheral vascular disease. These ulcers had been present for more than 12 months and the reverse peroneus brevis flap was offered to these patients as a last result. Flap survival was 100% with only 2 partial tip necrosis that healed uneventfully with local wound care. There were no reports of osteomyelitis or major amputation observed. The split-thickness skin graft from the donor site of the calf healed uneventfully as well. Results were satisfactory to both patient and surgeon with durable coverage and maintenance of limb length.

Discussion

The objective of this study was to review the current available literature for the outcomes of the reverse peroneus brevis muscle flap technique. This flap has been considered, however often overlooked, as a viable option for covering defects in the delicate area about the ankle and distal lower extremity. Neurofasciocutaneous flaps such as the sural flap have become more popular for defects of the distal lower extremity. Arguably, muscle flaps remain the best option for osteomyelitis, soft tissue infections, and cavities.[6] The peroneus brevis muscle flap was originally designed as a proximally based flap for pre-tibial effects. It has since been described for ankle wound coverage, heel ulcers and large leg ankle and foot defects.

Analysis of the 4 articles reviewed in this study included a total of 86 cases following a reverse peroneus brevis flap procedure for various indications. 7% of these patients reported an unfavorable outcome of distal tip necrosis of the peroneus brevis muscle. This complication is most likely due to the limited available literature regarding the reverse peroneus brevis transfer and can be attributed to a technical error regarding the careful dissection of the peroneus brevis muscle. It is imperative to preserve the blood supply of the muscle and Ensat et al describes this technique regarding the essential measurements regarding dissection that must be taken into account to avoid this technical problem. The articles by Ensat et al and by Nguyen and Collazo also emphasize pre-operative mapping of

the distal segmental branch of the peroneal artery using a Doppler to increase the reliability of the muscle flap.

Additionally, another rationale for the outcome of distal necrosis of the flap is the accompanied comorbidities of the included patients. For example, in the study by Nguyen and Collazo that follows 17 patients necessitating the reverse peroneus brevis muscle flap, all subjects included in this study had a known diagnosis of peripheral vascular disease. Other comorbidities reported in the other 3 articles included in this study consist of diabetes and hypertension, which are known diseases that compromise blood flow.

Nonetheless, one can theorize that the aforementioned outcome is multifactorial and Bach et al offers a clear summary on the possible different parameters that affect the reliability and survival of the reverse peroneus brevis muscle flap. The author mentions vascular risk factors, age of patients, arc of rotation and kinking of the pedicle area, inadequate preparation, unneeded tunneling of the flap, and tissue trauma due to accidents or irradiation, may negatively influence perfusion of the entire flap. Regardless of this negative outcome, 5 out of 6 patients that reported distal flap necrosis healed uneventfully with proper wound care techniques. These techniques include negative pressure therapy and daily dressing changes. Abd-Al-Moktader et al reports of the 1 instance where the distal tip necrosis resulted in loss of the distal portion of the peroneus brevis muscle. Here, the author attributes the loss of the muscle due to the patient's history of smoking.

Conversely, there are positive outcomes that are reported in the 4 articles included in this study, where 93% of the patients included in this review experienced complete flap survival and no need for further reconstructive procedure. The most significant outcome being the preservation of the ambulatory capacity of the patient. Bach et al and Ensat et al report that no functional impairment of the affected leg occurs due to flap harvest. Foot eversion and plantarflexion as well as ankle functionality were maintained due to preservation of the peroneus longus muscle. This allows patients to maintain their quality of life, as ambulation is a known key metric to improved health.

Furthermore, as seen in the article by Nguyen and Callazo, the reverse peroneus brevis muscle flap offers a better outcome for patients facing amputation. The 17 patients included in this study had non-healing ulcers and peripheral vascular disease with non palpable posterior and anterior tibial arteries however, a palpable peroneal artery. These patients had originally been referred to orthopedics for a below-the-knee amputation. Instead, the patients underwent a reverse peroneus brevis procedure and were able to salvage their limbs, allowing them to bear weight without prosthesis.

Alternatively, the 4 articles included in this study presented possible limitations. This includes the inherent non-randomized patient selection, due to the nature of amputation prevention. Small sample sizes in each article may also contribute to inaccuracy when applied to larger population sizes. Additionally, there were no control groups included in any of the studies to prevent bias.

Conclusion

Overall, the Reverse Peroneus Brevis flap should be considered as an option for surgical reconstruction of the distal lower extremity, as it has great outcomes for patients. The ability to reconstruct the distal lower extremity, a known challenging anatomical area, and the preservation of patients' ambulation makes this technique an attractive option for both patient and surgeon. Further research utilizing a larger series of patients with controls may better help reconstructive surgeons to optimize this technique for future use.

References:

1. Kadam D. Limb salvage surgery. *Indian J Plast Surg*. 2013;46(2):265-274.
2. Malahias M, Khalil H, Abdalbary SA, Abdelkader R. Distally-based Peroneus Brevis Turnover Muscle Flap in the Reconstruction of Soft Tissue Defects. *Plast Reconstr Surg Glob Open*. 2020;8(12):e3290. Published 2020 Dec 18.
3. Khouri, Roger K. M.D.; Shae, William W. M.D.. Reconstruction of the Lower Extremity with Microvascular Free Flaps: A 10-year Experience with 304 Consecutive Cases. The Journal of Trauma: Injury, Infection, and Critical Care: August 1989 - Volume 29 - Issue 8 - p 1086-1094
4. Podiatry Institute. Reverse Peroneus Brevis Muscle Flap for Dorsal Foot Wound Coverage: A Case Study . Chp 25
5. Eren S, Ghofrani A, Reifenrath M. The distally pedicled peroneus brevis muscle flap: A new flap for the lower leg. *Plastic and Reconstructive Surgery*. 2001;107(6):1443-1448.

6. Bach AD, Leffler M, Knese U, Kopp J, Horch RE. The versatility of the distally based peroneus brevis muscle flap in reconstructive surgery of the foot and lower leg. *Annals of plastic surgery*. 2007;58(4):397-404.
7. Abd-Al-Moktader. Distally Based Peroneus Brevis Muscle Flap for Large Leg, Ankle, and Foot Defects: Anatomical Finding and Clinical Application. *Journal of Reconstructive Microsurgery*. 2018;34(8):616-623. Ensat F, Hladik M, Larcher L, Mattiassich G, Wechselberger G. The distally based peroneus brevis muscle flap-clinical series and review of the literature. *Microsurgery*. 2014;34(3):203-208.
8. Nguyen T, Rodriguez-Collazo ER. Healing Heel Ulcers in High-Risk Patients: Distally Based Peroneus Brevis Muscle Flap Case Series. *Journal of Foot & Ankle Surgery*. 2019;58(2):341-346.
9. Rodriguez Collazo ER, Bibbo C, Mechell RJ, Arendt A. The Reverse Peroneus Brevis Muscle Flap for Ankle Wound Coverage. *Journal of Foot & Ankle Surgery*. 2013;52(4):543-54

Acute Achilles Tendon Rupture: An analysis of complications related to conservative and surgical treatment

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ABSTRACT

Objective: This review aims to analyze research on the post-procedure complications associated with conservative and surgical treatment of Achilles tendon (AT) ruptures.

Methods: Relevant research pertaining to Achilles tendon rupture conservative opposed to surgical treatment complications was completed using Western University Pumerantz Library database, Wiley Online Library, and PubMed. Key terms such as "Achilles tendon rupture treatment," "Achilles tendon rupture surgical," and "Achilles tendon rupture non-surgical," were used to find relevant literature.

Results: Surgical and non-surgical treatment of Achilles tendon rupture can cause varying complications such as re-rupture, deep vein thrombosis, nerve disturbances, contractures, scarring, and cosmetic concerns. Neither conservative nor surgical treatment can prevent complications from occurring.

Conclusion: There are no significant differences in post-procedure complication rates between the surgical and conservative treatment of Achilles tendon rupture repairs.

Introduction

The Achilles tendon (AT) serves as the strong tendinous culmination of the gastrocnemius and the soleus muscles, inserting on the calcaneus. Although this tendon is the strongest and largest tendon in the body, AT ruptures remain a relatively common injury affecting 31.71 per 100,000 people by some estimates.[1] AT injuries predominantly occur in white collar individuals in the 3rd and 4th decade of life while participating in sports activities.[2] Given the relative commonality of AT ruptures, the discussion between surgical and conservative treatment remains a controversial discussion. It is true that the initial decision when presented with an AT rupture is between surgical or non-surgical treatment, and in the past, aggressive surgical interventions were recommended over conservative management.[3] Different treatment options exist and more recent studies have indicated that conservative treatment may have more favorable outcomes such as reduced re-rupture rates when compared to surgical repair.[4] This serves as an important discussion point as complications and complication rates serve as the cornerstone when discussing whether surgical or conservative treatment, is best for each AT rupture patient.

The lack of consensus on the best treatment for each patient further indicates that AT rupture management will usually depend on the surgeon and patient preference.[1] In any case, the type and prevalence of complications associated with each procedure should be carefully considered. Therefore, this analysis will assess three articles and their findings related to complications and complication rates associated with surgical and conservative treatment of AT ruptures.

Methods

Relevant research articles pertaining to conservative and surgical treatment complications for Achilles tendon rupture from 2002-2020 were identified using Western University Pumerantz Library database, Wiley Online Library, and PubMed. Key terms such as "Achilles tendon rupture treatment," "Achilles tendon rupture surgical," and "Achilles tendon rupture non-surgical," were used to find relevant literature. Articles were included in this review if they were published in the last 20 years, and preference was given to studies that were conducted in the last 10 years. Studies were excluded from this review if they were published more than 20 years ago. The complications and complication rates for each of the examined studies were pulled directly from the article. This information was organized into the figures seen below in the results section. The percentage of complications seen in Table 4 was calculated in-house by dividing the number of

patients who experienced complications by the total number of patients included in that specific group.

Results

Olsson et al 2013

This study followed 101 patients, aged 18-65 years old with a male:female ratio of 39:10 in the surgical group and 47:4 in the non-surgical group. All patients presented with a midsubstance rupture, which was diagnosed on medical history and clinical examination which depended on a palpable gap and positive Thompson test result. After 101 patients were identified for inclusion into the study, they were then randomized into the surgical and non-surgical groups. One patient was initially included in the study despite having an ongoing skin infection and was excluded from the study directly after randomization. The surgical group AT ruptures were treated using core suturing with two strong semi absorbable sutures and a modified Kessler technique. The ankle was then postoperatively immobilized for six weeks in a pneumatic walker brace including three heel pads that produce a plantarflexion angle of approximately 22 degrees. The non-surgical group was treated immediately following randomization with the same brace used post-operatively with the surgical patients. The non-surgical group was immobilized in the brace for eight weeks. Follow-up examination for complications was performed at 2, 6, and 26 weeks for the surgical group and 8 and 26 weeks for the non-surgical group. Additionally, follow-up for functional analysis was performed at 6 months and 12 months for both groups. The complications noted in the patients involved in this study can be seen in Table 1. Not seen in Table 1 is one surgically treated patient who did sustain a partial re-rupture of the AT during a fall that occurred three weeks after the last day of immobilization.[5]

Group	Re-rupture	DVT	Superficial Skin Infection	Sural Nerve Disturbance	Macerated Skin and Pain/Pressure Induced Nerve Disturbance	Total Number of Patients
Surgical	0	1	6	1	13	49
Non-Surgical	5	2			2	51

Table 1: The complications reported by Olson et al 2013 and the number of patients that experienced said complications.

Keating and Will 2011

This study followed 80 patients, aged 25-58 years old with a female:male ratio of 28:11 in the surgical group and 32:9 in the non-surgical group. All patients presented with an acute rupture of the AT and were then randomly assigned to the surgical and non-surgical groups. The surgical group was scheduled as an urgent case and was operated on within seven days of presentation. The surgical procedure utilized an open technique where a core Kessler stitch with double-stranded PDS suture was used to oppose the tendon ends which was then supplemented with interrupted vicryl circumferential sutures. The patients were immobilized in a full equinus cast for four weeks and a semi-equinus cast for two weeks followed by the removal of the cast and full weight bearing. The non-surgical patients were put into a below-knee cast for 10 weeks in total. The first four weeks in full equinus, semi-equinus for four weeks and neutral for two weeks. Follow-up for both groups occurred for one year. Table 2 illustrates the total complications reported and the number of complications observed in the surgical and non-surgical group.[6]

Group	Re-rupture	DVT	Infection	Total Number of Patients
Surgical	2		3	39
Non-Surgical	4	2		41

Table 2: The complications reported in Keating and Will 2022 and the number of patients that experienced said complications.

Nilsson-Helander et al 2010

This study followed 100 patients ages 16-65 years old with a male:female ratio of 40:9 in the surgical group and 39:9 in the non-surgical group. All patients presented with an acute AT rupture which was diagnosed based on medical history and a clinical examination, which included tendon palpation and Thompson's test. Patients were randomized into either surgical or non-surgical groups. Two patients who were randomized to receive non-surgical treatment opted to receive surgical treatment. One patient who was randomized to the surgical treatment group was treated non-surgically because surgery was not possible within 72 hours. This led to 97 patients being included in

follow-up evaluations. The surgical group was treated using an open technique which conducted an end-to-end suture using the modified Kessler suture technique. Post-operatively the patients were placed in a below the knee cast with the foot in 30 degrees equinus position. Of note, the surgical group was treated with thromboprophylaxis consisting of 500 mL of high molecular weight dextran according to protocol. The non-surgical group was treated immediately with a below the knee cast with the foot in equinus position. Both the surgical and non-surgical groups were treated with below the knee casts for two weeks and then switched to an adjustable brace which limited dorsiflexion to 30 degrees and then 10 degrees for the following two weeks and four weeks respectively. Follow-up occurred for both groups at 2, 8, and 12 weeks in addition to the 6 month and 12 month marks. Table 3 demonstrates the complications reported in this study and the number of patients who experienced the complications.[3]

Group	Re-rupture	AT Contracture	Infection	DVT	Nerve Disturbance	Scaring Complaint	Cosmetic Complaint	Total Number of Patients
Surgical	2	1	2	14	2	13	10	49
Non-Surgical	6			18				48

Table 3: The complications reported in Nilsson-Helander et al 2010 and the number of patients that experienced said complications.

Discussion

AT rupture is a relatively common injury and this injury will often lead to long periods of immobilization and rehabilitation, therefore, treatment modality remains an important discussion.[7] Though much of the current research is focused on functional outcomes when comparing surgical and non-surgical repair of AT rupture, the complications associated with each treatment are important to consider. In each of the three randomized controlled studies reviewed, it was clear that re-rupture was a serious complication related to both surgical and non-surgical management of AT rupture.

Nilsson and Helander et al 2010 presented the prevalence of re-rupture to include "accidents" and how they may contribute to the AT re-rupture in the patients who were involved in their study. Within the study, they reported that two patients experienced re-rupture due to accidents. One patient in the surgical group had slipped two weeks after the initial injury resulting in re-rupture and one patient in the non-surgical group experienced re-rupture due to fall. Along the same lines, though accidents were not explicitly mentioned, Olson et al 2013 did report that one surgical patient did suffer from a partial re-rupture (which was not included in Table 1 or Table 4) after a fall three weeks following the final day of immobilization, and one non-surgical patient suffered re-rupture during a fall down the stairs. Although "accidents" were not common within the three studies, it does introduce discussion when considering treatment for an AT tear. Although accidents can occur unexpectedly, they are a part of daily living. Even though re-rupture due to accidents did occur in both groups, the potential for a patient to experience such an incident should be considered when treating an AT tear.

Re-rupture seemed to be among the most common complications related to AT tears. Across all three studies, the three reported complications in common were re-rupture, deep vein thrombosis (DVT), and infection. Within the three studies, the average percentage of these three complications combined were 21.9% with surgical treatment and 26.4% with non-surgical treatment. When viewing the combined data it would appear that the prevalence of re-rupture was significantly higher in the non-surgical group, however, when each study is examined alone, the prevalence of re-rupture between groups was not significant. Keating & Will 2011 reported that re-rupture rates were higher in the non-surgical group, but this difference was regarded as not statistically significant. Nilsson-Helander et al 2010 reported similar findings as there was no significant difference in re-rupture rates between surgical and non-surgical groups. Though the significance of re-rupture rates in Olson et al 2013 was not explicitly stated, it did mention that no major soft tissue complications were associated with the surgical group.

Holm, Kjaer, and Eliasson 2014 conducted a meta-analysis evaluating the complications surrounding surgical and non-surgical management of AT rupture and found that there was no significant difference in re-rupture rates between surgical and non-surgical treatment groups. They also cited Moller et al 2001 which did demonstrate a statistically significant difference in the rate of re-rupture rate of 20.8% and 1.7% in the non-surgical and surgical

groups respectively. Conversely, Holm, Kjaer, and Eliasson 2014 also cited meta-analysis Van der Eng et al 2013 which demonstrated that no statistical significance was found in re-rupture rates between the surgical and non-surgical treatment groups. Although no statistical analysis was conducted in the making of Table 4 or Graph 1, it is interesting to see such a noticeable difference in re-rupture rates between the two groups, but the results in each study when examined alone were not significant. Olson et al 2013 set the significance at $P < 0.05$, and the rate of re-rupture was determined to be $P = 0.057$. Similarly, Keating and Will 2011 determined the re-rupture rates between the two groups to not be significant via Fisher's exact test which yielded $P = 0.676$. Finally, Nilsson-Helander et al 2010 had similar results in that the significance was set at $P < 0.05$, and the rate of re-rupture was determined to be $P = 0.377$.

Given the findings, in addition to other reports from various studies, there is no accurate indication of which treatment yields lower rates of re-rupture as there are numerous studies with conflicting findings. Therefore, it seems that a larger scale study must be conducted in order to further verify which treatment is associated with high rates of re-rupture.

Though re-rupture represents a serious complication, DVT also serves as a complication that must be considered. As stated previously, no statistics were performed in the making of Table 4 and Graph 1, however, at first glance there does seem to be an increase in the prevalence of DVT in the non-surgical treatment group. This was initially surprising as DVTs are serious complications associated with orthopedic surgery. However, given the lack of statistics performed on the prevalence of DVT, it cannot be stated truly which group has a higher risk of DVT. The findings reported in Table 4 and Graph 1 are purely observations included for completeness. Of the three studies examined, Nillson-Helander et al 2010 was the only study that analyzed the differences in DVT prevalence between the two groups. They found 18 patients in the non-surgical group suffered from DVT whereas 14 patients in the surgical group suffered from DVT. This difference was found to be statistically insignificant.[8] Therefore, this leads us to believe that the findings in Table 4 and Graph 1 regarding DVT prevalence between the two groups may be due to a relatively small sample size and additional research must be conducted to draw a conclusion on which group has a higher prevalence of DVT.

When assessing each of these studies, it was noted that each had its own set of limitations and thus, the data reported for each study must be interpreted with these limitations in mind. Olsson et al 2013 reported five primary limitations to their study. First, it was reported there was a lack of biomechanical assessments following the suture technique, and instead used literature to appropriately construct their suture technique. Secondly, it was reported that the surgical group was subjected to an accelerated rehabilitation protocol postoperatively which the non-surgical group did not have. Therefore, the study recognized that it is unclear whether the surgery or the accelerated rehabilitation protocol made the difference. Thirdly, it was reported that the study was not blinded which has the potential to introduce bias. Fourth, it was reported that patients were instructed to weight bear as early as the 1st day, however, the degree of weight bearing was not measured. The fact that weight bearing was encouraged and not measured introduces an unaccounted variable. Finally, it was reported that the difference in re-ruptures between the surgical and non-surgical group could be due to type II error. This is an important consideration, as inappropriately concluding a treatment is superior can negatively affect patient outcomes.

Keating and Will 2011 mentioned a limitation of the study which said that the differences found between the surgical and non-surgical groups may have been statistically significant if a larger patient sample was used, and thus, a type II error is a possibility. Thus, further studies utilizing a larger sample size may be necessary to further verify the results reported.

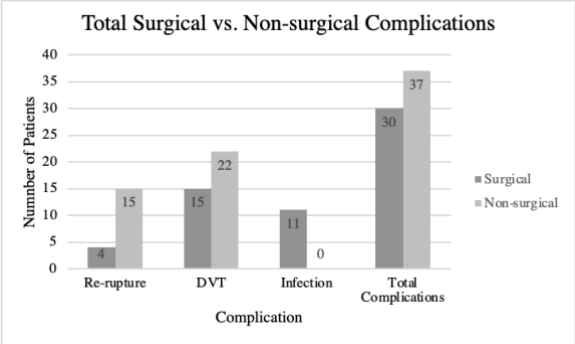
Nillson-Hendler et al 2010 noted that a potential limitation of their study involved the number of patients examined. It was noted that because there were relatively few patients included, their outcomes weighed more heavily upon the results than if the sample size was expanded. It was also noted that most other studies were plagued with this issue, therefore, substantiating the need for additional studies with larger sample sizes. Increasing the sample size would decrease the impact of individual complications within each group, allowing

for more accurate analysis of the prevalence of complications within the surgical and non-surgical groups.

Finally, it is important to acknowledge the potential bias the authors may have introduced in this study. Selection bias is an important consideration and its presence within this study must be assessed. When choosing studies to include in this analysis, the authors determined it would be in the best interest to analyze randomized studies which compared outcomes between surgical and non-surgical groups. Though this was effective to assess potential differences between the two treatment groups, this study did lack strength in that only three papers were included. This alone can contribute to bias as there is a wealth of data regarding surgical vs. non-surgical treatment for acute AT tears and a more thorough analysis would be required for a definitive conclusion. Additionally, each of the three papers assessed included relatively small sample sizes. This, coupled with the lack of additional studies, further contributes to the limited generalizability of the results and discussion report in this study. Furthermore, this study did not perform any statistical analysis, rather the results reported were simply percentages calculated across the included articles. The lack of statistical analysis contributes to relatively limited generalizability of the data reported. A thorough meta-analysis serves as a sensible next step for this investigation. Not only would this contribute to the current literature on the topic, it would serve as a valuable reference for clinicians tasked with treatment of acute AT ruptures.

Group	Re-rupture	DVT	Infection	Total Complications	Total Patients	Percentage of Complications
Surgical	4	15	11	30	137	21.9%
Non-surgical	15	22	0	37	140	26.4%

Table 4: The combined total number of reported Re-rupture, DVT, and Infection surgical vs. non-surgical complications, the number of total patients, and percentage of complications per patient, between all three studies.



Graph 1: The total number of reported Re-rupture, DVT, and Infection surgical vs. non-surgical complications between all three studies.

Conclusion

This review aimed to analyze the research on the post-procedure complications associated with conservative and surgical treatment of AT ruptures. The results determined that no single approach to AT rupture treatment will limit complications for patients. Without significant data to favor conservative or surgical treatment, it can be concluded that it is best to make the treatment decision based on the final goals and preferences of the patient and surgeon. However, further research could shift the paradigm from preference towards evidence based medicine which would innately improve outcomes and patient satisfaction.

References

1. Yasser Reda, Amr Farouk, Ibrahim Abdelmonem, et. al. (2020). Surgical versus non-surgical treatment for acute Achilles' tendon rupture. A systematic review of literature and meta-analysis, Foot and Ankle Surgery,Volume 26, Issue 3, 2020, Pages 280-288, ISSN 1268-7731,
2. Schepsis AA, Jones H, Haas AL. Achilles Tendon Disorders in Athletes. The American Journal of Sports Medicine. 2002;30(2):287-305.
3. Nilsson-Helander K, Grävare Silbernagel K, Thomeé R, et al. Acute Achilles Tendon Rupture: A Randomized, Controlled Study Comparing Surgical and Nonsurgical Treatments Using Validated Outcome Measures. The American Journal of Sports Medicine. 2010;38(11):2186-2193.
4. Park SH, Lee HS, Young KW, et. al. Treatment of Acute Achilles Tendon Rupture. Clin Orthop Surg. 2020 Mar;12(1):1-8.
5. Olsson N, Silbernagel KG, Eriksson BI, et al. Stable Surgical Repair With Accelerated Rehabilitation Versus Nonsurgical Treatment for Acute Achilles Tendon Ruptures: A Randomized Controlled Study. The

American Journal of Sports Medicine. 2013;41(12):2867-2876.
6. Keating J. F., and Will, E. M. Operative versus non-operative treatment of acute rupture of tendo achilles: A prospective randomized evaluation of functional outcome. The Bone & Joint Journal. 2011;93(8).
7. Schepull T, Aspenberg P. Early Controlled Tension Improves the Material Properties of Healing Human Achilles Tendons After Ruptures: A Randomized Trial. The American Journal of Sports Medicine. 2013;41(11):2550-2557.
8. Holm C, Kjaer M, Eliasson P. Achilles tendon rupture--treatment and complications: a systematic review. Scand J Med Sci Sports. 2015 Feb;25(1):e1-10.. Epub 2014 Mar 20. PMID: 24650079.
9. Moller M., Movin, T., Granhed, H., et al. A prospective, randomized study of comparison between surgical and non-surgical treatment. *The Bone & Joint Journal.* 2001;83(6).
10. Dorien M. van der Eng, Tim Schepers, J. et al,, Rerupture Rate after Early Weightbearing in Operative Versus Conservative Treatment of Achilles Tendon Ruptures: A Meta-analysis,The Journal of Foot and Ankle Surgery,Volume 52, Issue 5, 2013,Pages 622-628, ISSN 1067-2516.
11. Nilsson-Helander, K., Thurin,, a., Karlsson, J. et al. High incidence of deep venous thrombosis after Achilles tendon rupture: a prospective study. *Knee Surg Sports Traumatol arthrosc* 17, 1234-1238 (2009).

A Review of Recent Literature Comparing Straight versus Valgus Intramedullary Nails in Tibiotalocalcaneal Arthrodesis

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Abstract

Objective: This paper will review recent literature comparing the use of straight versus valgus intramedullary (IM) nails in tibiotalocalcaneal (TTC) arthrodesis in the treatment of ankle arthritis and deformity.

Methods: A literature search was performed on the Pumerantz Library, PubMed, and Google Scholar to identify recent articles that compared the use of valgus IM nails to ones that were straight in TTC arthrodesis procedures. The terms used in this search were "tibiotalocalcaneal arthrodesis," "tibiotalocalcaneal arthrodesis intramedullary nail," "comparison of valgus and straight tibiotalocalcaneal intramedullary nail," and "comparison of bent and straight tibiotalocalcaneal intramedullary nail."

Results: Retrograde intramedullary nails provide rigid internal fixation in TTC arthrodesis. The alignment of the hindfoot is key to the success of a TTC arthrodesis. Several studies have shown that a valgus bend to the intramedullary nail used in TTC arthrodesis may result in fewer insults to key anatomic structures. Conversely, recent literature also asserts there may not be a significant difference in damage to anatomic structures when using straight compared to valgus IM nails and that valgus nails may cause more pain.

Conclusion: TTC arthrodesis with valgus IM nail has been shown to yield promising results. However, little research has been conducted directly comparing the newest iteration of intramedullary tibiotalocalcaneal nails against straight nails.

Introduction

End-stage ankle arthritis is a debilitating disease. There are a variety of etiologies responsible for end-stage arthritis including primary arthritis, ankle trauma, and failure of previous ankle surgeries. End-stage ankle arthritis can significantly impact one's quality of life by limiting their ability to ambulate pain-free. Surgical correction is essential to treating these pathologies and helping patients return to activity.[1]

There are a variety of surgical approaches for fixation of TTC arthrodesis. These include plates, crossing cancellous screws, and retrograde IM nails. Retrograde IM nails are generally preferable to other internal fixation options. IM nails used in TTC arthrodesis can create compression across the ankle and subtalar joints, which is a key factor to achieving successful arthrodesis. Retrograde nails are difficult to insert due to the surrounding neurovascular anatomy.[2]

Recent iterations to the IM nail used in TTC arthrodesis accommodate for the anatomy of the hindfoot. One iteration includes a valgus bend to the intramedullary nail. This paper examines the hypothesis that the valgus bend in IM nails allows for improved clinical results following TTC arthrodesis.

Methods

A literature review was conducted utilizing databases such as the Pumerantz Library, PubMed, and Google Scholar. Key words used to identify articles of interest included: "tibiotalocalcaneal arthrodesis," "tibiotalocalcaneal arthrodesis intramedullary nail," "comparison of valgus and straight tibiotalocalcaneal intramedullary nail," and "comparison of bent and straight tibiotalocalcaneal intramedullary nail." This article is focused on papers which analyzed the use of retrograde IM nails in TTC arthrodesis. Articles greater than 20 years old were excluded to incorporate the most recent and relevant literature. Each of the articles were scrutinized based on the population size, treatments provided, and the outcomes as they relate to different types of IM nails.

Results

In an anatomic study, Mückley et al used six pairs of thawed fresh-frozen cadavers to compare TTC arthrodesis using a straight IM nail versus an IM nail with a valgus curve. After recreating the operative procedure, the nails were inserted, and the outcomes were assessed using radiographs and computed tomography (CT). The straight nail was designed with a lateral-medial locking tip with posterior to anterior locking in the calcaneus while the valgus-curved nail incorporated a 5-degree curve with a medial-lateral locking tip in the distal tibia and posterior to anterior locking in the calcaneus. This curve was intended to reduce risk of injury to vascular structures and musculature. The distance to various at-risk structures and the hardware were measured. The result of this study was that the valgus-curved IM nail was significantly farther from the flexor hallucis longus ($p = 0.047$), medial plantar artery ($p = 0.026$), and lateral plantar nerve ($p = 0.026$) compared to the straight nail. Additionally, the straight nail damaged anatomic

structures significantly more often. These include the extensor digitorum longus ($p = 0.007$), the anterior tibial artery ($p = 0.04$), and the deep and superficial peroneal arteries ($p = 0.03$). This demonstrates the possible benefits of this specific type of nail.[3]

A case series by Hernandez et al analyzed the radiographic and clinical outcomes of TTC arthrodesis using a straight IM nail. 49 patients were included in this study with an average follow-up of 70.7 months. Outcomes were measured using the American Orthopaedic Foot and Ankle Society (AOFAS) score which improved from 29.7 to 65.8 before and after TTC arthrodesis. An improvement in varus angulation also was noted from -3 degrees varus to 3.5 degrees valgus. Complications often associated with use of a straight nail including lateral plantar neurovascular disorders, cortical stress at the nail tip, and soft tissue injuries were not noted in this study.[4]

Fang et al performed a cohort study with 22 patients between June 2009 and January 2012 on the use of retrograde IM nail with a valgus curve in TTC arthrodesis. The IM nail used in this study had a 5-degree valgus curve with 10-degrees external rotation. The AOFAS ankle-hindfoot score in this group of patients was 69.9 after an average 22.3 months of follow-up. Six patients reported mild pain in the extended post-operative period. Patients in this study achieved 100% bony union and plantigrade fixation of the foot. Although some exhibited marked gait abnormalities or had difficulty ambulating on uneven terrain.[5]

Further study on TTC arthrodesis using valgus IM nails was conducted on 66 patients with ankle arthrosis or by Richter and Zech. The IM nail in this study employed a triple-bend and 60 patients completed a two-year follow-up. The Visual Analogue Scale Foot and Ankle (VAS FA) was used to assess the clinical outcomes. At two years, the mean VAS FA was 59.9 compared to 29.6 preoperatively ($p < 0.001$). This represents an improvement in clinical outcomes for 91% of the patients. Additionally, a 100% fusion rate was observed in patients and there were no neurovascular complications.[6]

Discussion

The current literature surrounding TTC arthrodesis lacks direct comparisons between implementation of straight and valgus IM nails. Mückley et al conducted one of the first comparative studies of straight IM nails compared to valgus IM nails.[3] This is significant as few studies before or since have been designed to directly compare any characteristics of the two systems. This study mostly focused on the damage that insertion of each type of nail may cause to surrounding anatomical structures. The increased risk of damaging structures such as the anterior tibial and peroneal arteries when using a straight IM nail is important for surgeons to consider. A weakness of anatomy in this study is that their sample size of six pairs of legs does little to account for the variations in human anatomy. Additionally, the study does not expand on other outcomes of TTC arthrodesis to compare these two systems.[3]

One such important outcome of TTC arthrodesis is fusion. Fusion is challenging to achieve, particularly due to the size of the joints and motion that typically occurs in the ankle and subtalar joints. Based on the study by Fang et al and Richter and Zech, most patients who underwent TTC arthrodesis with a valgus IM nail exhibited fusion by the 22 to 24 months post-op.[5,6]

The case series presented by Hernandez et al demonstrated notable improvement in AOFAS score when using a straight IM nail in TTC arthrodesis. While this study did not compare the use of a straight IM nail to one with a valgus curve, it demonstrated that the valgus curve is not crucial to achieving a correction from -3 degrees varus to 3.5 degrees valgus. This challenges the utility of the valgus IM nail. This study also showed that in this series of patients, the straight IM nail did not pose a risk to surrounding tendons and neurovascular structures. This contradicts the results by Mückley et al that the valgus IM nail preserves anatomic structures better than a straight IM nail.[3,4]

The study by Fang et al found that the use of valgus curved IM nails in TTC arthrodesis resulted in mild pain. Additional results from this study revealed that patients who underwent retrograde valgus IM nail insertion experienced marked gait abnormalities and difficulty ambulating on uneven terrain. This is to be expected from fusion of the subtalar and ankle joints. It can be expected that due to fusion of these joints, abnormal biomechanical stress is applied to the other joints and a significant loss in range of motion would be observed throughout the foot and ankle. This would ultimately result in changes in gait.[5]

Conclusion

The use of valgus IM nails in TTC arthrodesis is one of many options in the treatment of hindfoot arthritis. While recent literature has shown there may be a place for valgus TTC nails, other studies challenge the utility of a curved TTC nail, noting that there is no increased risk to anatomic structures with use of a straight nail and that valgus nails cause mild pain.[3,4] Additional research involving multi-center studies in a broader population are necessary to assess whether use of the valgus IM nail yields improved results over straight nails.

References

1. Martínez-de-Albornoz P, Monteagudo M. Tibiotalocalcaneal Arthrodesis in Severe Hindfoot Deformities. Foot Ankle Clin. Dec 2022;27(4):847-866.
2. Tarkin IS, Fourman MS. Retrograde Hindfoot Nailing for Acute Trauma. Curr Rev Musculoskelet Med. 2018 Sep;11(3):439-444.
3. Mückley T, Ullm S, Petrovitch A, et al. Comparison of two intramedullary nails for tibiotalocalcaneal fusion: anatomic and radiographic considerations. Foot Ankle Int. May 2007;28(5):605-13.
4. Lucas Y Hernandez J, Abad J, Remy S, Darcel V, Chauveaux D, Laffenetre O. Tibiotalocalcaneal arthrodesis using a straight intramedullary nail. *Foot Ankle Int*. May 2015;36(5):539-46.
5. Fang Z, Claaßen L, Windhagen H, Daniilidis K, Stukenborg-Colsman C, Waizy H. Tibiotalocalcaneal arthrodesis using a retrograde intramedullary nail with a valgus curve. Orthop Surg. May 2015;7(2):125-31.
6. Richter M, Zech S. Tibiotalocalcaneal arthrodesis with a triple-bend intramedullary nail (A3)-2-year follow-up in 60 patients. Foot Ankle Surg. Jun 2016;22(2):131-8.

EXTREMITAS

Conservative Treatment

Analyzing Mycological and Complete Cure Rates to Compare Efficacy of Various Topical Antifungals in the Pediatric Population: A Review

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ABSTRACT

Objective: To evaluate the efficacy of topical antifungal therapy for onychomycosis in the pediatric population.

Methods: A systematic review of available literature was conducted. Key terms regarding the topic were searched on six different databases (CINAHL, Cochrane, Embase, PubMed/Medline, Science Direct, and Web of Science). Inclusion and exclusion criteria were applied, and three relevant articles were selected. These articles were analyzed for their primary and secondary outcomes, and those results were tabulated and compared.

Results: Between 30 and 80% mycological cure was reported across all three studies ranging from 32 weeks to 52 weeks follow up. Complete cure, defined as mycological cure plus a form of clinical cure, was also reported for all included articles ranging between 8% and 40%. Secondary outcome measures regarding safety were reported with nine minor adverse events out of 157 patients (5.7%). The rapid review revealed significant heterogeneity in study design and insufficient numbers of high-quality randomized controlled trials available.

Conclusion: Overall, topical antifungal therapy appears to be an effective and safe treatment for pediatric onychomycosis. However, more high-quality controlled trials of greater sample size are needed in order to draw generalizable conclusions for the podiatric physician to feel comfortable and confident in effectively treating this unique and growing pediatric population.

Introduction

Onychomycosis is an infection of the nail that is more commonly seen in toenails than fingernails, and is caused by dermatophyte fungi, non-dermatophyte fungi, and yeast.[1] The most frequent infectious organism is the fungus Trichophyton rubrum.[2] Onychomycosis is the most common nail disorder in the United States. The prevalence in children, however, is much lower than in adults. Adults have an incidence of 3.2%, while children have one of 0.14%.[3] The frequency of childhood onychomycosis has been increasing recently worldwide, likely due to the rising number of children using shared spaces such as locker rooms, children with immunocompromised states, and the ill-fitting, tight quality of children's shoes.[4]

Although the infection is often not limb threatening, onychomycosis can cause thickened, discolored, dystrophic nails that are difficult to manage and can create pain from pressure in shoe gear or impingement against local tissues, as well as increase the risk for nail bed injury or secondary infection. As such, physical debridement of the nails as well as antifungal medications are used to treat both the appearance, pain, and prevent sequelae.

Topical and oral antifungal therapies are available for treatment of onychomycosis with varying degrees of efficacy and side effects. Topical therapies in adults tend to be well tolerated with little-to-no local or systemic side effects yet require long term use averaging one year with a low efficacy of around 30% for mycological cure, which is defined as no growth on fungal culture.[5] Contrastingly, oral therapies are more often effective in terms of mycological cure. [5] However, oral medications have higher risks for systemic side effects, such as liver damage and require laboratory monitoring while being used. For children, the systemic effects and invasive monitoring is not preferred by doctors and parents.[3] In the United States, there are no FDA approved oral therapies for treatment of onychomycosis in children currently.[6]

Where topical and oral therapies are well studied in adults, treatment protocols and outcomes for pediatric patients are less clear. As a population with an increasing frequency of incidence, it is important to understand the best options for the pediatric population instead of utilizing adult protocols for pediatric treatments. Due to their relative ease of use, accessibility, and safety profile, topical therapy is often recommended as a first line treatment for pediatric onychomycosis. Understanding the outcomes and efficacy of this therapy in the pediatric population can help practitioners better educate their patients and is the first step to determine if new or alternatives therapies may be needed.

The purpose of this investigation is to examine the available literature to evaluate the efficacy of topical antifungal therapies for treating pediatric onychomycosis.

Methods

A rapid systematic review was performed. CINAHL, Cochrane, Embase, PubMed/Medline, Science Direct, and Web of Science databases were queried for studies that examined the efficacy of topical antifungal therapies for onychomycosis in the pediatric population. Search terms "onychomycosis AND (pediatric OR child) AND (treatment OR antifungal) AND topical" were used for all six databases, rendering 1013 articles. Duplicate articles, non-English language articles, and articles older than 10 years (prior to 2012) were excluded, reducing the total articles to 433 articles. The remaining 433 articles were evaluated according to the following inclusion criteria: randomized control trials (RCTs) or high quality observational clinical trials, patient population under 18 years old, investigation of any topical antifungal therapy agent, and reporting of efficacy by mycological, clinical, or combined cure. Three articles met the inclusion criteria; data was collected, tabulated, and qualitatively assessed for the included articles.

Results

The study by Friendlander et al. conducted a randomized, double-blind, vehicle-controlled trial that investigated 8% Ciclopirox lacquer on 40 patients between the ages of two and 16 years old.[7] The primary outcome measure for efficacy was mycological cure at four weeks. Secondary outcome measures included complete cure, defined as Investigator Global Assessment (IGA) score (Table 2) of 0 with a negative culture; effective treatment defined as IGA score of two or less with a negative culture; quality of life assessment by questionnaire; and adverse events. Patients were assessed at eight, 12, 20, and 32 weeks. Within the randomized patients, there was a 3:1 ratio used, where for every three patients assigned to the ciclopirox lacquer arm of the investigation, one patient would be assigned to the vehicle group, which served as a control, resulting in 24 therapeutic and eight vehicle patients. Of note, at 12 weeks, if the patient's IGA score was greater than three or the patient had a positive fungal culture from the week 8 collection, the patient was crossed over to the treatment group. At week 12, the mycologic cure rate was 70% in the Ciclopirox group and 20% in the

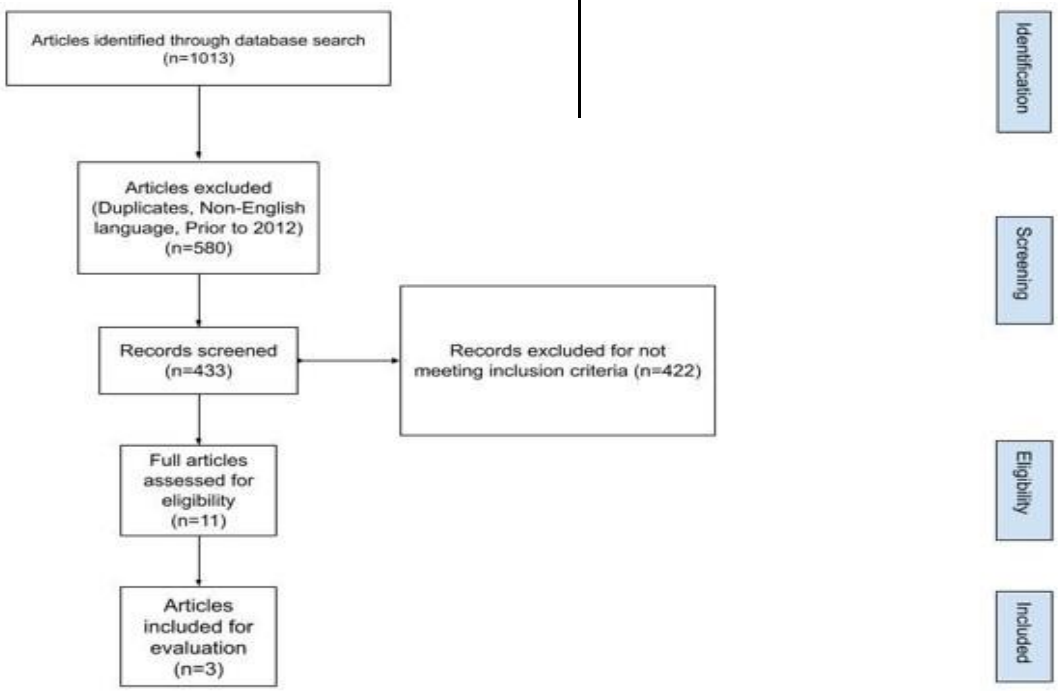
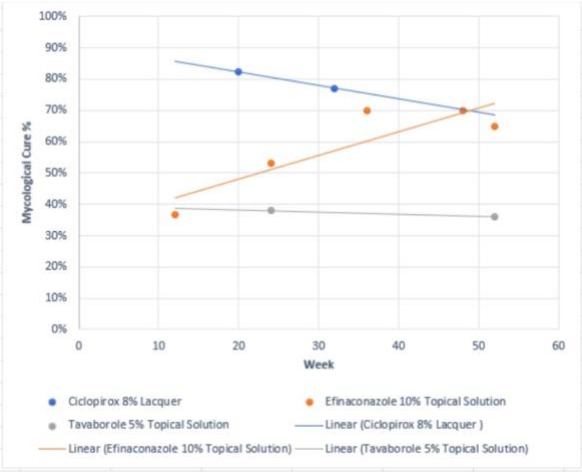


Table 1: *Summary of primary and secondary outcome measures in included studies*

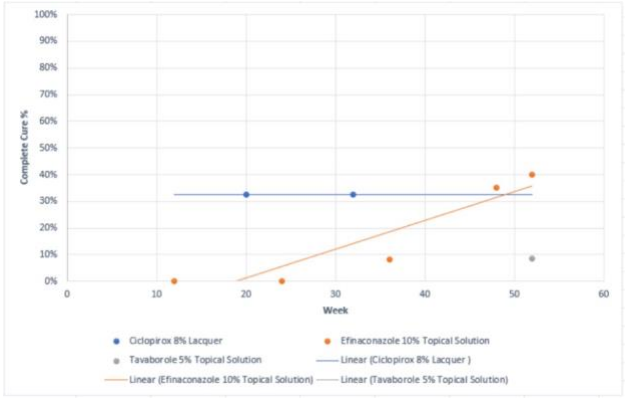
vehicle group (p = 0.31). Complete cure rates were almost equal between the ciclopirox and the vehicle around 20%, and seven patients in the vehicle group had positive fungal cultures or an IGA score greater than three and were switched to open-label active drug therapy. 82.2% of the patients had a mycological cure by 20 weeks and 77.1% of the patients had a mycological cure by the end of the 32-week study (Graph 1). 32.4% of patients had a complete cure in Week 20, and the percentage of patients remained the same in Week 32 (Graph 2). 71.4% of patients had effective treatment by the end of the study. Over 90% of patients stated they would undergo the treatment again in the quality-of-life questionnaire, and the only adverse event reported was a reversible faint yellow-brownish discoloration of the nail plate that resolved with acetone free nail polish remover applied once a week. Ciclopirox 8% is now FDA approved for use in children 12 years of age and older.[8]

Evaluate clinical appearance of the target toenail and documented with photography	
Score	Description
0	Complete clearance
1	75-99% clearance
2	50-74% clearance
3	<50% clearance
4	No significant change
5	Clinical worsening

Table 2: *Investigator Global Assessment Score*



Graph 1: *Mycological cure rates of 8% Ciclopirox, 5% Tavaborole, and 10% Efinaconazole from 12 to 52 weeks*



Graph 2: *Complete cure rates of 8% Ciclopirox, 5% Tavaborole, and 10% Efinaconazole from 12 to 52 weeks*

Next, the article by Eichenfield et al. was a phase four, multicenter, open-label study evaluating 10% solution of efinaconazole for topical treatment.[9] Efinaconazole 10% is FDA approved to treat pediatric onychomycosis in children at or over the age of 6 years.[8] This investigation studied 62 pediatric patients between the ages of six and 16 years for 48 weeks, with a four-week post-treatment follow up at week 52. The primary outcomes measures for this investigation were safety, pharmacokinetics, and efficacy. Safety was measured by incidence of adverse events (classified by the Medical Dictionary for Regulatory Activities (MedDRA)). Pharmacokinetics assessment included area under the concentration time curve from zero to 24 hours, maximum plasma concentration (Cmax), and time to Cmax (Tmax). Efficacy assessments included complete cure (0% clinical involvement of the target toenail and negative KOH and fungal culture), clinical efficacy rate (affected target great toenail area involvement of <10%), and mycologic cure (negative KOH examination and a negative fungal culture of the target great toenail sample). Mycological cure was reported as 36.7% of participants as early as 12 weeks (Graph 1). By week 24, the mycological cure rate was 53.3%, increased to 70% at 36 and 48 weeks, and was 65% by the end of study at 52 weeks (Graph 1). Complete cure was reported as 0% until week 36 when it was 8.3%, then 35% at 48 weeks, and 40% at 52 weeks (Graph 2). Clinical efficacy was reported as 8.3% at 24 weeks, 18.3% at 36 weeks, 43.3% at 48 weeks and 50% at 52 weeks. The investigators reported an overall safe profile with 38 participants (63.3%) experiencing 99 treatment-emergent adverse events, with only one treatment-related adverse event of ingrowing nail (eight events in two participants). Pharmacokinetic investigation revealed low systemic exposure and

only minor fluctuations in concentration over the 24-hour dose period.

The third study by Rich et al. is a phase four, open-label, single-arm study that evaluated 5% Tavaborole topical solution, an FDA approved therapy for children at or over the age of six years.[8,10] 55 patients were enrolled in this study, and 47 completed the study; all were between the ages of six and 17 years. The primary outcome measures for the study were safety/tolerability (patient reported adverse events and local tolerability reactions like burning, induration/edema, crusting, erythema, scaling), pharmacokinetic evaluation, and efficacy measured by mycological cure and complete cure. Complete cure was assessed at 52 weeks, and mycological cure was assessed at 24 and 52 weeks. 36.2% of patients were observed to have a mycological cure rate and 8.5% were observed to have a complete cure by week 52. The investigators reported an overall safe profile with only one treatment related to adverse event of paronychia that resolved before the end of the study despite continued treatment.

Discussion

The purpose of this investigation was to examine the efficacy of topical antifungal therapy for onychomycosis in the pediatric population. Currently, there are three topical treatments approved for pediatric use: ciclopirox 8% in children ≥12 years of age; tavaborole 5% in children ≥ six years of age, and efinaconazole 10% in children ≥ six years of age.

As presented, the included articles each investigated one of the three available FDA approved topical therapies. Mycological cure was measured across the three articles (negative culture for Friedlander, and negative culture plus negative KOH for Rich and Eichenfield) with between 30% and 80% mycological cure reported by the end of the study periods (ranging from 32 weeks to 52 weeks). Elewiski et al. investigated mycological cure, defined like Rich et al. as negative KOH and fungal culture, of adult patients treated with tavaborole 5% solution.[12] They reported 31.1-35.9% mycological cure at 52 weeks. Compared to the topical antifungals investigated in the pediatric population in the included articles, including tavaborole 5% with a 36.2%

Author (Year)	Friedlander, SF et al. (2012)	Eichenfield, LF et al. (2020)	Rich, P et al. (2019)
Article Title	Onychomycosis Does Not Always Require Systemic Treatment for Cure: A Trial Using Topical Therapy	Safety, Pharmacokinetics, and Efficacy of Efinaconazole 10% Topical Solution for Onychomycosis Treatment in Pediatric Patients	Tavaborole 5% Topical Solution for the Treatment Toenail Onychomycosis in Pediatric Patients: Results from a Phase 4 Open-Label Study
Topical Drug	Ciclopirox 8% Nail Lacquer	Efinaconazole 10% Topical Solution	Tavaborole 5% Topical Solution
Primary Outcome Measure	Mycological Cure	Safety: Patient reported Adverse events Pharmacokinetics: AUC and Cmax Efficacy: Mycological and Complete Cure	Safety: Patient reported adverse events and local tolerability reactions Pharmacokinetics: AUC and Cmax
Secondary Outcome Measure	Complete Cure Effective Treatment Adverse Events Quality of Life Questionnaire		Complete Cure, Mycological Cure

Image 1: *Systematic Review Article Selection Flowchart*

mycological cure rate at 52 weeks in the Rich et al. article, the pediatric population results are comparable or better than the efficacy rates seen in adults for the same medications.[5,12] This can be due to the thinner, faster-growing nails in children that make them better candidates for topical therapy when compared to adults as penetration of the medication is more likely.[11] Similarly, complete cure, which was defined as mycological cure plus a form of clinical cure (IGA score for Friedlander and clinical evaluation of percentage nail clearance for Rich and Eichenfield), was also reported for all included articles. This more stringent outcome measure was not surprisingly lower than mycological cure at the end of study with reported values between 8% and 40%. Similar to mycological cure, this was comparable to or better than adult populations (6.5-9.1% complete cure rates in adult population).[12]

Although not the primary objective of this study, all three articles additionally reported on safety measures, particularly adverse events for which, out of the combined 157 patients across all three articles, only nine treatment related adverse events of ingrowing nail and/or paronychia were reported. This is reassuring as a major factor in pursuing topical therapy for treatment of pediatric onychomycosis, over the more traditionally efficacious oral therapy used in the adult population, is avoidance of systemic adverse events.

Although the efficacy and safety profiles are promising for the three evaluated topical antifungals, there are many notable weaknesses to this rapid systematic review. There is significant heterogenicity between the study designs, particularly the difference in outcome measure definitions that impact the ability to combine data for quantitative meta-analysis. There was also a scarcity of high quality, high strength-of-study articles available. Of the three included, only one was blinded RCT, while the other two were non-controlled observational studies. This prevented the ability to draw a conclusion on the efficacy of each treatment compared to each other and their controls, as there was only one study with a control. The sample sizes are small, and further analysis would benefit from increased sample size for combined meta-analysis. Pediatric populations are also innately challenging to study as their rapid development can impact the interactions with medications in a relatively short time span. This can be a complicating factor when topical antifungal therapies require long periods of use averaging between 32 and 52 weeks, where there can be significant biological change within one year of pediatric development. Pharmacokinetic investigations, as presented in two studies, stratified across age groups may better help elucidate if this is a potential confounder. Ethical considerations are always important in human studies, and this is true when we consider subjecting children to a control in RCTs. As seen in the Friedlander article, subjects not responding to the therapy as anticipated at 12 weeks were crossed over to the therapy group. Although ethically allowing more subjects access to effective intervention, this does affect statistics comparing control and intervention groups at the end of therapy timelines, reducing the conclusions that can be drawn for these late-stage outcome measures. Additionally, as the only randomized and double-blinded trial, this reduced its strength of study.

Conclusion

Overall, topical antifungal therapy appears to be an effective and safe treatment for pediatric onychomycosis. However, more high-quality controlled trials with greater sample sizes are needed in order to draw generalizable conclusions for the podiatric physician to feel comfortable and confident in effectively treating this unique and growing pediatric population.

References

1. Arenas R, Torres-Guerrero E. Onychomycosis. *Nail Disorders*. 2019:31-35.
2. Mugge C, Haustein U-F, Nenoff P. Causative agents of onychomycosis - a retrospective study. *JDDG*. 2006;4(3):218-228.
3. Gupta AK, Mays RR, Versteeg SG, Shear NH, Friedlander SF. Onychomycosis in children: Safety and efficacy of antifungal agents. *Pediatric Dermatology*. 2018;35(5):552-559.
4. Kim DM, Suh MK, Ha GY. Onychomycosis in children: An experience of 59 cases. *Annals of Dermatology*. 2013;25(3):327.
5. Gupta AK, Stec N. Recent advances in therapies for onychomycosis and its management. *F1000Research*. 2019;8:968.
6. Vlahovic TC, Gupta AK. Efinaconazole topical solution (10%) for the treatment of onychomycosis in adult and pediatric patients. *Expert Review of Anti-infective Therapy*. 2021;20(1):3-15.
7. Friedlander SF, Chan YC, Chan YH, Eichenfield LF. Onychomycosis does not always require systemic treatment for cure: A trial using topical therapy. *Pediatric Dermatology*. 2012;30(3):316-322.
8. Gupta AK, Venkataraman M, Shear NH, Piguet V. Onychomycosis in children – review on treatment and management strategies. *Journal of Dermatological Treatment*. 2020;33(3):1213-1224.
9. Eichenfield L, Elewski B, Sugarman J, et al. Safety, pharmacokinetics, and efficacy of Efinaconazole 10% topical solution for onychomycosis treatment in pediatric patients. *Journal of Drugs in Dermatology*. 2020;19(9):867-872.
10. Rich P, Spellman M, Purohit V, Zang C, Crook TJ. Tavaborole 5% Topical Solution for the Treatment of

Toenail Onychomycosis in Pediatric Patients: Results from a Phase 4 Open-Label Study. *J Drugs Dermatol*. 2019;18(2):190-195.
11. Eichenfield LF, Friedlander SF. Pediatric Onychomycosis: The Emerging Role of Topical Therapy. *J Drugs Dermatol*. 2017;16(2):105-109.
12. Elewski BE, Aly R, Baldwin SL, González Soto RF, Rich P, Weisfeld M, Wiltz H, Zane LT, Pollak R. Efficacy and safety of tavaborole topical solution, 5%, a novel boron-based antifungal agent, for the treatment of toenail onychomycosis: Results from 2 randomized phase-III studies. J Am Acad Dermatol. 2015 Jul;73(1):62-9.

The Efficacy of Night Splints as Adjunct Therapy in the Treatment of Plantar Fasciitis: A Comprehensive Literature Review

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ABSTRACT

Objective: To determine if the current literature supports night splints as an effective conservative treatment method for plantar fasciitis.

Methods: A literature search of Pubmed, Google Scholar, and Embase was conducted with the key terms "plantar fasciitis", "night splint", "treatment of plantar fasciitis" and "heel pain". Studies were included based on inclusion and exclusion criteria and relevance to the project.

Results: The posterior night splint demonstrated to be an effective treatment method for acute and chronic plantar fasciitis when used with other conservative treatment methods in four of the six studies that were evaluated. However, the night splint alone did not show to cause a statistically significant improvement in patient symptoms.

Conclusion: The use of a posterior night splint can be an effective conservative treatment modality for plantar fasciitis. However, it is most effective when used conjunctively with other conservative treatment methods such as NSAIDs, a stretching and exercise program, and activity modification. Due to the conflicting nature of the results, further studies should be conducted to validate the use of night splints as an effective treatment for plantar fasciitis.

Introduction

Plantar fasciitis is the primary cause of 80% of heel pain and is present in 10% of the United States population.[1-4] It is categorized as an overuse injury and is clinically correlated with stabbing heel pain upon first stepping out of bed in the morning, post-static dyskinesia, and substantial heel pain after prolonged standing and walking. In the acute phase, plantar fasciitis occurs when the plantar aponeurosis becomes inflamed and irritated from repetitive strain and microtrauma. The diagnosis of plantar fasciitis is typically established from clinical history and physical examination alone. Patients will complain of heel pain tenderness localized 1 cm distal to the insertion of the plantar fascia. Diagnostic imaging generally does not help with the diagnosis and treatment plan; however, it does stand as a tool to help rule out other pathology.[1-6]

There is a myriad of options that encompass the treatment regimen for plantar fasciitis. While it is normally self-limiting (<12 months), it can lead to years of pain and limitation of activity. The first step in treatment encompasses rest, ice, activity modification, and stretching exercises- primarily of the lower extremity posterior chain muscles. Corticosteroid injections into the plantar fascia have also been shown to help with inflammatory symptoms, but are not typically a permanent solution and include the risk of plantar fascia rupture and fat pad atrophy.[6] The idea to use a posterior night splint for plantar fasciitis began in 1991.[7] This device aims to maintain the ankle in a dorsiflexed position and toes in an extended position in order to stretch out the plantar fascia and triceps surae; typically to be worn overnight. The purpose of this paper is to evaluate the effectiveness of the posterior night splint as a conservative treatment method for both acute and chronic plantar fasciitis.

Methods

A search of the literature was completed with the key terms "plantar fasciitis", "night splint", "treatment of plantar fasciitis" and "heel pain". The databases of Google Scholar, Embase, and PubMed were searched for peer-reviewed journal articles pertaining to the aforementioned key terms. Inclusion criteria required the study to be focused on the use of treatment of night splints as a treatment method for plantar fasciitis.

Results

Wapner et. al[7] was the first paper to be published suggesting the use of a posterior night splint for the treatment of plantar fasciitis. This case study hypothesized that the use of a custom molded posterior night splint orthotic with the foot dorsiflexed at five degrees would help stretch the plantar fascia leading to pain relief in patients with chronic plantar fasciitis

of at least 1 year. This night splint was utilized as a last resort for patients who had otherwise failed other conservative treatments including activity modification, NSAIDs, custom shoe orthotics, and a series of corticosteroid injections. The patients were an average of 37 years old and 20 lbs. over normal range BMI. The night splint was instructed to be worn every night while the patient slept for a total of three months. Following the initial three months, the patient was weaned off their night splint in two-week intervals, beginning with wearing the device every night, then every other, and finally, every three nights, and so on. The study involved a total of 14 patients with 18 affected feet. After 4 months of total night splint usage, 11 of the 14 patients reported complete resolution of their symptoms. They determined that one patient failed treatment due to lack of compliance, and another due to the development of medial nerve entrapment complexing her symptoms. The last patient who failed treatment was 60 lb overweight and it was determined his weight contributed to his persistent pain.

Powell et. al[8] completed a 6-month randomized crossover study examining 37 patients (52 total feet) being treated for recalcitrant plantar fasciitis. The authors hypothesized that the daily use of a dorsiflexion night splint for 1 month would effectively treat patients with recalcitrant plantar fasciitis. The patient was fitted and placed in a night splint with approximately 5 degrees of dorsiflexion at the ankle with a firm foam wedge anchored to the distal aspect of the footplate of the night splint which also provided 30 degrees of dorsiflexion at the metatarsophalangeal (MTP) joints. Each patient was asked to discontinue all their other treatment modalities (NSAIDs, PT, custom shoe orthotics) during the time they were participating in the study. The patients were randomized and split into two groups. Group A wore the splint for the first month, then took one month off, and was then monitored for an additional four months. Group B did not wear the splint for the first month, then did wear the splint for the second month, and was then monitored for an additional four months. Each patient was evaluated at 30 days, 60 days, and 6 months. At both the beginning and end of the study, the patient's overall satisfaction with the splint treatment was recorded and compared. 88% of the patients reported decreased pain with an average pain improvement of +5.9 on a 10-point scale. 73% overall of patients reported being satisfied with the methods of treatment and treatment itself.

In 1999, Probe et al[9] conducted a prospective randomized study of 116 participants with plantar fasciitis with the objective to determine the effectiveness of adjuvant over-the-counter night splints in alleviating acute (<12 months) symptoms of plantar fasciitis. Both Group 1 and 2 were treated with a baseline protocol of 1 month of daily anti-inflammatory medication (Piroxicam 20mg), Achilles stretching exercises (10 repetitions of 10 seconds three times per day) and wearing shoes with supportive arches and cushioned heels. Patients in Group 2 used the 5-degree dorsiflexion night splint for 3 months in addition to the baseline treatment. Blinded clinical reviews were performed at 4 weeks, 6 weeks, 12 weeks, and 19 months (follow-up) using the Health Status Data Short Form 36. Data analysis was performed using student's t-tests to compare between groups. Variables analyzed included demographics, group randomization, presence of a heel spur on radiographs, and weight above or below the 195 lb. median weight. 81 of the patients were women, and 35 were men; the mean age of patients was 46 years, with a SD of 11 years. The average duration of symptoms prior to treatment was 19 weeks. 59% of patients had plantar spurs on radiographs. Prior treatment included: orthotics in 35 patients, injections in 11, and taping in 29; 69 patients received no treatment prior to the study. Overall, the rate of subjective improvement of at least one pain grade on a 4-point scale was 68% after 12 weeks (most improvement was seen in the first 4 weeks) and 84% at the 19-month follow-up. No statistical difference was seen with the presence or absence of a night splint. Second, the presence of a bone spur, bilateral symptoms, obesity, gender, duration symptoms, previous treatment, and group allocation did not statistically affect improvement rates. However, age older than 45 years old was statistically significant for poorer prognostic at the 12-week follow-up ($p=.03$) but was comparable to younger counterparts at the 19-month follow-up. This study concluded that using night splints with the ankle in dorsiflexion did not prove to be significantly beneficial as adjuvant therapy in patients with "acute" plantar fasciitis (<12 months).

Beyzadeoglu et. al.[10] evaluated the effectiveness of an 8-week night splint treatment for plantar fasciitis. The splint was to be fitted to the

patient's foot, custom molded, and then worn daily while the patient slept. The authors treated 44 patients (53 pedal complaints) who had had plantar fasciitis for a mean symptom duration of 7.2 +/- 5.9 weeks. A Pearson Chi-square test was conducted for the subcategories of height, weight, level of sport daily, daily standing duration, and type of shoe usage. The patients were randomized and placed into two groups and a Mann-WhitneyU test was conducted. Group 1 was treated with silicone heel cushions, oral NSAIDs, activity modification, stretching, exercises, and diet modification. In contrast, Group 2 was treated with all the same conservative care management and additionally, a night splint that maintained 5 degrees of dorsiflexion. Both groups continued this treatment for 8 weeks. Group 2 patients showed a statistically significant pain decrease compared to Group 1. Patients also filled out evaluations with the AOFAS and VAS (visual analog scale) before and after two months of treatment. A statistically significant difference in VAS score was found between the two groups ($p=0.001$) and group 2 patients showed a pain reduction of 79% with a reduction of 62% in the conservative treatment group. No statistical difference was seen when looking at the demographic subcategories of the data. Regarding the patients' satisfaction with the treatment, in group 1, 44% of the patients were satisfied with 28% of patients very satisfied. Whereas group 2 reported being very satisfied in 42% of patients and 42% satisfied. However, 42% of patients also complained of sleep disruption from wearing the night splint.

In 2012, Lee et al[2] conducted a prospective study consisting of 28 patients to evaluate the effectiveness of a self-adjustable dorsiflexion night splint in combination with an accommodative OTC foot orthosis (Group B) versus the use of a 5-degree dorsiflexion night splint alone (Group A). Patients had not received any prior treatment and were assigned to Group A or B using a consecutive sampling approach. A Foot Function Index (FFI) questionnaire was used to evaluate the pain and function at baseline, as well as two and eight weeks after treatment. To assess the differences between the two groups, a Bonferroni t-test was performed at three different time intervals. There was no statistically significant difference in scores for pain, disability, activity limitation, and total FFI between the groups at baseline and at week two. However, the pain score and total FFI score in group B were significantly lower than in Group A at week 8. This study suggests that the treatment of orthotic insoles and night splints was more effective in relieving acute plantar fasciitis pain than the orthotic insole alone.

One of the most recent studies on this topic was conducted by Wheeler[11] in 2017 who sought to investigate any improvements in pain or function in patients with chronic plantar fasciitis with the use of tension night splints (TNS). This was a single-blinded randomized controlled trial of 40 patients, divided evenly into group 1- TNS and a home exercises program (HEP) and group 2- only HEP. Of note, all patients in both groups had already undergone HEP alone without relief of pain. The mean age of the patients was 52.1 years, 33% were male, mean BMI was 30.8 kg/m^2 and mean duration of symptoms was 25 months. Patients were followed up at 6 weeks and 3 months regarding pain and quality of life using various questionnaires (1-10 scale, FFI, FFI-R, SF-36, MOXFQ, AOFAS, FAAM, and EQ-5D), as well as flexibility (measured via goniometer) and sleep quality (PSQI) questionnaire. Data analysis was conducted by performing paired-sample t-tests for comparison within groups, and independent-sample t-tests for comparison between groups. Both control and intervention groups showed statistically significant improvement in self-reported "average pain" from baseline to week 6 and at 3 months; however, there was no statistical significance between the groups. Again, improvements were also observed in self-reported "worst pain", "pain walking", "pain first thing in the morning", and FFI for both groups at all time periods; but no statistically significant difference between groups. Lastly, there were no significant changes in sleep quality in either group. Overall, this study concluded that even in patients with very chronic symptoms of plantar fasciitis, improvements can be seen in pain and function using a structured HEB; however, the addition of a TNS does not have much, if any benefit as an addition to HEP.

Discussion

The focus of this study was to evaluate the current literature surrounding the use of posterior night splints as a conservative treatment method in plantar fasciitis. With post-static dyskinesia being a key clinical feature of plantar fasciitis, stretching the plantar fascia and triceps surae overnight to prevent

tightness addresses the biomechanical components of this condition.

Wapner et. al[7] was the first study to evaluate the use of a posterior night splint. They performed a case study that evaluated 14 patients with plantar fasciitis with a duration of at least 1 year. The patients were treated with the use of a custom molded polypropylene night splint with 5 degrees of DF nightly for 9 months. They allowed patients to have continued use of other conservative treatment modalities such as NSAID usage, Tuli heel cups, and general stretching exercises. With the use of the night splint, every patient reported relief of the pain with their first step in the morning within 1 week of use. However, there were some innate limitations of this study. There was no control group, and they studied a small treatment group with an insufficient number needed to treat. The study also failed to mention compliance to the night splint or the sleep quality of the patient while using the night splint. Furthermore, it did not evaluate the patient's satisfaction with the night splint treatment or their use of other conservative treatments. This makes it difficult to know if 11 out of 14 patients demonstrated improvement from night splint usage or if they improved from the use of the combination therapy. Finally, the patients were using a custom orthotic night splint, so these results could theoretically differ if they had used an over-the-counter night splint, which is something often prescribed to patients.

Powell et al[8] conducted a 6-month prospective randomized crossover study where they evaluated 2 groups of patients who had recalcitrant plantar fasciitis. They had patients wear a night splint that not only dorsiflexed the ankle at 5 degrees but also provided 30 degrees of dorsiflexion at the MTPJ. The benefits of this study are that it incorporated a control group, utilized randomization, and instructed patients to discontinue all other conservative treatment methods. They also ran a multiple subcategory study with a chi-square test to consider the multi-factorial nature of plantar fasciitis. The limitations of this study are that there was no mention or measure of compliance from the patients to the night splint, there was no true blinded control group and there was no guarantee that the patients weren't using other treatments to aid with pain relief. Similar to the Wapner paper, the patients were using a custom orthotic night splint, so these results could differ if they had used an over-the-counter night splint

Probe et al[9] conducted their 116-participant study to test the conclusions made by Wapner and Powell et al.[7,8] In contrast to the two former authors, Probe concluded that the use of night splints with the ankle in dorsiflexion did not prove to be significantly beneficial as an adjuvant therapy to NSAIDS, supportive shoes, and stretching in patients with “acute” plantar fasciitis (<12 months). The strengths of this study include its design as a randomized control trial and its larger participant number. Compared with previous literature, Wapner et al[7] studied 14 patients with recalcitrant symptoms, and the average duration of antecedent symptoms was 17 months. Powell et al[8] study patients showed improvement in 80% of affected feet, were also recalcitrant cases, and their average duration of antecedent symptoms was 33.4 months. Therefore, it is of note that while the night splints were not of benefit to the acute phase of plantar fasciitis, they might prove to be more effective as adjuvant therapy in chronic cases.

Beyzadeoglu et al[10] analyzed 44 patients (53 feet) with plantar fasciitis who had a mean symptom duration of 7.2 +/- 5.9 weeks. They determined that patients who have not been previously treated for plantar fasciitis can obtain significant relief of heel pain in the short term with the use of a night splint in conjunction with other conservative measures. Some benefits of this study are that they had a control group and evaluated the patient’s level of physical activity. However, they did not keep track of patient compliance and had a limited follow-up time frame of 24 months. This study negated the findings previously made by Probe et al.[9] However, these conclusions must be interpreted with caution as Beyzadeoglu et al[10] study was of a smaller participant number, and the treatment time was only 8 weeks (versus Powell et al[8] of 3 months).

Subsequently, Lee et al[2] suggested that the treatment of orthotic insoles and night splints was more effective in relieving pain than the orthotic insole alone. It is imperative to note that the design of this study differs from the studies that have previously been analyzed in this paper. Only Wapner and Powell included custom orthotics in their evaluation. Limitations to this study include the wide variability there is in models of custom orthotics and the lack of control of other treatments including shoe wear or at-

home stretching exercises. However, a benefit of this study and perhaps their success in demonstrating the benefit of the night splint is their patient education on adjusting the night splint to fewer degrees of DF as needed. Patients are more likely to comply with treatment if they are able to adjust the splint at night.

Most recently, Wheeler et al[11] concluded that even in patients with very chronic symptoms of plantar fasciitis, improvements can be seen in pain and function using a structured home exercises program; however, the addition of a tension night splint does not have much, if any benefit as an addition to home exercises. This publication contradicts the first 2 publications evaluated in this paper. Similar to Wapner and Powell, a limitation of this study is that the treatment was conducted on a small population of participants. Furthermore, due to the nature of the treatment, only a single-blinded methodology was possible. However, the introduction of a "sham", night splint-look-like device could be placed on a control group to accurately measure the effectiveness of the night splint in a future double-blinded randomized trial.

Conclusion

In conclusion, our study demonstrated that the use of a posterior night splint may be an effective conservative treatment modality for acute and chronic plantar fasciitis, although the studies reviewed show conflicting data. It is likely most effective as a treatment method when used adjunctively with other conservative treatment methods such as NSAIDs, stretching and exercise programs, activity modification, custom orthotics, and supportive shoe gear. Currently, there is not sufficient evidence in the literature to effectively support the efficacy of the night splint as a stand-alone treatment and there is conflicting evidence in its evaluation as an adjunctive treatment. There is a need for more research to be conducted with larger study populations and double-blinded randomized controlled trials.

References

1. Cole C, Seto CK, Gazewood JD. Plantar Fasciitis: Evidence-Based Review of Diagnosis and Therapy. *American Family Physician*. 2005;72(11):2237-2242.
2. Lee WCC, Wong WY, Kung E, Leung AKL. Effectiveness of adjustable dorsiflexion night splint in combination with accommodative foot orthosis on plantar fasciitis. *The Journal of Rehabilitation Research and Development*. 2012;49(10):1557.
3. Martin RL, Irrgang JJ, Conti SF. Outcome Study of Subjects with Insertional Plantar Fasciitis. *Foot & Ankle International*. 1998;19(12):803-811.
4. Ryan J. Use of posterior night splints in the treatment of plantar fasciitis. *American family physician*. 1995;52(3):891-898, 901-902. Accessed December 10, 2022.
5. Melvin T, Tankersly Z, Quazi Z, Jasko J, Odono R, Shuler F. Primary Care Management of Plantar Fasciitis. *Orthopaedics*. Published online November 1, 2015. Accessed December 10, 2022.
6. Young CC, Rutherford DS, Niedfeldt MW. Treatment of Plantar Fasciitis. *American Family Physician*. 2001;63(3):467.
7. Wapner KL, Sharkey PF. The Use of Night Splints for Treatment of Recalcitrant Plantar Fasciitis. *Foot & Ankle*. 1991;12(3):135-137.
8. Powell M, Post WR, Keener J, Wearden S. Effective Treatment of Chronic Plantar Fasciitis with Dorsiflexion Night Splints: A Crossover Prospective Randomized Outcome Study. *Foot & Ankle International*. 1998;19(1):10-18.
9. Probe RA, Baca M, Adams R, Preece C. Night Splint Treatment for Plantar Fasciitis a Prospective Randomized Study. *Clinical Orthopaedics and Related Research®*. 1999;368:190-195. Accessed December 10, 2022.
10. Beyzadeoglu T, Gokce A, Bekler H. *The Effectiveness of Dorsiflexion Night Splint Added to Conservative Treatment for Plantar Fasciitis Plantar Fasiitis İçin Konservatif Tedaviye Eklenen Dorsifleksiyon Gece Atelinin Etkinliği*.; 2007.
11. Wheeler PC. The addition of a tension night splint to a structured home rehabilitation programme in patients with chronic plantar fasciitis does not lead to significant additional benefits in either pain, function, or flexibility: a single-blinded randomized controlled trial. *BMJ Open Sport & Exercise Medicine*. 2017;3(1):e000234.

Exercise Intervention of Pediatric Obesity in the Mitigation of Lower Extremity Pathomechanics: A Literature Review

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ABSTRACT

Objective: The purpose of this study is to evaluate the outcomes of exercise intervention of pediatric obesity in the prevention of lower extremity pathomechanics in children.

Methods: A literature review on relevant research articles pertaining to the interventions of pediatric obesity and its impact on functional gait was conducted using PubMed and Google Scholar databases. Search terms/phrases such as "pediatric obesity", "obesity intervention", and "exercise pes planus" were used.

Results: Studies demonstrate minimal changes of plantar foot pressures after weight loss in children. Additionally, locomotive training ($p=0.015$) and physical strengthening ($p<0.05$) serve as additive factors in weight loss intervention when improving biomechanical function in children.

Conclusions: Physicians should value holistic pediatric care and consider treatment plans revolving around weight loss and functional training as prophylaxis or treatment of overweight/obese children.

Introduction

As the prevalence of obesity increases in the In the United States, it is important to focus on the consequences of such a trend in healthcare.[1] It has been shown that obesity has a profound influence on musculoskeletal disease due to the abnormal load on bones and joints.[2] As children around the age of seven years develop into an adult gait pattern, excessive body weight could increase the subtalar joint's pronatory moment as the talus receives axial load from the tibia creating a medially-deviated joint inferiorly with the calcaneus. Consequently, this loading pattern causes the individual to compensate via excessive pronation of the subtalar joint.[3] This common biomechanical phenomenon serves as foundation for symptomatic feet represented by increased plantar pressures.

Functional capacity of the foot may be influenced by malalignment of the hip, knee, and ankle joints. This is worsened if excessive childhood weight continues into adulthood as axial load increases stress on the musculoskeletal structures of the lower extremity.[4] The purpose of this literature review is to evaluate the outcomes of early exercise interventions to reduce plantar pressures and pathomechanics in the pediatric population.

Methods

The design of the report is non-experimental and serves to review current literature. PubMed and Google Scholar databases were used to search for relevant studies pertaining to pediatric exercise intervention and its effect on the lower extremity. Search terms include: "pediatric obesity," "pediatric weight loss," "obesity intervention," "pediatric exercise intervention," "exercise pes planus," "plantar pressure weight loss," and "obesity musculoskeletal."

Studies in the English language that pertained to only pediatric cases were included. Data involving patients at or above the age of 18 were excluded from the literature review.

Results

In a 2014 study, Riddiford-Harland et al evaluated the effects of weight-bearing physical activity on the plantar peak pressures generated by the feet of overweight and obese children. 24 children (age range: 5 to 9) participated in a physical activity (PA) group requiring completion of a 10-week exercise program focused on the fundamental moving skills of running, jumping, leaping, hopping, sliding, galloping, striking, rolling, kicking, throwing, catching, and bouncing a ball. Changes from baseline were evaluated 6 months after initial measurements were taken. Results indicated that there was no significant increase or decrease to the subjects' peak

plantar distributions (force per unit area) in normal ambulation.

Molina-Garcia et al performed a similar study in 2019 in which 23 overweight/obese children who participated in a 13-week early exercise program were compared to 28 overweight/obese children who did not participate in the intervention program. For three days a week, participants of the intervention group were instructed on movement quality for 30 minutes and given 60 minutes for moderate-vigorous aerobic exercise. At the end of the 13-weeks, the intervention group had a lower plantar pressure surface area average of 53.89 cm^2 whereas the control group recorded an average of 56.35 cm^2 (p=0.015). This value for the intervention group was relatively the same after 13-weeks when compared to the pre-program average.

In 2017, Steinberg et al performed a study in which 30 overweight children were divided into three groups:

- Group 1: 6-month obesity weight-loss intervention (n=10, mean age: 10.7 +/- 1.7)
- Group 2: 6-month obesity weight-loss intervention with locomotion training for biomechanical improvement (n=10, mean age: 9.4 +/- 0.8)
- Group 3: no intervention (n=10)

All individuals were either in 4th or 5th grade and based in Israel. There was no significant difference in age between the three groups. Individuals in group 1 experienced a significant decrease in weight in comparison to Groups 2 and 3 who experienced a significant increase in weight. Despite the weight loss in Group 1, there was no significant improvement of biomechanical function, solely an increase in peak plantar pressures and maximum force when walking or running. Significant improvement in biomechanical function was only observed in Group 2 as subjects demonstrated decreased peak plantar pressures in heel strike (127.0 to 90.3), the medial midfoot (129.85 to 99.56), and the lateral forefoot (140.45 to 106.25) when walking or running (p=0.044). Group 2 also showed a decrease in maximum force in heel strike (20.28 to 12.81), the medial midfoot (20.36 to 12.44), and the lateral forefoot (19.63 to 12.44) when walking or running (p=0.015).

Horsak et al performed a study in 2019 that evaluated the effects of weight-bearing physical activity on the plantar pressures and foot structures of overweight and obese minors. 35 subjects were randomly assigned to an exercise program (EP) (n=19) or a control group (n=16). The exercise group performed 60-minute progressive group training sessions twice a week for 12 weeks. The control group received no exercise program, but was allowed participation after the study. Each group was evaluated after 12 weeks. When walking, the EP group demonstrated a decreased hip adduction and contralateral pelvic drop when compared to the control group (p=0.018 and p=0.006, respectively). When descending a flight of stairs, the EP group demonstrated decreased hip adduction and contralateral pelvic drop when compared to the control group (p=0.027 and p=0.016, respectively). Finally, there was a 30% increase in isometric strength of hip abductors seen in the EP group in comparison to the control group (p=0.047).

Discussion

When evaluating the results of weight intervention in the studies performed by Riddiford-Harland et al and Molina-Garcia et al, plantar pressures were not decreased; instead, they were maintained. This is mainly due to the development of an adult pattern gait with the growth of musculoskeletal structures. We must expect plantar pressures to increase over time in the pediatric population due to normal development, especially when studies are conducted over a period of months. Maintenance of plantar pressures over time in the context of pediatric growth and development, may be viewed as an overall decrease in plantar pressure. It is expected for plantar pressures to increase as children grow. Therefore, minimal increases or no changes in plantar pressure over time may be considered beneficial in children and a sign of improved functionality.[6]

The question that the Riddiford-Harland et al and Molina-Garcia et al studies leave unanswered is: Why is functionality improved outside of the observed decreased plantar pressures? Muscle strength and gait patterns can greatly influence plantar pressures. For example, genu valgum due to weak hip external rotation may cause excessive tibial internal rotation leading to overpronation of the subtalar joint. Evaluating changes in muscle strength allows researchers to observe functional changes in relation to early weight loss intervention which was shown to

decrease plantar pressures in the Riddiford-Harland et al and Molina-Garcia et al studies.

Although the two aforementioned studies showed that weight loss alone is effective in the reduction of plantar pressures, the study by Steinberg et al further demonstrated that weight loss combined with locomotive training in the reduction of plantar foot pressures in gait is more effective. Their study showed that locomotion training was the primary variable that improved functional gait in children $p<0.05$). Therefore, we must consider functional variables of pathomechanics that increase plantar foot pressures, rather than just weight loss alone. These variables include muscle strength and gait patterns.

The study conducted by Horsak et al demonstrated the physiological changes of a proposed pediatric physical training program and its influence on children's gait. The observed reduction in hip adduction and contralateral hip drop in this study ($p<0.05$) are symbolic of an increase in strength of the hip abductors (gluteal muscle group and tensor fascia latae). The increase of isometric strength in hip abductors leads to control of hip joint motion primarily in the frontal plane, as excessive hip adduction is reduced. Control of the hip joint, due to its proximity to the body's center of gravity, plays a pivotal role in the distal kinetic reaction of the knee and ankle joints. Hip stabilization therefore leads to greater control of medial knee collapse in dynamic gait. Furthermore, control of genu valgum and varum deformities decreases the likelihood of developing tibial valgum and varum deformities.

Horsak et al's study primarily aimed to evaluate hip motion and failed to measure forces related to genu valgum/varum and tibial valgum/varum. Of the 35 subjects evaluated, 29 total children had observable pes planus and genu valgum. The study only includes measurements of hip abduction and adduction; there is no mention of the impact of early exercise intervention on the knee and ankle joints. Key muscles that future studies should evaluate include those of the lower leg. These more distal muscles play an integral part in the gait cycle in the balance of pronatory and supinatory forces during the contact phase of gait.

Additionally, if the goal is to see long-term results of pediatric exercise intervention, then studies should aim to follow children into adulthood. Duration of study ranged from 10 weeks to 6 months. Although this is enough time to see functional change in children, the true impact of physical improvement must be evaluated years later into adulthood.

The primary limitation of the four studies presented is the small sample size presented within each study. Only 24 children in Riddiford-Harland, 51 children in Molina-Garcia et al, 30 children in Steinberg et al, and 35 children in Horsak et al were evaluated, which is not representative of the general pediatric population. The study performed by Steinberg et al was only limited to children in Israel within grades 4 and 5. These data sets cannot be considered representative of the general pediatric population due to the small sample size and lack of geographic diversity. Future studies should be conducted with randomized subject selection with individuals from various locations.

Conclusion

Pathomechanics predispose overweight and obese children to discomfort and possible injuries. The impact of poor gait is seen when children experience pain or injuries due to the development of pathomechanics. In contrast, proper alignment of the lower extremity and reduced plantar pressures decrease the likelihood of lower extremity pathomechanics.

Children are learning and adapting to their bodies everyday. They do not know or understand what a normal gait is until they are informed of such, or if symptoms and injuries occur. Therefore, it is imperative to intervene on the overweight/obese pediatric population and encourage weight loss and locomotive training through physical activity to foster a healthier adult population. Future randomized, prospective studies of pediatric weight intervention and physical training could focus on the specific exercises and training protocols that effectively produce functional results into adulthood.

References:

1. Sanyaolu A, Okorie C, Qi X, Locke J, Rehman S. Childhood and Adolescent Obesity in the United States: A Public Health Concern. *Glob Pediatr Health*. 2019;6.
2. Anandacoomarasamy A, Caterson I, Sambrook P, Fransen M, March L. The impact of obesity on the musculoskeletal system. *Int J Obes (Lond)*. 2008;32(2):211-222.
3. Froehle AW, Nahhas RW, Sherwood RJ, Duren DL. Age-related changes in spatiotemporal characteristics of gait accompany ongoing lower limb linear growth in late

childhood and early adolescence. *Gait Posture*. 2013;38(1):14-19.
4. Adoracion Villarroya M, Manuel Esquivel J, Tomas C, Buenafe A, Moreno L. Foot structure in overweight and obese children. Int J Pediatr Obes. 2008; 3:39–45.
5. Riddiford-Harland DL, Steele JR, Cliff DP, Okely AD, Morgan PJ, Baur LA. Does participation in a physical activity program impact upon the feet of overweight and obese children?. *J Sci Med Sport*. 2016;19(1):51-55.
6. Molina-Garcia P, Miranda-Aparicio D, Molina-Molina A, et al. Effects of Exercise on Plantar Pressure during Walking in Children with Overweight/Obesity. *Med Sci Sports Exerc*. 2020;52(3):654-662.
7. Steinberg N, Rubinstein M, Nemet D, et al. Effects of a Program for Improving Biomechanical Characteristics During Walking and Running in Children Who Are Obese. *Pediatr Phys Ther*. 2017;29(4):330-340.
8. Horsak B, Schwab C, Baca A, et al. Effects of a lower extremity exercise program on gait biomechanics and clinical outcomes in children and adolescents with obesity: A randomized controlled trial. *Gait Posture*. 2019;70:122-129.

Evidence Based Non-surgical Treatment of Plantar Plate Injury

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ABSTRACT

Objective: Plantar plate injuries are a common cause of metatarsalgia. While there are several non-surgical treatment modalities that exist to treat these injuries, there is a lack of strong evidence-based protocols that demonstrate reproducible results. The purpose of this literature review aims to examine evidence-based theories for non-surgical treatment modalities used to treat plantar plate injuries.

Methods: A literature review was conducted using keyword searches in PubMed and Google Scholar. Keywords used were "non-surgical," "conservative," "efficacy," "biomechanical," "follow-up," and "sample size." Articles were reviewed for the efficacy of evidence-based non-surgical treatment modalities used to treat plantar plate injuries.

Results: Despite the lack of clear evidence for the efficacy of non-surgical treatments for plantar plate injuries, few studies have adequately evaluated these treatments using appropriate follow-up periods and sample sizes. Most research in this area relies on self-reported symptom improvement as the primary measure of treatment success.

Conclusion: There is a scarcity of evidence supporting the effectiveness of non-surgical treatments for plantar plate injuries, as few studies have used appropriate modalities to track their success. While some studies have used MRI scans to assess improvement, these are often limited to case studies. To better understand the effectiveness of these treatments and develop evidence-based treatment protocols that can be generalized to a larger population, further research with larger sample sizes should consider various methods of measuring their efficacy.

Introduction

Plantar plate injuries are a common cause of metatarsalgia. They can be treated non-surgically or surgically, but when it comes to treating them non-surgically, there is little to no supporting evidence that backs up current treatment protocols. The causes of this pathology may be multifactorial and the progression can be detrimental to patients and can adversely affect their activities of daily living while decreasing one's quality of life. Swelling, pain, and metatarsophalangeal instability are common manifestations of plantar plate injuries.[1] Other conditions such as hallux abductovalgus and hallux varus may coexist alongside plantar plate dysfunction, resulting in difficulty with treating the condition.[1] The current non-surgical treatments used to treat plantar plate injuries include platelet rich plasma injections, prolotherapy injections, orthotics, and toe tape. However, there is a lack of sufficient evidence based theories as well as large enough sample sizes that demonstrate the efficacy of these treatments.

Background

The metatarsophalangeal joint (MPJ) is a structure composed of different tissue stabilizers. Lesser metatarsophalangeal instability is a common condition accounting for several cases of metatarsalgia. The plantar plate contributes as the main stabilizer of the metatarsophalangeal joint which prevents the toes from moving dorsally. If left untreated, the digit will experience a gradual tear and eventually shift dorsally, as well as deviate medially. The second digit is most commonly affected and is most often seen in women and elderly.[2] Athletes who undergo hyperextension on a fixed foot, axial loading, and valgus forces are also subject to such injuries.[3] Although there are studies on athletes and plantar plate injuries, the incidence and epidemiology of this injury remain uncertain. This is due to a lack of large studies on the topic, with most of the literature focusing on diagnosis and treatment rather than epidemiology and prevention.[4] Other conditions such as having a longer second metatarsal as well as a hypermobile hallux valgus deformity also contribute to lesser metatarsophalangeal joint instability.

Biomechanics

During gait, the forefoot endures much of the body weight. The 2nd MPJ is most susceptible to injuries in the area causing gradual wear and tear to the plantar plate.[5] Chronic tear of the plantar plate will eventually cause subluxation to the joint with medial displacement and crossover of the digit.[1]

Etiology

On MRI, plantar plate tears are commonly found as lateral full-thickness tears at the proximal phalanx insertion.[1] The most common cause of a second MPJ plantar plate tear is gradual wear and tear of the plantar plate and structures found around the metatarsophalangeal joint. Extrinsic factors play a large role in gradual tear of the plantar plate which include overloading the metatarsophalangeal joint, having a hypermobile first ray, and a long second metatarsal.[1] The most common test used in clinics to diagnose plantar plate instability is the drawer test where the metatarsal is held in neutral while displacing the proximal phalanx dorsally.[1] Another common and reliable indicator of joint instability is the Lachman test.[3]

Non-surgical Management of Plantar Plate Tears

While there are surgical options to treat plantar plate tears, they are typically reserved for more severe stages of the injury where major anatomical deformation has occurred or when non-surgical treatment has failed.[6,7] With surgery, there is the potential for complications and long term follow-up care, which results in considering the use of non-operative treatments as the first line of care for stable injuries.[5] Detecting plantar plate tears at earlier stages are critical for the success of non-surgical care.[8] There are multiple non-surgical treatments that may relieve or heal plantar plate tears such as the use of: toe tape, walking boots, stiff soled shoes, shoe inserts, corticosteroids, toe spacers, and addressing issues of equinus.[7,9] These modalities are used in conjunction with physical therapy, non weight bearing exercises that transition to weight bearing as allowed, limited ROM activities, and NSAIDs to produce a rehabilitation program.[10,11] It is also possible to follow the progression of plantar plate tears through serial MRI imaging for follow-up care.[12,13] Non-operative treatment of plantar plate injuries require less follow up care with a reduced risk of complications compared to surgical treatments, however, most literature that covers evidence based theories treating plantar plate disorders are surgical.[5] The purpose of this literature review aims to examine evidence-based theories for non-surgical treatment modalities used to treat plantar plate injuries.

Methods

A literature review was conducted from various online research journals which met certain inclusion and exclusion criteria in order to extract relevant information regarding various non-surgical treatment modalities used and the evidence-based theories surrounding the efficacy of these treatments on individuals who underwent treatment for plantar plate injuries. Inclusion criteria required the study to focus on evidence-based non-surgical treatments for plantar plate injuries. Papers that were outside of the focus of this study were disregarded. PubMed and Google Scholar were used as the primary databases. Keywords and phrases used included “plantar plate, non-surgical, treatment,” “plantar plate, conservative, treatment,” “plantar plate, non-surgical, biomechanical,” “plantar plate, non-surgical, sample size,” “ plantar plate, non-surgical, follow up.” Treatment outcomes, duration of follow-up, sample size, and biomechanical explanations for various non-surgical treatment modalities were investigated.

Results

The studies reviewed suggest that non-surgical treatment options aim to limit the progression of the deformity, while also managing pain, with the ultimate goal of stabilizing the affected digit to the point where the periarticular structures can undergo fibrosis.[14,15,16] While these treatments are widely accepted, there is a lack of supportive evidence on the successes of these conservative treatments through different measuring modalities that track the efficacy of these treatments on plantar plate tears.[5,17] Although evidence is scarcely available, four articles attempted to measure the efficacy of non-surgical treatments through MRI’s, self-report, and other measurement modalities, and were limited to one patient having short term success per study.

Labbad et al utilized extracorporeal pulse activation technology (EPAT) for seven weeks and

measured the efficacy of the treatment on MRI for a single patient who reported a full recovery after the treatment.[18] Over the course of seven weeks, the patient received five EPAT treatments on their left forefoot. Each treatment consisted of 3000 pulses at 2.8 bars applied directly to the MPJ of the affected foot. The patient's progress was monitored through weekly pain assessments using a 0-10 scale, MRI scans, and their ability to return to normal activities. After the final treatment, the patient reported being able to walk pain-free and resumed all normal activities. An MRI scan performed 5.5 months after the final EPAT treatment showed evidence of repair in the previously torn plantar plate, as well as improvement in the overall structural integrity of the plantar plate. These results suggest that shockwave therapy may be a viable option for treating plantar plate tears.[18]

Kinter and Hodgkins conducted a case series study that utilized various forms of non-surgical treatments, including taping and the use of a post-op shoe, and were applied to individuals with plantar plate injuries. In the largest study of conservative care for this condition, 99 patients were treated with non-surgical methods, compared to 55 patients who underwent surgical treatment. Among the conservative group, 52% reported satisfaction with their treatment plan, which involved nonsteroidal anti-inflammatory drugs (NSAIDs), advice on appropriate footwear, steroid injections, functional taping, or a combination of these options. This suggests that conservative care may be a viable option for managing lesser MPJ instability. The results showed that the combination of a post-op shoe and taping was most effective in the acute phase of the injury and there was proof on serial MRI that the injury incrementally healed over one year. It was also noted that discontinuing these non-surgical options may lead to re-injury. One particular case, involving a ballerina with a grade 2 tear, was able to fully recover with the use of sling taping and a post-op shoe over a period of approximately 3.5 months.[2]

Ojofeitimi et al conducted a case study on a ballerina who had been diagnosed with osteoarthritis of the 1st MPJ, calcification of the 2nd MPJ, capsulitis, and a plantar plate tear, leading to MTPJ instability and functional deficits in walking barefoot and performing demi releve or demi pointe. The dancer was treated with a multimodal conservative treatment plan comprising three phases, along with physical therapy and prolotherapy injections. Phase 1, starting one week after the first prolotherapy injection, included stationary cycle training, non-weightbearing core and lower extremity strengthening, technique re-education, and alternative dancing class performed in supine, prone, and sidelying positions. Phase 2 restricted the dancer to ballet without jumping or demi pointe for two weeks, with the aid of sling tape and padding. Foot doming exercises were initiated at the end of this phase. Phase 3 focused on intrinsic toe flexor strengthening and soft tissue mobilization of the second and third DIP and PIP joints. The dancer's mental and physical status were assessed throughout the rehab period using SF-36 and DFOS scores. One year after discharge, the dancer was able to perform without sling tape or other aids and reported no pain.[11]

A case report conducted by Jordan et al described the successful non-operative treatment of a plantar plate rupture. The patient was a 48-year-old female recreational athlete who sustained the injury in a water skiing accident. Initial treatment included taping the toe in plantarflexion and wearing a forefoot unloading shoe with a selective cushioning insole. The patient was also instructed in exercises to stretch the plantar fascia and strengthen the intrinsic muscles of the foot. Follow-up evaluations, including MRI scans, were conducted at regular intervals over a 12-month period. By the final follow-up, the patient had experienced a complete resolution of symptoms and demonstrated no signs of instability in the MPJ.[13]

Discussion

The research on non-surgical treatment modalities for plantar plate tears is limited and inconclusive. The studies reviewed suggest that these treatments can reduce the progression of deformities, manage pain, and stabilize the digit to allow for fibrosis of the periarticular structures. While these treatments are widely accepted, there is a lack of supportive evidence on their successes. Four studies have attempted to measure the efficacy of non-surgical treatments through MRI and a few other measuring scales, but were limited to one patient showing short-term success per study.

Labbad et al found that shockwave therapy utilizing extracorporeal pulse activation technology (EPAT) on a single patient for seven weeks may be a

viable option for treating plantar plate tears, and monitored the patient's progress through weekly pain assessments, MRI scans, and their ability to return to normal activities. The patient reported being able to walk pain-free after five and a half months along with an MRI scan that showed improvements in the structural integrity of the plantar plate.[18] However, the results of this study cannot be generalized to the larger population due to the small sample size and short duration of follow-up. In addition, pain perception is subjective, the correlation between pain reduction and healing is still a matter of debate in the medical community. A decrease in pain may indicate healing, but it is not a foolproof diagnostic tool as other health conditions can affect the perception of pain and obscure underlying pathologies. The paper was also authored by a physician utilizing EPAT services, which could potentially introduce bias in the reporting of the patient's outcomes.

Kinter and Hodgkins looked at various forms of conservative treatments, including taping and the use of a post-op shoe, for individuals with plantar plate injuries which showed that the combination of a post-op shoe and taping was most effective in the acute phase of the injury, and discontinuing these treatments may lead to re-injury.[2] While this study did show success with the healing of the plantar plate injury, this study was subject to several limitations which include leaving out the sample size, the mechanism of injury that caused re-injury in patients, and failing to mention the duration of the study. The same paper mentioned the case involving a ballerina with a grade 2 tear who was able to fully recover with sling taping and a post-op shoe over a period of approximately 3.5 months.[2] Although the ballerina was able to fully recover from the non-surgical treatments, this study is limited due to the small sample size and its short study duration limiting the generalizability of the results.

Ojofeitimi et al conducted a case study on a ballerina with a plantar plate tear and other foot conditions and was treated with a multimodal conservative treatment plan comprising three phases, along with physical therapy and prolotherapy injections. The dancer's mental and physical status were assessed throughout the rehab period using SF-36 and DFOS scores.[11] One year after discharge, the dancer was able to perform without sling tape or other aids and reported no pain. While the duration of follow-up was longer than other studies, the study concluded that it was not clear which part of the multimodal treatment was most effective in treating the patient and again was limited to a single patient.

The case report by Jordan et al described the successful non-operative treatment of a plantar plate rupture in a 48-year-old female recreational athlete. The patient was treated with taping the toe in plantarflexion and wearing a forefoot unloading shoe with a selective cushioning insole.[13] The patient was able to return to normal activities and had no pain after six months of treatment. As mentioned before, the small sample size of this study limits the generalizability of the results along with the short period of follow-up.

Considering the healing rates between athletes and the general population is crucial when considering the efficacy of treatments. It is possible that athletes may experience a slower healing process and a greater risk of re-injury compared to non-athletes when dealing with plantar plate injuries. This could be due to the increased physical demands placed on the foot during athletic activities, as well as the higher frequency and intensity of training and competition. Moreover, athletes may be more inclined to continue participating in sports despite pain, which could worsen the injury and delay the healing process. Further investigation is necessary to explore this hypothesis and establish if there are notable differences in healing outcomes between athletes and non-athletes with plantar plate injuries.

The current evidence on non-surgical treatment options for plantar plate tears is scarce and inconsistent, marked by small sample sizes and conflicting outcomes. Further exploration is necessary to fully assess the effectiveness of these treatments and determine the best evidence-based approach for various grades of injury. The lack of longer follow-up periods and comparative evaluations between different modalities hinders the ability to draw conclusive findings at this time.

Conclusion

Current treatment approaches for plantar plate tears involve non-surgical methods aimed at managing the condition. However, the effectiveness of these non-surgical treatments lacks comprehensive evidence-based theories behind the treatments. In conclusion, it is imperative to take a multi-faceted

approach to evaluate the healing process and accurately measure its progress. Future research should aim to establish the efficacy of these treatments through larger sample sizes, extended follow-up periods, more rigorous evaluation of the methods used to measure their effectiveness, and establishing objective measures of pain and healing.

References

1. Akoh CC, Phisitkul P. Plantar Plate Injury and Angular Toe Deformity. *Foot and Ankle Clinics*. 2018;23(4):703.
2. Kinter CW, Hodgkins CW. Lesser Metatarsophalangeal Instability: Diagnosis and Conservative Management of a Common Cause of Metatarsalgia. *Sports Health-A Multidisciplinary Approach*. 2020:390-394.
3. Faltas J, Mullenix K, Moorman CT, Beatty K, Easley ME. Case Series of First Metatarsophalangeal Joint Injuries in Division 1 College Athletes. Sports Health. 2014; 6(6):519-526.
4. George E, Harris AHS, Dragoo JL, Hunt KJ. Incidence and Risk Factors for turf Toe Injuries in Intercollegiate Football: Data From the National Collegiate Athletic Association Injury Surveillance System. *Foot Ankle Int*. 2014; 35(2):108-115.
5. Coughlin MJ. Second metatarsophalangeal joint instability in the athlete. *Foot & ankle*. 1993;14(6):309-319.
6. Seow D, Yusof TNBT, Yasui Y, Shimozono Y, Kennedy JG. Treatment Options for Turf Toe: A Systematic Review. *Journal of Foot & Ankle Surgery*. 2020;59(1):112-116.
7. Nery C, Fonseca LF, Gonçalves JP, et al. First MTP joint instability - Expanding the concept of "Turf-toe" injuries. *Foot and ankle surgery : official journal of the European Society of Foot and Ankle Surgeons*. 2020;26(1):47-53.
8. Malani K, Ravine M, Schneider HP. Nonoperative Treatment of Plantar Plate Tears. *Clinics in Podiatric Medicine and Surgery*. 2022;39(3):451-459.
9. Suero EM, Meyers KN, Bohne WH. Stability of the metatarsophalangeal joint of the lesser toes: a cadaveric study. *J Orthop Res*. 2012;30(12):1995-1998.
10. Doty JF, Coughlin MJ, Weil L Jr, Nery C. Etiology and management of lesser toe metatarsophalangeal joint instability. *Foot and ankle clinic*s. 2014;19(3):385-405.
11. Ojofeitimi S, Bronner S, Becica L. Conservative Management of Second Metatarsophalangeal Joint Instability in a Professional Dancer: A Case Report. *Journal of Orthopaedic & Sports Physical Therapy*. 2016;46(2):114-123.
12. Drakos MC, Fiore R, Murphy C, DiGiovanni CW. Plantar-Plate Disruptions: "The Severe Turf-Toe Injury." Three Cases in Contact Athletes. *Journal of Athletic Training*. 2015;50(5):553-560.
13. Jordan M, Thomas M, Fischer W. Nonoperative Treatment of a Lesser Toe Plantar Plate Tear with Serial MRI Follow-up: A Case Report. *Journal of Foot & Ankle Surgery*. 2017;56(4):857-861.
14. Mendicino RW, Statler TK, Saltrick KR, Catanzariti AR. Predislocation syndrome: a review and retrospective analysis of eight patients. *Journal of Foot & Ankle Surgery*. 2001;40(4):214-267.
15. Shane A, Reeves C, Wobst G, Thurston P. Second metatarsophalangeal joint pathology and freiberg disease. *Clinics in podiatric medicine and surgery*. 2013;30(3):313-325.
16. Yu G, Judge M, Hudson J, Seidelmann F. Predislocation syndrome - Progressive subluxation/dislocation of the lesser metatarsophalangeal joint. *Journal of the American Podiatric Medical Association*. 2002;92(4):182-199.
17. Peck CN, Macleod A, Barrie J. Lesser Metatarsophalangeal Instability: Presentation, Management, and Outcomes. *Foot & Ankle International*. 2012;33(7):565-570.
18. Labbad ZG, Love E, Shah DN, Kihira Y, Grinberg V. Treatment of lesser metatarsophalangeal joint plantar plate tear via Extracorporeal Pulse Activation Technology (EPAT) with MRI Follow-up: A case report. *Foot & Ankle Online Journal*. 2020;13(2):1-5.

The Effectiveness of Corticosteroid Injections for the Treatment and Management of Morton's Neuroma

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Abstract

Objective: To examine the effectiveness of corticosteroid injections on the treatment and management of Morton's neuroma, a condition resulting from nerve compression in the intermetatarsal spaces.

Methods: Five articles that investigated the effects of corticosteroids on patients diagnosed with Morton's neuroma were searched using different databases such as Pubmed, Cochrane, Embase, and Google Scholar. Relevant publications included in this study were randomized controlled trials (RCT), prospective, and retrospective studies. Articles older than 2012 were excluded.

Results: The use of corticosteroid injections and a local anesthesia for the relief of pain from Morton's neuroma showed a significant reduction in patient's pain from one week to three months after initial injection. There were no significant differences in pain relief after three months of corticosteroid injection therapy indicating that the use of corticosteroids for injections are best for short-term relief.

Conclusion: The use of corticosteroid injections for the treatment of Morton's neuroma shows short-term effectiveness in the relief of pain. It is not a permanent treatment in which patients would look at repeating injections or turn to surgical removal of the neuroma.

Introduction

Morton's neuroma was discovered by Thomas Morton, an American orthopedic surgeon, who was able to identify the source of the neuroma, in a case study.[1] Neuroma, also known as nerve pain, is one of the most common causes of foot pain in adults within the presence of a diverse range of disease conditions.[1] Adults are more commonly prone to neuromas and more specifically among adults, women are 10 times more likely compared to men in developing neuromas with 75-95% of cases.[1] A neuroma is also commonly found in athletes such as runners or dancers who work extensively with their metatarsal joints by engaging in hyperextension or hyperpronation of the foot. [2]

Often mistaken as a tumor, Morton's neuroma is characterized by proliferative fibrosis or perineural tissue in the foot. [3] It is the result of nerve compression in the intermetatarsal spaces and is most commonly found in the third intermetatarsal space.[3] The third intermetatarsal space is the most common as it contains the digital nerve which receives a large amount of sensation from the lateral plantar nerve which is connected deep into the deep transverse metatarsal ligament (DTML).[3] Some commonly reported symptoms are tingling, numbness, radiating pain, the feeling of a lump at the bottom of the foot, and the feeling of walking on a wrinkled sock. [4] Factors that may increase the severity of the symptoms are ill-fitting, closed-toe shoes and weight bearing activities.[4]

There are several diagnostic tests that are utilized to help determine the diagnosis of Morton's neuroma and to help rule out other conditions as there are a wide-range of diseases and conditions that share the same symptoms. These tests include using ultrasounds, magnetic resonance imaging (MRI), Mulder's sign test, Grautheir's test, and the Bratkowski test.[4] Ultrasounds and MRIs are the most commonly used tests to help aid in the diagnosis process and determine the location of the neuroma in the intermetatarsal spaces.[4] Once identified, there are several treatments to help relieve nerve pain for patients to choose from which include non-pharmacological and pharmacological therapies.

Depending on the severity of the neuroma, non-pharmacological is often the first line of treatment before utilizing invasive therapies as it helps to relieve pain and pressure.[4] Non-pharmacological therapies include avoiding ill-fitted shoes, wearing shoes with a wide toe, avoiding high heels, or by wearing shoe cushion pads.[3] These therapies are beneficial to assist with spreading out the metatarsals while keeping irritation and pressure off of the compressed nerve.[3] Alternatively, pharmacological therapy includes infiltrative treatments which comprise of anesthesia injections, corticosteroid injections, or surgical procedures.[4]

Corticosteroid injections are often used as a treatment of pain relief in many patients.[4] Once the exact location of the neuroma is identified and other disease states are ruled out, patients can choose whether or not to receive corticosteroid injections. Corticosteroid injections are usually injected into the intermetatarsal spaces where the neuroma is identified with the guidance of an ultrasound or x-ray.[4] Once injected, patients often feel a relief of pain from hours to months after the initial treatment. However, there

have only been a limited number of recent studies showing the efficacy of corticosteroid injections in investigating their short term effects which ranges from three months to two years. Additionally, there have been fewer studies investigating the long-term effects of corticosteroid injections as the use of corticosteroid injections long term may result in complications such as nerve injury, infections, plantar fascia rupture, and fat pad atrophy.[4]

The purpose of this literature review is to investigate the effectiveness of corticosteroid injections for the treatment and pain management of a Morton's neuroma.

Methods

A literature search was conducted to identify relevant publications through databases such as PubMed, Cochrane, Embase, and Google Scholar. Various articles were included from 2012 to the present in order to include the most updated clinical research pertaining to the use of corticosteroid injections in patients for the relief of Morton's neuroma. Articles published prior to 2012 were excluded. Keywords used to identify relevant articles were "Morton's neuroma," "corticosteroid injections," and "Morton's neuroma injection." Publications include randomized controlled trials (RCT), prospective, and retrospective studies, for a comprehensive insight into the treatment of Morton's neuroma.

Results

In a patient-blinded randomized trial conducted by Thomson et al, they investigated the effects of corticosteroid injections with ultrasonographic guidance. Radiologists administering the injections could not be blinded as they needed to confirm the exact drug given to the patient and were independent of the data analysis. Patients included were characterized by either having pain or paresthesia in the second or third intermetatarsal spaces with worsening of symptoms by certain footwear, relief of symptoms when removing pressure such as shoes, a positive compression test, a painful click, or a Mulder sign.[5] Study investigators diagnosed Morton's neuroma when a soft-tissue mass measured ≥5 mm in diameter when compressed. Soft-tissue masses that measured less were not significant enough to be considered a neuroma. After diagnosis, participants in the experimental group received a corticosteroid and anesthetic injection of mL methylprednisolone 40 mg and participants in the control group received an injection of anesthetic alone which was 1 ml 2% lidocaine.[5] Participants were followed up at one, three, and twelve months after initial injection. At follow-up, participants were given a questionnaire which they were asked using the modified Foot Health Thermometer that uses a scoring scale from "not better at all" to "completely better."[5] Investigators found that at three months, the global assessment of foot health in the experimental group was significantly better compared to the control group ($p = 0.002$).[5] However, at 3 and 12 month follow-up, the differences in pain were less significant between both groups.[5]

In a prospective, double-blinded, randomized control trial, Lizano et al investigated the effects of corticosteroid injections with a local anesthetic compared to a local anesthetic alone in the treatment for Morton's neuroma. Investigators included patients who were diagnosed with Morton's neuroma from January 2013 to January 2015. Clinical findings in patients included paresthesia in the second and/or third interdigital space of the foot, worsening of symptoms upon tight footwear, improvement in symptoms upon removal of tight footwear, a positive metatarsal compression test, or a positive Mulder's sign.[6] Patients who received previous injections, are under current treatment, are on anticoagulation, analgesics, anti-inflammatory, or has any conditions that may affect treatment such as rheumatoid arthritis were excluded from the study.[6] Thirty-five patients met the inclusion criteria and were randomized using a computer program to be in the experimental group receiving a corticosteroid injection with a local anesthetic or to the control group receiving a local anesthetic alone. The experimental group received three injections of 1 mL mepivacaine 2% with 1 mL of triamcinolone 40 mg each. The control group received three injections of 2 mL mepivacaine 2% each.[6] Injections were given one week apart without ultrasound guidance. Follow-ups were conducted at 3 and 6 months after the completion of treatment. The primary outcome was measured using the visual analog scale (VAS) in which patients ranked their pain on a scale from 0 to 100 with 0 being "no pain" and 100 being "the worst imaginable pain." There were significant improvements in pain three months after the completion of treatment for both groups. However, there were no significant differences in satisfaction between the experimental and control groups at 6 months after treatment. Older patients, patients with short duration of symptoms, and patients who had an absence of radiating pain had better improvement in pain at 6 months following treatment ($p = 0.027$).[6]

In a retrospective study conducted by Park et al, they explored the prognosis after corticosteroid injections. They included 201 patients who had received corticosteroid injections for Morton's neuroma between January 2010 and March 2016 at their local institution by reviewing diagnostic imaging studies. A total of 161 patients received an injection of

1 mL dexamethasone (5 mg) and 1 mL of 1% lidocaine with ultrasound guidance. Follow up was monthly until six months after the injection in which surgical removal of the neuroma was recommended. Using the Johnson scale, 41 patients (20.4%) were satisfied ($p<0.001$). Furthermore, 104 (51.8%) were satisfied with minor reservations, 26 (12.9%) were satisfied with major reservations, and 30 (14.9%) were dissatisfied.[7] Furthermore, the need for additional corticosteroid injections correlated with the patient's age and size of the neuroma. Patients who needed further treatment had an average size of the neuroma of 9.1 mm whereas patients who did not need further treatment had an average size of 4.9 mm ($p<0.001$). Of the patients who had a larger size neuroma, the mean age was 52 years and the mean age for the smaller size neuroma was 58 years ($p=0.004$).[7]

In another retrospective study conducted by Grice et al, investigators explored the effects of corticosteroid injections in various foot and ankle diseases including Morton's neuroma. Telephone and questionnaires were reviewed of patients who underwent ultrasound or x-ray guided injections. Injections included 0.5% marcaine with 40 mg Depo-Medrone.[8] However, how much of the injections patients were given with were unknown. Out of 67 patients who received corticosteroid injections for the treatment of Morton's neuroma, 58 (85%) patients reported complete or partial relief of pain. Two years after the completion of treatment, 21 patients remained asymptomatic, 16 patients had minor relief of pain, 11 patients repeated injection treatment, 19 of patients received surgical removal of the neuroma after treatment, and only one patient reported worse pain after treatment.[8]

In a double-blind randomized controlled trial, Mahadevan et al investigated the efficacy of corticosteroid injections with or without ultrasound guidance. Patients included were clinically diagnosed with Morton's neuroma and had not received any corticosteroid injections within the last 12 months up to recruitment. Forty-five patients were randomly assigned to group A which included ultrasound guidance or group B which included no ultrasound guidance.[9] Patients had a follow up at 3, 6, and 12 months. Patients were given a mixture of 1 mL of 40 mg triamcinolone acetonide and 2 mL of 1% lidocaine. Primary outcomes were measured using VAS pain score. Investigators found a significant reduction in pain in both groups following injection ($p<0.001$).[9] However, the difference between the two groups was not statistically significant at each follow up. Of the 45 patients, 23 went on to receive either further injections or surgical removal after 12 months following treatment. Furthermore, 13% of patients did not have any response to treatment in both groups combined.[9] In conclusion, investigators found no significant differences when giving treatment with or without ultrasound guidance as satisfaction reported were similar in both groups but saw a decrease in symptoms up until 12 months using corticosteroid injections.

Discussion

With corticosteroids being a common treatment for pain for patients with Morton's neuroma after the use of non-pharmacological therapies, relief of pain is often experienced ranging from one month to six months after injection. However, some patients have reported feeling no pain up to two years as seen in the study conducted by Grice et al where 21 patients who have received corticosteroid treatment remained asymptomatic.[8] Despite the current investigations of corticosteroid injections, the therapeutic effects are short-term but vary between each patient. Among those studies, participants eventually resort to surgical removal of the neuroma even after receiving injections or receive more injections.

The results of all studies showed that there is significant improvement in pain amongst patients who receive injections at the site of their neuroma. More specifically, patients across studies reported significant reduction in pain ranging from one week after injection to about three months. According to the studies, there were no significant differences in the location of the injection that was administered whether it was administered at the dorsal, plantar, or web-spaces.

In Thomson et al, significant differences were found at one month after injection in the experimental group where patients reported better quality of life as they were able to walk and do activities in the absence of pain [5]. Investigators also found that the size of the neuroma did not correlate with the outcome of the study. This conflicts with the study conducted by Park et al, where a correlation was found between the size of the neuroma and the prognosis of receiving surgical removal later on.[7] However, this can be due to the short follow up of three months by Thomson et al as they were not able to continue the study after three months.

All studies except for Park et al used ultrasound guidance during the treatment process to help guide in the location of the neuroma. In the study conducted by Mahadevan et al, there were no significant differences between injecting with ultrasound guidance compared to without guidance.[9] However, ultrasound guidance may provide a more accurate placement of the injection. Furthermore, an ultrasound may not be present in all clinics causing physicians to resort to blinded injections.[6]

Limitations of all studies were the lack of sample size, the short follow up length, and conflicting

results. There are some studies that show improvement in pain at three months and others that show no significant differences between the experimental and control groups at 3 months. Due to the nature of the studies with short follow ups and sample sizes, there is great variability in the results of the studies on whether there is a significant effect of pain relief. Thus, making it difficult for it to be generalizable to the general population. Furthermore, it is unclear in certain studies why certain corticosteroids were chosen over another and reasoning for a certain dosage.

Conclusion

Management of pain due to Morton's neuroma proves to be difficult as there are multiple factors to consider such as the patient's pain level, location of neuroma, and the size of the neuroma. Corticosteroid injections are proven to be effective in having a significant reduction of pain in as short as three months to as long as two years. Since the use of corticosteroids long term may result in further complications, most patients often resort to surgical removals of the neuroma. Taking this into account, further research should compare the effectiveness of using different agents used in the treatment of Morton's neuroma.

References

1. Edwards SR, Fleming S, Landorf KB. Efficacy of a single corticosteroid injection for Morton's neuroma in adults: a systematic review. *J Am Podiatr Med Assoc.* 2021;111(4).
2. Di Caprio F, Meringolo R, Eddine MS, et al. Morton's interdigital neuroma of the foot: a literature review. *Foot ankle Surg.* 2018;24(2):92-98.
3. Jain S, Mannan K. Diagnosis and management of Morton's neuroma: a literature review. *Foot Ankle Spec.* 2013;6(4):307-17.
4. Thomas JL, Blitch EL, Chaney DM, et al. Diagnosis and treatment of forefoot disorders. section 3. Morton's intermetatarsal neuroma. *J Foot Ankle Surg.* 2009;48(2):251-6.
5. Thomson CE, Beggs I, Martin DJ, et al. Methylprednisolone injections for the treatment of Morton neuroma. *J Bone Joint Surg Am.* 2013;95:790-8.
6. Lizano-Diez X, Gines-Cespedosa A, Alentorn-Geli E, et al. Corticosteroid injection for the treatment of Morton's neuroma: a prospective, double-blinded, randomized, placebo controlled trial. *Foot Ankle Int.* 2017;38(9):944-51
7. Park YH, Lee JW, Choi GW, et al. Risk factors and the associated cutoff values for failure of corticosteroid injection in treatment of Morton's neuroma. *Int Orthop.* 2018;42(2):323-329.
8. Grice J, Marsland D, Smith G, Calder J. Efficacy of foot and ankle corticosteroid injections. *Foot Ankle Int.* 2017;38(1):8- 13.
9. Mahadevan D, Attwal M, Bhatt R, Bhatia M. Corticosteroid injection for Morton's neuroma with or without ultrasound guidance: a randomised controlled trial. *Bone Joint J.* 2016;98(4):498-503.

Outcomes of Postoperative Neutral Tensioned Immobilization after Achilles Tendon Repair: A Literature Review

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ABSTRACT

Objective: The purpose of this review is to evaluate the available information on the outcomes of postoperative neutral tensioned immobilization after surgical repair of the Achilles tendon.

Methods: A literature review on relevant research articles pertaining to neutral tensioned immobilization after surgical repair of the Achilles tendon was conducted using PubMed and Google Scholar databases. Search terms/phrases such as "Achilles tendon surgery", "neutral tension", and "Achilles tendon immobilization" were used.

Results: Multiple studies reveal that postsurgical neutral immobilization of the ankle joint in 90 degrees has varying postoperative complication rates, mainly re-rupture and infection (0% to 18.2%). Additionally, long-term subjective and objective follow-up assessments via Leppilahti, VAS, and AOFAS Hindfoot scores indicate strong performance of surgically repaired tendons after immediate tensioned immobilization with the ankle joint in the neutral position..

Conclusion: Postoperative immobilization of the ankle joint in neutral position after Achilles tendon repair serves as a viable option when splinting/casting patients.

Introduction

The Achilles tendon is one of the strongest and thickest tendons in the human body and can support tensile loads up to eight times the amount of body weight during movement.[1] The gastrocnemius and soleus are the primary muscles in the Achilles tendon and act together to plantarflex the ankle, flex the knee, and to supinate the subtalar joint. The plantaris muscle, though present in this system, is a minor contributor to Achilles tendon functionality due to it being a thin vestigial tendon.[1] These muscles attach to the calcaneus via the Achilles tendon and function in conjunction with one another to propel the body forward during the propulsion phase of gait.

The Achilles tendon is most commonly damaged during athletic activity and occurs primarily in male athletes between the ages 30-40.[1] Many studies have confirmed that the most common site of damage occurs at the "watershed area" located at the midportion of the Achilles tendon, located 2 to 6 cm above its posterior insertion at the calcaneal tuberosity, due to poor vascularization.[1] This anatomical arrangement of the Achilles tendon may in fact contribute to a high rate of rupture, tenosynovitis, and tendinitis.

Conservative approaches have been used to repair the Achilles tendon due to significant caution when treating this major soft tissue structure. Traditional care typically involves postoperative splinting of the ankle in equinus to limit the patient's dorsiflexion capabilities in an effort to reduce tension on the newly repaired tendon. However, the purpose of this study is to review the viability of neutral tensioned immobilization after surgical Achilles tendon repair. The reliability of this immobilization method is measurable via postoperative complication rates and follow-up assessments.

Methods

A search for relevant research articles regarding Achilles tendon ruptures and postoperative neutral casting were conducted through the PubMed and Google Scholar databases. Search terms and keywords included: "Achilles tendon," "tendon length," "tendon strength," "neutral casting," "tendon healing," and "tensioned immobilization."

Inclusion criteria included cases of neutral position casting following operative treatment of the Achilles tendon and research written in the English language. Exclusion criteria included non-operative treatment of the Achilles tendon. Neutral tensioned splinting was defined as cast immobilization of the ankle joint at 90 degrees.

Results

A study performed by Rantanen et al in 1993 retrospectively analyzed 22 individuals who underwent surgical repair of Achilles tendon ruptures. These patients received an end-to-end repair with 1 or

2 Bunnell-sutures and small adaptive sutures, and were later immobilized in a short, heel-supported walking cast with the ankle in the neutral position. The neutral ankle position casts were worn for 6 weeks postoperatively. After removal of the cast, these patients were encouraged to ambulate immediately. Of the 14 patients in the group who were athletes, 13 (92.9%) were able to return to regular intensity activity within an average of 10 months. 4 of the 22 (18.2%) individuals had minor complications including mild infection, sural nerve lesion, or severe pain. There were no incidences of re-rupture within the group of patients who were immobilized in neutral tension.

A randomized, prospective study by Lantto et al in 2015, evaluated 25 patients with surgically-repaired acute Achilles tendon ruptures. Tendons were repaired via 2-suture Kessler technique with PDS and vicryl, with an additional gastrocnemius flap to cover the suture line. All patients were immobilized in a below-knee plaster splint with the ankle in the neutral position. Patients were then immobilized for 6 weeks with weight-bearing allowed at 3 weeks. Of the 25 patients, two (8%) experienced re-rupture of the Achilles tendon. One of the re-ruptures involved deep infection and eventual loss of the tendon. 18 of the 25 patients followed up 11 years after surgery for evaluation using the Leppilahti score. 14 patients (78%) reported excellent outcomes, while the other 4 patients (22%) reported good outcomes. The mean Leppilahti score at the 11-year follow up was 93.6 +/- 7.2 out of 100 (p=0.68).

In 2021, Subbannan et al performed a retrospective study of 30 surgically repaired Achilles tendon ruptures which were postoperatively immobilized in neutral ankle position with a below-knee cast for 4 weeks. Surgeons performed tendinoachilles lengthenings proximally via Z-plasty (in defects <2.5cm) or via turnplasty (in defects >2.5cm) followed by end-to-end repair via preloaded suture anchor. Of the 30 subjects, there was a 13:2 ratio of men to women and an average age of 52 (range: 29-68 years). No re-ruptures or wound-related complications were reported.

A 2021 retrospective cohort study performed by Xu et al involved 258 patients who sustained Achilles tendon ruptures from sports-related activities. Surgeons performed open repairs via Krackow locking loop and modified Kessler. 224 of the total patients were immobilized postoperatively with the ankle joint in the neutral position for either 2, 4, or 6 weeks. Patients were then evaluated every two weeks after surgery for 16-weeks. Of the neutral-tension immobilized ankles, there were 2 total deep venous thrombosis (0.89%), 3 total re-ruptures (1.34%), and 3 superficial infections (1.34%). The average visual analogue scale (VAS) pain scores for the three groups at 2-weeks was 1.94/10. All VAS average scores were 0/10 by the 12-week mark. The three groups had an average of 99.5/100 on the American Orthopaedic Foot and Ankle Society (AOFAS) hindfoot score by week 14 after an initial average score of 54.6/100 during week 2 follow-ups.

Discussion

The purpose of postoperative splinting or casting is to protect the integrity of the surgical repair, supporting a basis for healing. The idea of immediate immobilization of the ankle joint in the neutral position after Achilles tendon surgery was a foregone thought due to the increased tension applied to newly repaired tendon. However these studies indicate relatively low postoperative complication rates ranging from 0% to 18.2% with varying numbers of subjects.

The primary concern with tensioned immobilization is tendon integrity, but collectively, only 5 of the 301 (1.7%) total Achilles tendons in the four studies were re-ruptured. When considering effectiveness of neutral-tensioned casting and the incidence of re-rupture, weight-bearing protocol serves as a crucial factor since excessive tension could ultimately weaken surgical repair of the Achilles tendon. Weight-bearing protocol varied in all four presented studies: Subbannan et al allowed weight-bearing after 4 weeks, Lantto et al allowed weight-bearing after 3 weeks, Rantanen et al allowed weight-bearing after 2 weeks, and Xu et al allowed weight-bearing within a range of 2-8 weeks. This inconsistency of non-weightbearing timelines serve as a major confounding variable when considering the re-rupture rates as a collective whole. Furthermore, the studies presented in this review failed to mention how patient compliance to weight-bearing instructions was managed and monitored. Strict patient compliance to weight-bearing protocol serves as a major barrier when effectively evaluating postoperative outcomes.

6 of the 301 (2.0%) total Achilles tendons studied in the four studies of this review were

complicated by either superficial, deep infections, and tendon loss. Tendon loss occurred to only one patient (0.3%) in this review as a complication of deep infection following achilles tendon repair. There are many reasons for infections such as increased tourniquet time and increased surgical blood loss intraoperatively. Pre- and post-operatively, behavioral factors such as smoking and potential non-sterile care of dressings may increase risk for postoperative infections. Such variables were not mentioned in these four studies and therefore should be targeted as potential confounding variables in future studies.

When performing surgery on Achilles tendon, risk for developing deep venous thrombosis (DVT) is elevated due to the immobilization of the lower limb with the usage of a thigh tourniquet causing blood flow stasis. Of the four studies presented, Xu et al reported 2 total DVTs after neutral immobilization of the Achilles tendon (0.07%). The use of DVT prophylaxis was not mentioned in the four studies presented in this review. Although only a small percentage of DVTs were reported, it is important to consider that DVTs are an inherent risk in any surgery especially if prophylactic measures such as perioperative anticoagulation and postoperative movement are not followed. Therefore, future studies should control such variables through a consistent protocol for DVT prophylaxis.

Sural nerve injuries, such as the one case (0.3%) mentioned in the Rantanen et al study, are an intrinsic risk whenever surgery is being performed in the region of the Achilles tendon. The sural nerve runs intimately with the lateral border of the Achilles tendon and is at risk to damage during the initial skin incision or resection of the tendon. Injury to this nerve should be avoided as much as possible, but remains at-risk due to its anatomical relationship to the Achilles tendon.

Postoperative complications may also be greatly influenced by medical conditions and medications that impair the body's immune system such as diabetes, autoimmune disorders, malignancies, and use of corticosteroids. There was no mention in any of these studies that aimed to control any of these variables.

Subjective and objective assessments at follow-ups via the Leppilahti, VAS, and AOFAS hindfoot scores indicate strong performance of the surgically-repaired tendons after tensioned casting.[3,4] The study performed by Lantto et al produced a 93.6 +/- 7.2 out of 100 (p=0.68) at the 11-year follow-up indicating both high patient satisfaction and excellent clinical assessment. The downside to this finding is the low statistical significance, which is most likely due to the small patient pool in the study (n=18). The results produced by Subbannan et al showed tremendous improvement of VAS pain scores and AOFAS Hindfoot scores for functionality. Pain scores drastically decreased between the 2- and 4-week follow-ups, with a steady downtrend towards the 16-week follow-up. With the understanding that surgical repair of an Achilles tendon rupture will likely never yield a completely recovered tendon (score of 100/100), the AOFAS Hindfoot scores indicate full functional recovery by week 14. After an initial average of 54.6/100 at week 2, the week-14 follow-ups and onward begin to show average scores of at least 99/100. Regardless of these results, it is still unclear if there is a direct correlation between these subjective and objective measurements and neutral-tensioned casting.

The studies performed by Rantanen and Lantto, show that immobilization in neutral ankle position may serve as an effective option when considering preservation of muscle strength and return to activity. Neutral tensioned immobilization allowed athletes to return to sports at original intensity within a year.[2] Long-term isokinetic strength was also maintained when compared to the contralateral leg.[3] Additionally, data demonstrated greater retention of isometric strength in plantarflexion upon follow-up in the neutral tensioned group.[3] Other miscellaneous benefits include wound care access, reduction in the development of equinus deformity, and less pain experienced when rehabilitating range of motion.[4] Such observations and data serve to demonstrate that not only is neutral tensioned-casting a viable option in patients, but that it could serve to provide greater benefits for patients.

There are many limitations to the studies mentioned in this review. The primary weakness of these results is the low yield of patients evaluated within the individual studies (n=22, 25, 30, and 224). Each individual study provided statistically significant findings. However, the small sample sizes provided by each study, except for the Xu et al study (n=224), may not be representative of the general population. Furthermore, the studies performed by Rantanen et al,

Subbannan et al, and Xu et al were all retrospectively-designed, unlike the prospective design of the Lantto et al study. The intrinsic bias of retrospective studies reduces the reliability of the results, which should be avoided in later research.

Conclusion

Regardless of these studies' weaknesses, it was never deemed that neutral-tensioned casting negatively impacts postoperative care of surgically repaired Achilles tendons. Additionally, there is not a significant amount of focused literature written in regards to the direct comparison of neutral-tensioned Achilles tendon immobilization versus other methods.

There is no conclusive data provided that demonstrates that neutral tensioned immobilization is a primary factor in the reduction of re-rupture and infection rates. Nevertheless, these studies indicate that immobilization in this manner has been involved in the rehabilitative success of patients. Further research should aim to provide statistical significance of a possible correlation between neutral immobilization and positive postoperative outcomes. Studies should control confounding variables such as medical conditions, medications, age, gender, activity level, etc. Future studies should also be prospectively designed with randomized patient selection.

References

1. Yinger K, Mandelbaum BR, Almekinders LC. Achilles rupture in the Athlete. *Clinics in Podiatric Medicine and Surgery*. 2002;19(2):231-250.
2. Rantanen J, Hurme T, Paananen M. Immobilization in neutral versus equinus position after Achilles tendon repair. A review of 32 patients. *Acta orthopaedica Scandinavica*. 1993;64(3):333-335. doi:10.3109/17453679308993638
3. Lantto I, Heikkinen J, Flinkkila T, et al. Early functional treatment versus cast immobilization in tension after achilles rupture repair: results of a prospective randomized trial with 10 or more years of follow-up. *Am J Sports Med*. 2015;43(9):2302-2309.
4. Subbannan SK, N C. A retrospective review of Tendoachilles repair in complete avulsion rupture with lengthening of Achilles tendon and suture anchor with immediate post operative neutral ankle immobilization. *European Journal of Plastic Surgery*. 2022;45(5):779-786.
5. Xu, X.Y., Gao, S., Lv, Y. *et al.* Duration of immobilisation after Achilles tendon rupture repair by open surgery: a retrospective cohort study. *J Orthop Surg Res* 16, 196 (2021).

Medication Reconciliation in Rheumatic Patients Undergoing Lower Extremity Joint Procedure

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ABSTRACT

Objective: Rheumatoid arthritis (RA) is a common autoimmune disease which presents with progressive disability systemic complications. Current treatment of RA is with immunomodulatory medications, which presents challenges for the patient in the perioperative period seeking surgical treatment for their lower extremity complications. The objective of this paper is to perform a literature review on the importance of medication reconciliation in RA patients in the preoperative setting in order to manage post-surgical complications.

Methods: Multiple peer-reviewed journal databases were used to collect literature. These databases included ScienceDirect, Google Scholar, and EBSCOhost. Keywords included "rheumatoid arthritis", "surgical intervention", and "medication management".

Results: A total of four peer-reviewed studies were included in the data collection. These studies compared the postoperative wound healing delays and infectious complications in patients being treated with methotrexate in the setting of rheumatoid arthritis. Each study compared the treatment group to a control.

Conclusion: Immunosuppressive medication regimen in the gold standard treatment to achieve clinical remission for patients suffering from RA. The first-line choice has been methotrexate which has shown no significant risk for increased post-op complications. Other DMARDS do present a statistical significance and further research should be done to understand the risks of each drug.

Introduction

Rheumatoid arthritis (RA) is a common autoimmune disease which presents with progressive systemic complications. It is characterized by synovial inflammation, autoantibody production, cartilage and bone destruction, and systemic features affecting the cardiovascular, pulmonary, psychological, and skeletal systems. Although there is no definitive cause of RA, there has been an established association between the human leukocyte antigen (HLA)-DRB1 locus and patients positive for rheumatoid factor or anti citrullinated protein antibody (ACPA).[1] The synovitis in these patients is a result of the transmigration of lymphocytes and polymorphonuclear leukocytes into the synovial fluid.[2]

The bone erosion and joint destruction in RA is specifically a result of the macrophage colony-stimulating factor and receptor activator of NF-kB ligand (RANKL) which promote osteoclast differentiation and invasion of the periosteal surface.[2] Additionally, mechanical factors predispose certain sites to increased erosion. This chronic inflammatory disorder primarily involves the small synovial joints and studies have shown that approximately 16-19% of patients with RA presents with foot and ankle pain as the initial complaint.[3] Overtime, there is an increase in foot-related complaints equating to around 90% of RA cases.[3] The metatarsophalangeal joint is the most commonly affected with progressive articular damage and structural deformities.[3] The deformities contribute to negative effects on patients' mobility and functional capacity. The current treatment strategy for the structural deformities involve aggressive therapy and surgical intervention.

Although the structural deformities are managed from a surgical approach, the primary goal of treatment in patients with RA is to achieve long-term clinical remission and optimize their quality of life in the absence of symptoms of the disease. These patients are placed on long-term medication regimens which essentially suppress the immune system and inflammatory cells contributing to the pathology. Given the immunosuppressive effects of these drugs, there was a notion that these drugs could lead to increased risk of infection and postoperative wound healing delay.[4] These medications include traditional, nonbiologic disease modifying antirheumatic drugs

(DMARDS) and analgesic and anti-inflammatory medications.[1] The results of this paper will focus on the conventional non-biologic DMARDS given that these are the first-line agents in the treatment of RA.

Disease Modifying Antirheumatic Drugs (DMARDS)	Conventional Drugs: methotrexate, leflunomide, hydroxychloroquine, sulfasalazine, minocycline
	Anti-TNF: adalimumab, etanercept, infliximab, certolizumab, golimumab, canakinumab
	Non-TNF: abatacept, rituximab, tocilizumab
	Immunosuppressants: cyclosporin, cyclophosphamide, azathioprine
Analgesics/ Anti-Inflammatory	Topical analgesics: Capsaicin, NSAIDs, Salicylates
	Oral analgesics: NSAIDs, Acetaminophen, Opioids
	Oral anti-inflammatory: Corticosteroids

Figure 1.1 Lists the potential therapeutic agents used in the management of RA.

Due to the immunomodulatory effects of these medications, increased consideration must be taken in the preoperative period. Patients with RA suffer higher rates of infection and wound healing complications at baselines compared to patients without RA due to the aggressive immunosuppression treatment regimen.[5-7] RA is a pathology that has significant detrimental contribution to the podiatric patient community and as such it is important to understand the implications of the medication regimen. The objective of this paper is to perform a literature review to understand the need for medication reconciliation in RA patients in the preoperative setting in order to minimize the post-surgical complications.

Methods

Multiple peer-reviewed journal databases were searched to collect literature. These databases included ScienceDirect, Google Scholar, and EBSCOhost. Keywords included “rheumatoid arthritis”, “surgical intervention”, “rheumatoid arthritis surgery”, and “medication management”. In order for a study to be included, it must involve RA patients prescribed biologic DMARDs who have undergone a surgical procedure. Studies included could be retrospective and prospective cohort studies, case reports, literature reviews, and randomized control trials. The exclusion criteria were those studies that did include conventional DMARDs in their trials and did not test for post-operative outcomes in the setting of surgical procedure.

Results

Perhala et al performed a 10-year retrospective analysis at the Cleveland Clinic Foundation of the occurrence of postoperative infectious complications in patients who underwent total joint arthroplasties as a result of rheumatoid arthritic joint deformities.[8] The study had two groups of patients whom were both treated with total joint arthroplasties: the first group consisted of 60 patients (92 procedures) who were taking methotrexate (MTX) and the second group had 61 patients (110 procedures) who were not prescribed MTX. Eight patients (8.7% of procedures) experienced complications in the MTX group versus five patients (5.5% of procedures) experienced complications in the non-MTX group. The complications in group one included three infected prosthesis, two infected hematomas, two necrotic eschars, and one prolonged wound drainage. The complications in group two included two infected prosthesis, one infected hematoma, one deep wound abscess, and one prolonged wound drainage.[8]

Grennan et al conducted a prospective study at Wrightington Hospital with 388 patients diagnosed with RA who were to undergo elective orthopedic surgery due to the arthritic joint complications.[9] Their sample size was divided into three groups: those who continued methotrexate, those who discontinued methotrexate two weeks before surgery until two weeks after surgery and the control group of 228 RA patients were not receiving MTX therapy and underwent similar surgeries. A total of 88 procedures

in Group 1, 72 procedures in Group 2, and 228 procedures in group 3 were analyzed. Signs of infection or surgical complications occurred in two of 88 procedures in group 1 (2%), 11 of 72 procedures in Group 2 (15%), and 24 of 228 in group 3 (10.5%).[9]

Jacques et al conducted a randomized prospective study in 64 patients with RA treated with MTX and who underwent orthopedic surgery.[10] There were two groups, each consisting of 32 patients. In group A, MTX was interrupted seven days prior to surgery whereas in group B there was no discontinuation of MTX. The procedures performed included arthroplasties, synovectomies, and arthrodesis all secondary to RA complications. Patients were seen for regular follow ups for a total of eight months after the surgery. A total of 89 orthopedic surgeries were performed. There were no postoperative infections recorded within either group. Prolonged wound healing was recorded in six cases in group A and in four cases in group B. The complications observed included wound dehiscence, skin necrosis, and delayed wound healing.

A prospective study by Fuerst et al compared whether treatment with conventional DMARDS including methotrexate versus leflunomide increased the risk of wound-healing complications after elective orthopedic surgery in patients with rheumatoid arthritis.[11] Leflunomide acts by inhibiting the de novo synthesis of pyrimidine nucleotides in immune response cells.[11] 201 patients were included in this study over the space of March 2002 to September 2003. 124 patients received methotrexate therapy and 57 patients received leflunomide therapy. All patients were required to have taken a DMARD for at least three months. The overall complication rate in patients undergoing methotrexate therapy was 12.9% and overall complication rate in patients undergoing leflunomide was 40.6%.[11] These complications included necrotic eschars, wound dehiscence with prolonged wound drainage, and superficial wound infections with coagulase-negative staphylococcus.

Discussion

RA presents with debilitating symptoms which require both strict medication regimen and invasive surgical treatment. The frequency of foot deformities in RA patients was as high as 78.8% with the most frequent deformity being hallux abductovalgus.[3] The deterioration of these joints warrants treatment with surgical intervention. However, given the immunosuppressive nature of the medications that RA patients are prescribed, a balance must be obtained in the perioperative period in regard to immunomodulation and the risk of RA symptomatic flare. Thus, the goal of this literature review was to answer the question of whether methotrexate requires a medication reconciliation in the perioperative setting when treating RA joint pathology.

The four studies referenced each analyzed the risk of postoperative complications in patients being treated with MTX in the setting of RA. Each study was able to account for age, sex distribution, and duration of RA as factors in order to ensure they were not significant confounders in the study designs.[8-11] Of the four studies in this review, all of them were localized to joint procedures in the lower extremity. Subsequently, the findings from this literature review can serve as insights when understanding the RA pathology.

The study by Perhala et al compared patient's prescribed MTX versus those not taking MTX in the setting of total joint arthroplasty to treat RA joint complications. When a logistic regression analysis was conducted, the results were a p-value of 0.366 and a chi-squared value of 0.816.[8] From this, we are lead to the conclusion that there is no statistical significance in regard to increased frequency of local postoperative infectious complications in the setting of methotrexate regimen. This suggests that the treatment in the perioperative period with doses of MTX does not increase the risk of infectious complications or wound healing delay in the postoperative setting.

Furthermore, the study conducted by Grennan et al sought to analyze the postoperative complications in patients continuing versus discontinuing MTX treatment in the pre and postoperative setting. The logistic regression analysis showed that the surgical complication or infection frequency in group one was less than that in either group two or three.[9] This allows for the inferences that patients with RA who are undergoing MTX therapy can continue to do so without increased risk of complications in the postoperative setting. The previously mentioned study further corroborates the results of this study. The main limitation addressed in

this study was that it merely followed the short-term postoperative complications within one year of the surgery. Although group one had the fewest complications, this may be due to the immediate anti-chemotactic effect of methotrexate.[9] Thus, this study warrants a longer duration of follow up to confirm whether there is a correlation between increased infection rate and medication continuation.

The study by Jaques et al. further contributes to the thought that methotrexate can be safely administered in the perioperative period. When performing a logistic regression with a statistical significance set of 0.05, there was no significance found between those that continued to take MTX as opposed to those that discontinued MTX seven days prior to surgery.[10] Although there were complications observed in each group, it should be noted that some of the patients were prescribed prednisolone which had not been discontinued. Prednisolone is a glucocorticoid which acts to decrease inflammation via suppression of leukocytes.[13] This study raises the concern for the potential of confounding variables contributing to complication risks. Although this paper focused its findings on the use of MTX, patients with RA are prescribed a multitude of immunomodulatory medications each with the potential of postoperative complications. All of the studies took into consideration age and sex as potential confounding variables, but this was the only one that mentioned other immunosuppressive agents as an additional variable.

The study for Feurst et at. was unique in that the MTX group was compared to another DMARD group rather than a non-MTX group. This difference in study design leads to findings which parallel those in prior studies but also raise questions for future research navigation in this field. When a logistic regression analysis was done, it was found that methotrexate therapy did not increase the risk of surgical complications, however leflunomide did increase the risk significantly. The p value for the MTX group was 0.98 verses the p-value for the leflunomide group was 0.01.[11] The odds ratio for the MTX group was 0.99 verses the odds ratio for the leflunomide group was 3.48.[11] The overall data from the Fuerst et al study shows that in patients undergoing orthopedic surgery as a result of rheumatoid arthritic deformity, the use of leflunomide increased the risk of early healing or infection complications whereas there was no significance with methotrexate. Although each of these drugs fall in the same category as a conventional DMARD, their specific mechanism of action is quite different at a physiological level. Methotrexate is a folate derivative that inhibits several enzymes responsible for nucleotide synthesis and thus acts as an immunomodulator that affects intracellular metabolic pathways of purine metabolism.[12] Leflunomide acts by inhibiting the de novo synthesis of pyrimidine nucleotides in immune response cells.[11] This difference in physiological target may contribute to the statistical significance in postoperative complications. This specific study warrants further research on the difference between the conventional DMARDS in their perioperative management in the setting of RA patients. It can be inferred that although MTX is an immunosuppressive agent, it's mechanism of action does not directly affect the physiological process of wound healing but rather may target more of the inflammatory markers involved in the pathogenesis of RA.

It is important to discuss the other reasons for which some patients did experience delayed wound healing and infections. This doubles back to the concept of potentially confounding variables. Many patients present with comorbidities which contribute to impaired wound healing and increased risk of infection. Some of these comorbidities include diabetes, history of tobacco use, and cardiovascular disease. Another reason includes patient compliance with postoperative instructions such as time to being weightbearing or incision site maintenance. The aforementioned studies did not directly mention these within their study design and, thus, could be potential reasons for complications.

A limitation of the results of this study was that not all the studies were randomized nor blinded.[11] Additionally, most of these studies followed patients only in the short-term postoperative period. The study by Grennan et al mentioned that the decreased infection risk may be attributed to the immediate anti-chemotactic effect of MTX in the biologic setting.[10] Given that methotrexate is the first-line agent in the treatment of RA, most studies evaluating DMARDs focus only on that agent. The mechanism of each medication used to treat RA varies and as such further investigation is needed to assess the potential increased risk of postoperative

complications with these medications. Future studies should follow patients in a long-term postoperative setting to see prospective complications.

Conclusion

Immunosuppressive medication regimen in the gold standard treatment to achieve clinical remission for patients suffering from RA. The first-line choice has been MTX which has shown no significant risk for increased post-op complications. Other DMARDS do present a statistical significance and further research should be done to understand the risks of these medications.

Citations

1. Karatepe, A.G., et al Foot deformities in patients with rheumatoid arthritis : the relationship with foot functions. *International Journal of Rheumatic Disease.* 13: 158-163, 2010.
2. McInnes I.B. Schett, G. The Pathogenesis of Rheumatoid Arthritis. *The New England Journal of Medicine.* 365: 2205-19, 2011.
3. Chauhan, K., Jandu, J.S., Goyal, A., et al Rheumatoid Arthritis. *StatPearls Publishing.* 2022. https://www.ncbi.nlm.nih.gov/books/NBK441999/
4. Doran, M.F., Crowson, C.S., Pond, G.R., O'Fallon, W.N., Gabriel, S.F. Frequency of Infection in Patients with Rheumatoid Arthritis Compared with Controls: A Population-Based Study. *Arthritis & Rheumatism.* 46(9): 2287-2293, 2002.
5. Bibbo C. Wound healing complications and infection following surgery for rheumatoid arthritis. *Foot Ankle Clinics.* 12:509–524, 2007.
6. Bibbo C, Goldberg JW. Infectious and healing complications after elective orthopedic foot and ankle surgery during tumor necrosis factor-alpha inhibition. *Foot Ankle Int* 25:331–335, 2004.
7. Ishie S, Ito H, Azukizawa M, Furu M, Ishikawa M, Ogino H, Hamamoto Y, Matsuda S. Delayed wound healing after forefoot surgery in patients with rheumatoid arthritis. *Mod Rheumatol* 25:367–372, 2015.
8. Perhala, R.S., Wilke, W.S., Clough, J.D., and Segal, A. Local infectious complication following large joint replacement in rheumatoid arthritis patients treated with methotrexate versus those not treated with methotrexate. *Arthritis & Rheumatism.* 34(2): 146-152, 1991.
9. Grennan, D.M., Gray J., Loudon, J., Fear S. Methotrexate and early postoperative complications in patients with rheumatoid arthritis undergoing elective orthopedic surgery. *Ann Rheum Dis.* 60(3): 214-217, 2001.
10. Sany, J., Anaya, J., Canovas, F., Combe, B., Jorgensen, C. The fluence of Methotrexate on the Frequency of Postoperative Infectious Complications in Patients with Rheumatoid Arthritis. *The Journal of Rheumatology.* 20: 1129-32, 1193.
11. Fuerst, M., Moehl, H., Baumgaertel, K., Ruether, W. Leflunomide increases the risk of early healing complications in patients with rheumatoid arthritis undergoing elective surgery. *Rheumatology & International.* 26(12): 1138-1142, 2006.
12. Krause, Mg. & Matteson, E.L. Perioperative management of the patient with rheumatoid arthritis. *World Journal of Orthopedics.* 5(3): 283-291, 2014
13. Ramammorthy, S. & Cidlowski, J. Corticosteroids-Mechanisms of Action in Health and Disease. *Rheum Dis Clin North Am.* 42(1): 15-31, 2016

Botulinum Toxin A Treatment of Post-Stroke Lower Limb Spasticity

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ABSTRACT

Objective: This study aims to investigate the effectiveness of botulinum toxin A (BTX-A) treatment and to compare the Modified Ashworth Scale (MAS) outcomes of patients recovering from lower limb post-stroke spasticity (PSS) who have undergone BTX-A therapy.

Methods: We conducted a literature search analysis of peer-reviewed publications regarding "botulinum treatment of post-stroke lower limb spasticity" through PubMed, Science Direct, Google Scholar, and the Journal of Advanced Academics (JOAA) from patient reports made between 2014 and 2021. Search terms included: lower limb post-stroke spasticity, botulinum A toxin therapy, post-stroke rehabilitation, botulinum toxin injection for spasticity.

Results: Across the studies discussed on botulinum toxin A therapy, patients who had received BTX-A treatment demonstrated lower Modified Ashworth Scale (MAS) scores at the end of treatment when compared to placebo group.

Conclusion: Botulinum toxin A is an effective form of treatment for post-stroke lower extremity spasticity.

Introduction

Stroke is a major cause of mortality and of adult disability worldwide. It is estimated that 42.6% of stroke patients will develop post-stroke spasticity, with 15.6% of cases progressing to severe spasticity. Lower extremity spasticity is a common complication following stroke and can have many negative effects on a patient's overall quality of life. This condition involves involuntary contractions of the skeletal muscle, which can lead to a muscle stiffness that impedes both lower and upper extremity mobility and gait. Spasticity can be characterized by muscle weakness, increased muscle tone, and muscle and joint deformities. [1-7]

The goal of post-stroke spasticity (PSS) treatment is to decrease symptoms by minimizing hyperactive stretch reflexes and skeletal muscle excitation-contraction coupling. Botulinum toxin A (BTX-A, BonT-A) is a potent exotoxin produced by bacterium Clostridium botulinum. This is a treatment administered intramuscularly. The toxin inhibits acetylcholine release and synaptic transmission, leading to relaxation of hypercontracted muscles seen in post-stroke spasticity.[8] It has been suggested in previous studies that early management of spasticity with BTX-A leads to more favorable outcomes in post-stroke patients. The goal of this systematic review is to discuss the efficacy of Botulinum toxin A in treatment of post-stroke lower extremity spasticity.

Methods

A review of current literature regarding "botulinum treatment of post-stroke lower limb spasticity" was conducted through keyword search engines, PubMed, Science Direct, Google Scholar, and the Journal of Advanced Academics (JOAA).

Search terms included: lower limb post-stroke spasticity, botulinum A toxin therapy, post-stroke rehabilitation, botulinum toxin injection for spasticity. We reviewed articles published from 2014 to 2021 with the main emphasis on Botulinum toxin A treatment of PSS. Initially, 186 results were found. Exclusion criteria included studies that used other forms of Botulinum toxin (ie. BTX-B), those that were published before 2014 and after 2021, and those that had a sample size of less than twenty participants. After filtering for articles that used similar methods in evaluation of BTX-A therapy on PSS, five papers were selected. The studies were longitudinal observational investigations, with durations that ranged from twelve weeks to greater than six months.

Results

Study Characteristics

A summary of the results for the selected articles is shown in Table 1. Modified Ashworth Scale (MAS) was used as the main method of assessing spasticity, which evaluated both neural and biomechanical components of spasticity. Additionally, some studies have also included Fugl-Myer Assessment scale (FMA), Sway area (SA), Gait Velocity (GV), Functional Ambulation Classification (FAC), and Functional Independence Measure (FIM). For this paper, we will focus on addressing the changes in MAS scores. The study duration ranged from three to six months, with a sample size of 21 to 104 subjects. All investigations that were included used Botulinum Toxin A with doses and concentrations that varied across studies.

Comparison of BTX-A Treatment of Lower Limb PSS

Study	Sample Size	Duration	Dose of Botulinum Toxin	Outcome Measurements	Results
Pietrzak, 2014	52	<3 months	230 or 460 U	Modified Ashworth Scale (MAS)	The muscular hypertonicity was reduced with BTX-A treatment given during the first 3 months after injury.
Li, 2017	104	12 weeks	200 U or 400 U; 50 U/mL or 100 U/mL	Modified Ashworth Scale (MAS), Gait Velocity (FPV)	BTX-A effectively and safely treated foot spasm after stroke at an optimal dose of 400 U with a concentration of 50 U/mL (high dose/low concentration).
Picelli, 2021	83	136.1 days (±95.1 days)	300 U	Modified Ashworth Scale (MAS), Medical Research Council (MRC), Motricity Index (MI)	The use of BTX-A treatment for PSS should be initiated within 3 months of stroke onset to obtain greater reductions in muscle tone after 1 and 3 months.
Pimentel, 2004	21	>6 months	300 UI 100 UI	Modified Ashworth Scale (MAS), Functional Independence Motor Score (MFIM)	There was improved spasticity in the 300U group was better than in the BTX-A 100U group.
Tao, 2015	23	3 weeks	50 IU	Modified Ashworth Scale (MAS), Fugl-Meyer Assessment (FMA)	BTX-A injections at low doses may improve the gait, spasticity, and independent capabilities in post-stroke spasticity patients.

Table 1. Summary of the five studies on Botulinum Toxin A intervention for lower extremity spasticity. [1-5]

In Pietrzak et al, 52 patients with unilateral or bilateral spasticity and a MAS score of at least 1+ were recruited. A total dose of 230 U was injected into each target muscle group. Patients with unilateral stroke received 230 U and patients with bilateral spasticity were treated with 460 U (230 U on each affected leg). All patients received similar standardized rehabilitative care during the duration of the study. Twelve weeks after the initial injection, the patients were injected again using the same methodology. The study found that patients who received treatment showed improvement in spasticity with an average of 0.6 points reduction in MAS at week 12 as compared to an increase in MAS score seen in the placebo group.[3]

In Li et al, 104 patients participated in the 2017 study, which explored the benefits of BTX-A at varying dose and concentration combinations. The subjects were divided into four groups; each group received either 200 U or 400 U and one of the two concentrations (50 or 100 U/mL). Throughout the study, MAS scores varied between groups, with significantly lower scores in the high dose/high concentration group after 4 days of treatment. After 12 weeks, the study concluded that BTX-4 at a higher dose and lower concentration showed the most improvement.[4]

In a longitudinal study by Picelli et al, 83 patients had an average age of 63.9 (±12.5 years) and had an average time since stroke onset of 136.1 days (±95.1 days). A significant decrease in MAS score was observed at week 4 after post-stroke spasticity treatment, but the reductions were smaller at weeks 12 and 24 after treatment. The study also found the time between stroke onset and BTX-A treatment could play a role in MAS score. Patients who received treatment after 90 days of stroke onset showed higher MAS score at week 4 and 12 than 24 compared to patients who were treated <90 days post stroke. [2]

In Pimentel et al, 21 patients with a diagnosis of ischemic and/or hemorrhagic stroke (MAS score of 3 or 4) participated in the study. The first treatment group (age: 50.5±6.8) received 300 UI distributed to different regions of the target muscle and the second treatment group (47.9±3.8) received 100 UI. After 8- and 12-weeks post-treatment, both groups showed significant improvement. However, the first treatment group showed greater improvement with the higher dosage (300 UI). [5]

A study conducted by Tao et al aimed to understand whether a low-dose of BTX-A can improve spasticity. In this study, 23 patients with ischemic and/or hemorrhagic stroke were recruited, with the average age of 55±12 for the treatment group and 58±14 for the control group. In the treatment group, 200 U of BTX-A was injected into the gastrocnemius muscle and a lower dose of 50 U was administered to the posterior tibial muscle. At week 8, the treatment group showed lower MAS score compared to the control group.[1]

Discussion

The present analysis found that early administration of botulinum toxin A is an effective treatment in reduction of lower extremity hypertonicity and spasticity seen in post-stroke patients. The studies in focus used the Modified Ashworth Scale (MAS). MAS scores were correlated with lower limb movement quality and motor performance.[1-6] The studies also included other additional scales such as Gait Velocity, Modified Barthel Index (MBI), Sway Area, Functional Ambulation Classification (FAC), and Functional Independence Measure (mFIM). [1-6]

In a study by Picelli et al on eighty-three patients with PSS, MAS showed a significant reduction in PSS at 4 and 12 weeks following botulinum toxin A treatment.[3] In Tao et al, there was significant improvement of gait analysis (using assessment of speed, cadence and step length) seen in the BTX-A treatment group compared to those in the control group.[1] Additionally, it was found that the botulinum treatment was associated with improved MBI scores for quality of life and daily living activities. In a study involving 104 patients by Li et al, the treatment of BTX-A led to significant improvements in MAS and other quantitative scores.[4] Several of the studies found that botulinum toxin A treatment should be administered during early onset of stroke spasticity.[1,3] However, the guidelines and definitions of early BTX-A administration are still under investigation and yet to be determined. Picelli et al suggests that BTX-A treatment should be administered within 3 months following stroke for optimal muscle tone reduction.[3] On the other hand, Tao et al recommends that lower limb PSS treatment with BTX-A is ideal within 4-6 weeks following stroke.[1] Additionally, several of the studies recommend that combination therapy resulted in more favorable outcomes in patients than a single treatment alone. It is suggested that BTX-A treatment in combination with techniques such as physical therapy and rehabilitation can lead to correction of locomotion and walking patterns impacted by stroke spasticity.[1]

Patients did experience some adverse effects associated with BTX-A administration which included allergic reactions, pain, bleeding and/or swelling at the injection site, and dysphagia. However, none of these reported symptoms led to severe adverse complications.[2,4] Two patients died during the Pietrzak study with the first death from intracranial bleeding and the second death from relapsing stroke. However, both deaths were considered to be causally unrelated to the study procedures. [5]

There were several limitations to this systematic review. The PSS studies were limited to those that used the Modified Ashworth Scale (MAS) as the primary outcome measurement. However, many PSS studies utilized other measurement scales to assess BTX-A efficacy, including Functional Independence Motor Score (mFIM) and Maximum Voluntary Contraction (MVC) tasks.[2,5] Common limitations across studies used for this analysis are small sample sizes and the lack of standardized optimal doses for BTX-A. Additionally, as noted by Picelli et al, the absence of measurement regarding treatment goal attainment and the lack of blinded outcome assessment may introduce bias in the assessment of outcomes.

Conclusion

Botulinum toxin A treatment in post-stroke patients may reduce lower extremity spasticity, enhance gait, and improve overall ability for daily life activities. While dosage and concentration differences were observed between studies, BTX-A treatment demonstrated safety and efficacy in patients with lower limp spasms. However, these findings need to be further evaluated to develop a set of guidelines for early BTX-A therapy in PSS.

References

1. Tao W., Yan H., Li J.-H., Shi Z.-H. Gait improvement by low-dose botulinum toxin a injection treatment of the lower limbs in subacute stroke patients. J. Phys. Ther. Sci. 2013;27:759–762.
2. Pimentel L.H.C., Almazor F.J., Rodrigues L.R.S., et al. Effects of botulinum toxin type A for spastic foot in post-stroke patients enrolled in a rehabilitation program. Arq. Neuro-Psiquiatria. 2014;72:28–32.
3. Picelli,A.;Santamato,A.; Cosma, M. et al. Early Botulinum Toxin Type A Injection for Post-Stroke Spasticity: A Longitudinal Cohort Study. Toxins 2021,13,374.
4. Li J, Zhang R, Cai BL, et al. Therapeutic efficacy and safety of various botulinum toxin A doses and concentrations in spastic foot after stroke: a randomized controlled trial. Neural Regen Res 2017; 12(9):1431-1437.
5. Pietrzak HM, Kaszuwski P., Schelusky L., et al. Early botulinum toxin treatment for spastic pes equinovarus—A randomized double-blind placebo-controlled study. Eur. J. Neurol. 2014;21:1089–1095.
6. Wein T, Esquenazi A, Jost WH, et al. OnabotulinumtoxinA for the Treatment of Poststroke Distal Lower Limb Spasticity: A Randomized Trial. *PM R*. 2018;10(7):693-703.
7. Harb A, Kishner S. Modified Ashworth Scale. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; May 8, 2022.
8. Chen YT, Zhang C, Liu Y, et al. The Effects of Botulinum Toxin Injections on Spasticity and Motor Performance in Chronic Stroke with Spastic Hemiplegia. *Toxins (Basel)*. 2020;12(8):492. Published 2020 Jul 31.

EXTREMITAS

Dermatopathology

Juvenile plantar dermatosis: a review of diagnosis, management, and differentiation from its mimics

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Abstract

Objective: Juvenile plantar dermatosis (JPD) is a common dermatological condition that is easily mistaken for common podiatric dermatological conditions such as tinea pedis and atopic dermatitis. This study reviews the clinical features and management of JPD, as well as how to rule out its mimics.

Methods: This review identified literature from January 31st 1985 to December 31st 2022 using the PubMed database. The following search key words were used: *Juvenile plantar dermatosis OR pediatric foot dermatoses.*

Results: A review of the relevant literature shows that JPD is a clinical diagnosis that does not require testing. Plantar distribution, history, and histopathological changes help differentiate JPD from its mimics of atopic dermatitis and tinea pedis. JPD can appear concurrently or coexist with one of its mimics, irritant contact dermatitis, as proven by patch testing in several studies. The consensus treatment is to have regular change of socks and shoes in addition to improved foot hygiene and emollients.

Conclusion: JPD is a disease limited to children and adolescents, with a male predominance. It is a clinical diagnosis that often mistaken for its mimics, atopic dermatitis, irritant contact dermatitis, and tinea pedis. Although there is a consensus treatment for JPD in the literature, recent studies have uncovered new potential treatments that require further investigation to potentially reduce the duration of JPD treatment.

Introduction

Juvenile plantar dermatosis (JPD) is a common cause of foot rash seen in school aged children and adolescents, typically 4 to 15 years old with a male predominance. The etiology of juvenile plantar dermatosis is due to a combination of repetitive frictional movements, occlusive footwear, and excessive sweating, but the exact pathophysiology is not known. The dry-wet cycling causes chronically dry feet that present as symmetrical, shiny erythema on the weightbearing surfaces of the feet with fissuring and superficial desquamation of the skin folds and loss of the epidermal ridge pattern.[1-3] Symptoms can persist for 2.5-4.5 years.[4] The prevalence of JPD is unknown due to the limited research. JPD presents as an erythematous rash of the weight-bearing plantar aspects of the feet with the distal one-third of the plantar surface of the feet and toes tending to be involved more frequently.[2] Studies have shown that 93% of patients have rashes on the ball of big toe and 77% of patients will have rashes on the ball of their foot, while only 23% have a rash on their heel.[3]

Treatment is conservative with patients being encouraged to wear thick cotton socks with breathable shoes, preferably leather and not made of synthetic materials, and applying an occlusive emollient such as petroleum jelly after bathing and before bed.[1,5-7] Treatment is unrewarding with slow improvement or unsuccessful therapy.

Diagnosis of JPD is done clinically with a thorough examination of the feet.[6] Common mimics such as and as atopic dermatitis, irritant contact dermatitis, or tinea pedis can be ruled out through biopsy, patch testing, and KOH test. However, these tests are not necessary if the clinician is able to recognize JPD based on clinical features and patient history. Healthcare providers with a better understanding of JPD's historical and clinical features can help reduce unnecessary testing to rule out its mimics of atopic dermatitis and tinea pedis and stop protracted symptoms before treatment.[7] The goal of this paper is to review the clinical features of JPD and its mimics to allow clinicians to quickly identify JPD, in addition to reviewing the treatment modalities.

Methods

This review identified literature from January 31, 1985, to present using PubMed. The following search strategy was used: *Juvenile plantar dermatosis OR pediatric foot dermatoses.* Articles not written in the English language were excluded, articles pertaining to JPD were included. In total, the search yielded four prospective uncontrolled studies, one retrospective uncontrolled study, one case series, one case study, and four literature reviews.

Results

Clinical Presentation

Ashton, Jones et al conducted a prospective uncontrolled study on 56 patients and found that JPD affects children aged 3 to 14 with mean onset of 7.3 years and disease duration is 2.5 to 4.5 years and has

a male predominance.[3] Emollient usage proved more beneficial with 48% reporting an improvement of symptoms.[3]

Zagne et al conducted a case series exploring the histopathology of JPD and found that on histopathology JPD is characterized by spongiotic dermatitis and eccrine duct inflammation.[3,8] These findings when seen on biopsy can help rule in a diagnosis of JPD.

Kumar et al conducted an open prospective uncontrolled study of 25 patients with JPD. Their results were in line with other studies conducted. They found that 16% of patients had a personal history of atopy, 36% of patients had risk factors such as irritating footwear or prolonged contact with water, and 12% of patients were positive in patch testing.[2] Fungal scrapings were negative, ruling out tinea pedis.

Treatments

A case study done by Shipley et al found that topical 0.1% tacrolimus applied twice per day for one month nearly resolved their patient's JPD.[9] This is a proposed new treatment option other than the more traditional treatment of emollient and wearing clean, dry socks.

Graham et al conducted a retrospective case series involving 98 patients with JPD whose parents were surveyed. Results showed that 75% of parents felt that appropriate footwear changes did not help the disorder; 60% felt that treatment was generally ineffective, with the most effective treatments being white/yellow soft paraffin with salicylic acid, Neutrogena hand cream, and creams utilizing 10% urea.[10] Additionally, patch testing for irritants yielded positive results for two patients.

Mimics

The reviews of Rasner et al, Silverberg et al, Vlahovic et al, and Guenst et al all compared the presentation and history of JPD with atopic dermatitis, irritant contact dermatitis, and tinea pedis. The distribution of JPD, atopic dermatitis, and tinea pedis over the foot varies. JPD was found to originate from the base of the big toe, sparing webbed spaces. The foot rash from JPD is typically not pruritic or painful.[5]

Atopic dermatitis of the foot is similar to JPD as it is typically bilateral and typically painless. It contrasts from JPD as atopic dermatitis is pruritic, and the plantar surface is typically spared. There is an association of JPD with atopy, with about 15% of patients with JPD reporting a personal history of atopy.[3,11]

JPD can be mistaken for irritant contact dermatitis due to similar presentation. Irritant contact dermatitis presents as erythematous, localized, well-defined lesion and chronically with dryness and cracking of the skin in response to a causative agent. It is important to perform patch testing if contact dermatitis is suspected. In Jones et al's study, an uncontrolled 8-year prospective study was conducted via questionnaire to assess the association with JPD and skin irritants. 102 patients with JPD underwent patch testing to materials in their own shoes and socks, with five yielding positive results. Similarly, Ashton and Griffiths conducted a controlled study where 218 patients with JPD were patch tested for contact allergens against controls. They found that 2-9% of patients with JPD tested positive for a relevant irritant.[4] Treatment of plantar irritant contact dermatitis is similar to JPD in that it involves removal of the synthetic fabrics that is causing irritation.

Tinea pedis differs most from JPD compared to atopic dermatitis. The three main types of tinea pedis are intertriginous, moccasin, and vesicular. Intertriginous tinea pedis is characterized by peeling and fissuring of the toe web spaces and can spread to the dorsal foot. Moccasin pattern tinea pedis presents as dry, scaly, patches on the plantar and lateral aspects of the foot. Vesicular tinea pedis presents as vesicles and pustules over the anterior plantar surface.[5] A clinical differentiator between tinea pedis and JPD is the distribution. JPD is localized to the weight bearing plantar surface of the feet such as the ball of the big toe and ball of the foot. It typically is not seen in the interdigital web spaces, lateral foot, and dorsal foot as seen in tinea pedis. Diagnosis of tinea pedis can be confirmed with KOH wet mount and is treated with topical antifungals and foot creams. Tinea pedis is found unilaterally or bilaterally and is typically pruritic and painful.

Atopic dermatitis was found to be in geometrical formations throughout the affected foot and tinea pedis was found to be in the 4th to 5th web space. This puts great emphasis on conducting a thorough dermatologic exam in the interdigital web space to rule in or rule out JPD.[6,12]

There is no associated seasonal variation, though some individuals report worsening symptoms in the summer or winter.[3] A theory for why symptoms persist despite treatment recommendations is that the skin barrier is broken from aggravated friction, and the threshold for precipitation of the problem is lowered. Thus, even if appropriate changes are made, symptoms persist because there is a low threshold for aggravation.[10]

Discussion

The literature showed that the consensus is that JPD is a clinical diagnosis that does not require

additional testing, such as biopsy. However, histopathological testing has proven reliable to rule in JPD if there is any uncertainty about the diagnosis.[3,8] Vlahovic, Rasner et al, and Guenst et al, agreed that the treatment of choice for JPD is improved foot hygiene, frequent changing of socks, and emollients as needed.[1,5-7] Additionally, Rasner et al, and Guenst et al, found steroid creams are useful for pain relief. In contrast, Graham et al concluded that topical steroids were the most irritating treatment. None of the studies suggested that steroid creams showed benefit towards the pathology of JPD. Shipley et al showed in a case study that tacrolimus was a new and promising treatment for JPD, fully resolving the patient's JPD within a month.[9] This vastly differs from the recovery timeline seen in Jones et al's case series of 102 patients with JPD. Jones et al found the average length of disease was 8.4 years. Many of the subjects in that study felt typical treatment was ineffective. This compares to Ashton et al who found JPD duration is closer to 2.5-4.5 years with typical treatment.[4]

JPD is a common but understudied dermatological pathology. The literature is highly limited and original research on JPD was primarily done in the 1960s-1980s. The original research was also highly limited due lack of control and small sample sizes, the highest being Ashton et al having 218 subjects in their controlled case series. Current literature is far and few between. This could be because JPD is a low acuity and non-debilitating disease. The lack of research also creates discrepancies for discussing clinical timelines of JPD. As mentioned above, the literature showed JPD's duration ranging from 2.5-8.4 years depending on the source, a grossly large range.[3,11]

Future directions for research on JPD that are needed are increased epidemiological studies that can provide incidence, prevalence, and length of treatment, as well as updated age ranges of presentation. There is also a need for improved treatments. Shipley et al showed tacrolimus ointment can resolve JPD in 1 month, years faster than the most conservative range from prior studies.[4,9] Shipley et al's studies suggest other calcineurin inhibitors or immunosuppressant ointments could be promising avenues for improved treatment of JPD.

Conclusion

Juvenile plantar dermatosis is a chronic condition that is prevalent in childhood and adolescence. JPD is diagnosed in clinic with minimal testing; a history showing repeated sweating and drying of the feet and an erythematous rash of the weight-bearing plantar aspects of the feet and toes is enough clinical suspicion to rule in JPD. Treatment using emollients are effective initially, but due to the longevity of the disease course, progress becomes slow and ineffective. Due to the chronic, slowly improving nature of this condition, patient education is paramount to manage patient expectations and treatment goals. A recent case study showed presented tacrolimus as a novel and promising treatment option for JPD. Due to the limited research on alternative treatments for JPD, other than emollients, further research into the efficacy of alternative therapies for JPD is needed.

References

1. Vlahovic TC. Dermatologic Concerns of the Lower Extremity in the Pediatric Patient. *Clinics in Podiatric Medicine and Surgery.* 2016;33(3):367-384.
2. Kumar HK, Naveen S, Shankar K. Juvenile plantar dermatosis: A barrier disease beyond eczema: An open prospective uncontrolled study in a tertiary care hospital of South India. *Indian Journal of Paediatric Dermatology.* 2016;17(1):13-17.
3. Ashton RE, Jones RR, Griffiths A. Juvenile plantar dermatosis. A clinicopathologic study. *Arch Dermatol.* 1985;121(2):225-228.
4. Ashton RE, Griffiths WAD. Juvenile Plantar Dermatosis—atopy or footwear? *Clinical and Experimental Dermatology.* 1986;11(6):529-534.
5. Guenst BJ. Common pediatric foot dermatoses. *J Pediatr Health Care.* 1999;13(2):68-71.
6. Rasner CJ, Kullberg SA, Pearson DR, Boull CL. Diagnosis and Management of Plantar Dermatoses. *The Journal of the American Board of Family Medicine.* 2022;35(2):435-442.
7. Browning JC, Brown M. Juvenile Plantar Dermatosis. In: *Harper's Textbook of Pediatric Dermatology.*2019:335-337.
8. Zagne V, Fernandes NC, Cuzzi T. Histopathological Aspects of Juvenile Plantar Dermatosis. *The American Journal of Dermatopathology.* 2014;36(4).
9. Shipley DR, Kennedy CTC. Juvenile plantar dermatosis responding to topical tacrolimus ointment. *Clinical and Experimental Dermatology.* 2006;31(3):453-454.
10. Graham RM, Verbov JL, Vickers CFH. Juvenile plantar dermatosis. *Clinical and Experimental Dermatology.* 1987;12(6):468-469.
11. Jones SK, English JSC, Forsyth A, Mackie RM. Juvenile Plantar Dermatosis—an 8-year follow-up of 102 patients. *Clinical and Experimental Dermatology.* 1987;12(1):5-7.
12. Silverberg NB. Typical and atypical clinical appearance of atopic dermatitis. *Clinics in Dermatology.* 2017;35(4):354-359.

A Review of Palmoplantar Psoriasis Treatments

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Abstract

Objective: Palmoplantar psoriasis is a regional variant of psoriasis that is associated with various comorbidities, significant functional disability, and reduced health-related quality of life. Treatment of this condition proves to be complex, as it typically does not respond successfully to the classic psoriasis regimen. The purpose of this paper is to discuss palmoplantar psoriasis treatments to improve familiarity with various pharmacological agents and reduce patient burden.

Methods: A literature review was performed using the NCBI PubMed database. The search strategy involved the following combination of terms and Boolean operators: (palmoplantar) AND (psoriasis) AND (treatment). Papers that were not accessible through the WesternU library were excluded.

Results: In comparing the various pharmacological treatments, there are major side effects that must be considered. Particularly, the systemic agents prove to have the highest risk-to-benefit ratio. Despite these medications being in use for so long, the emergence of biologics and phototherapy seem to provide better alternatives when topical corticosteroids are not successful.

Conclusion: Superpotent topical corticosteroids and phototherapy agents serve as important first-line treatments in palmoplantar psoriasis. When recalcitrant, biologic agents should be considered next. Systemic agents represent a last-line therapy due to their limited effectiveness and significant adverse effects.

Introduction

Palmoplantar psoriasis is a bilateral, symmetric, and difficult-to-treat variant of psoriasis that characteristically affects the skin of the palms and soles. Psoriasis is defined as a skin disease marked by erythematous scaly patches or plaques that affects an estimated 125 million people worldwide.[1] The palmoplantar variant comprises 3% to 4% of all cases of psoriasis. The morphology of palmoplantar psoriasis can range from hyperkeratotic, pustular, or mixed, with hyperkeratotic being the most common subtype. Symptoms of this condition include itching, pain, scaling, and fissuring.[2] Compared to patients with psoriasis without palm and sole involvement, those with palmoplantar psoriasis have been found to have greater physical disability.[3] The location of the lesions significantly impairs a patient's ability to work as well as walk, resulting in physical, psychosocial, and economic burdens that decrease quality of life.[4] In addition, palmoplantar psoriasis is associated with metabolic comorbidities, including diabetes mellitus, hypertension, obesity, and metabolic syndrome.[5]

Psoriasis may be triggered by infections, mechanical irritation, or drugs in genetically susceptible individuals.[2] The mechanism causing psoriasis is not yet well understood, however, has been associated with keratinocyte proliferation, acanthosis, parakeratosis, and inflammatory cytokines secreted by T-helper cell type 17 (Th17).[1,5] There is no cure for this condition, and most patients will require drug treatment eventually.

The first line treatment for palmoplantar psoriasis follows the conventional psoriasis treatment regimen with topical steroids, typically to no avail. The bulk of topical drug absorption is through the stratum corneum, which is the most superficial layer of the skin. Palmoplantar psoriasis produces hyper keratinization within this layer, resulting in increased thickness. Most patients require treatments other than topical corticosteroids.[6] Other treatment options include phototherapy, systemic medications, or biologic agents. Each of these treatments is characterized by their own risks of adverse effects that may limit their use in clinical practice[7]. Despite the increasing number of medications available, palmoplantar psoriasis remains a difficult dermatologic disorder to treat. Herein, the purpose of this paper is to discuss the mechanisms of action, efficacies, and adverse effects of the pharmacologic agents available to treat palmoplantar psoriasis.

Methods

A review of the current literature regarding palmoplantar psoriasis treatments was performed using the NCBI PubMed database. The search strategy involved the following combination of terms and Boolean operators: (palmoplantar) AND (psoriasis) AND (treatment). Papers that were not accessible through the WesternU library were excluded. 45 articles were selected based on relevance to the topic.

Results

Superpotent Topical Corticosteroids

First-line therapy for palmoplantar psoriasis is highly potent topical corticosteroids. Topical corticosteroids have anti-inflammatory, anti-proliferative, immunosuppressive, and vasoconstrictive effects that are exerted via intracellular corticosteroid receptors.[1] Depending on vasoconstrictive activity, topical corticosteroids are classified into seven categories, with class one being the highest and class seven being the lowest. Areas with thick, chronic plaques such as those in palmoplantar psoriasis often require treatment with class one (highly potent) corticosteroids.[6] As mentioned previously, the thickened stratum corneum present in palmoplantar psoriasis remains a significant barrier to topical medications alone. A retrospective study by Adisen *et al* found that only 27% of patients (n = 62) solely treated with corticosteroids twice a day for greater than, or equal to, twelve weeks had marked improvements.[8] Using highly potent corticosteroids for a prolonged amount of time poses many risks, including skin atrophy, striae, and rebound (disease recurrence that is more severe than initial presentation).[8,9] Use of class one corticosteroids should be limited to no more than twice daily for up to four weeks. If use extends past this time frame, close monitoring of the patient is required to reduce the event of adverse effects.[9] As topical corticosteroid monotherapy typically does not achieve management of symptoms, these are frequently used as adjunctive therapies for patients on systemic agents, phototherapies, or biologics. Since corticosteroids have relatively minor side effects when used for short periods of time, they should still be used as first-line agents for treatment (Figure 1).

Light Therapies

While topical treatments are considered first line therapy for palmoplantar psoriasis, phototherapy has proven to be an effective treatment. The two most frequently used forms of phototherapy include psoralen plus ultraviolet A (PUVA) and narrowband ultraviolet B (nb-UVB). PUVA consists of UV-A radiation (320-400 nm) given with a photosensitizing agent called psoralen. Nb-UVB delivers UV-B radiation (308-311 nm) without a photosensitizing agent. UV-B penetrates at most into papillary dermis, whereas longer wavelengths in UV-A can reach subcutaneous tissue.[10] Research also exists highlighting the usage of UVA-1 (UV-A radiation without a photosensitizing agent) and 308-nm excimer laser (high energy UVB phototherapy focusing on individual lesions) as comparable treatments. There is currently no defined regimen of treatment strength or duration for phototherapy treatment in palmoplantar psoriasis due to varying success and side effects of these three delivery modalities.

One study by Su, et. al. sought to compare nb-UVB to UVA-1 treatment. 64 patients were split into two groups, one for nb-UVB and one for UVA-1, with treatment three times weekly for up to 30 sessions. The Palmoplantar Pustular Psoriasis Area and Severity Index (PPPASI) score was utilized to assess improvement. While both groups showed statistically significant reduction in PPPASI, the UVA-1 group showed a significantly greater mean reduction (6.0 ± 2.4) compared to the nb-UVB group (4.4 ± 1.4) at 30 sessions.[11] In a study by Sezer, et. al., PUVA was compared with nb-UVB, with reductions in the severity index score of 85.45 and 61.03 % with PUVA and nb-UVB, respectively.[12] While UVB therapy appears to yield less clinical improvement than PUVA, a major advantage of UVB therapy is decreased skin penetrance and the lack of chemical adjuvants, reducing cancer risk when compared to PUVA.[13]

In a study by Chen, et. al., 308-nm excimer laser therapy was delivered to 77 patients in 3 groups consisting of low, medium, and high irradiated dosage. Dosage was determined using minimal erythema dose (MED), defined as the minimal dose required to produce erythema on uninvolved skin, with low (2-fold MED), medium (4-fold MED), and high (6-fold MED). 95% of patients in the high dose group reached remission at 12 weeks, 29.17% of patients in the medium dose group, and 8.3% of patients in the low dose group.[14] In a study by Nistico, et. al. of 33 patients, the use of long-wave ultraviolet A (UVA-1) was also shown to achieve complete remission in >75 % patients.[15]

A retrospective study by Richer, et. al. revealed that one of the main variables to treatment is commitment to continued treatments, a requirement for clinical improvement.[16] The evidence suggests that phototherapy is an effective method of treating palmoplantar psoriasis as a first- or second line therapy.[13]

Biologics

The American Academy of Dermatology currently recommends biologics as third or fourth-line therapies for palmoplantar psoriasis due to potential side effects and costs.[56] Palmoplantar psoriasis has been historically excluded from many biologic approval and safety studies. As a result, data is limited on their usage.[13]

Al Muqrin, et. al. reported a case of palmoplantar psoriasis resistant to topical corticosteroid treatment who experienced nearly complete clearing after 6 weeks with two doses of

Risankizumab, one dose given at baseline and the other at week 4. Risankizumab is an interleukin-23 inhibitor (IL-23).[17] In another study by Morales, et. al., 5 patients with severe refractory palmoplantar pustular psoriasis received treatment with Ustekinumab, another IL-23 inhibitor. The patients received an initial 45 mg dose, another 45 mg dose 4 weeks later, and then every 12 weeks thereafter. The patients all experienced complete clearing at week 20.[18] The positive results of IL-23 inhibitors may be attributed to the presence of IL-23 on type 17 helper T (TH17) cells, aiding in survival and proliferation, which have a role in psoriasis pathogenesis.[19] Guselkumab, another IL-23 inhibitor, is currently approved for treatment of palmoplantar psoriasis in Japan with continued success.[20] A 28-week retrospective study by Megna, et. al., compared three IL-23 inhibitors (guselkumab, tildrakizumab, and Risankizumab) who all proved high efficacy with no significant differences in results and little to no adverse effects.[21]

TH17 cells release interleukin-17 (IL-17), a cytokine elevated in palmoplantar psoriasis.[22] Secukinumab is an anti-IL-17 biologic FDA-approved for the treatment of palmoplantar psoriasis.[23] In a study by Galluzzo, et. al., 43 patients were treated with secukinumab successfully with a Psoriasis Area and Severity Index (PASI) reduction of 78.2% at 16 weeks. Half of the patients achieved complete skin clearance at 40 weeks and there were no relevant treatment-related adverse events reported.[24] Ixekizumab, another IL-17 antagonist, has shown efficacy in a local, low-dose hypodermic injection.[25]

While biologics have been shown to treat palmoplantar psoriasis, they have also been indicated as causes of development. A study by Lu, et. al., identified 155 patients who developed palmoplantar psoriasis during biologic treatment. The reported biologics were adalimumab (43.9%), infliximab (33.3%), secukinumab (7.6%), and brodalumab (1.5%). Overall, 58.8% of patients had complete remission in 3.6 months.[25] Adalimumab, the most associated causative biologic, is an anti-tumor necrosis factor (TNF) agent. Anti-TNF agents have been associated with palmoplantar psoriasis induction in inflammatory patients, specifically inflammatory bowel disease (IBD) or existing psoriasis.[26,27] Interestingly, Gkalpaktiotis, et. al. describes a case of a patient with psoriasis vulgaris who developed palmoplantar pustulosis while being treated with adalimumab. The patient was subsequently treated with ixekizumab with near-complete healing by 16 weeks.[28]

Systemic Agents

Systemic agents like methotrexate or cyclosporine are indicated for patients with severe, recalcitrant disease who may have limited access to biologics, prefer noninjectable medications, or do not respond to topical therapy.[6,29] No significant differences in efficacy were found between these two systemic agents.[30] The benefits of treatment versus risk should be highly considered when prescribing either methotrexate or cyclosporine. The emergence of biologics has largely surpassed the efficacy of systemic agents as well as have less side effects, therefore systemic agents should be considered a last-treat agent for treatment (Figure 1).

Systemic Agents: Methotrexate

Methotrexate has commonly been used off-label to treat psoriasis for the past four decades. It acts as a competitive inhibitor of dihydrofolate reductase to reduce the synthesis of nucleic acids and decrease cell proliferation.[31] Rather than decreasing proliferation of keratinocytes, methotrexate decreases proliferation of lymphoid cells to improve psoriasis.[32,33] Methotrexate is usually given orally, however it can also be administered parenterally. Concomitant supplementation with folic acid is recommended to decrease the rate of adverse effects associated with this therapy.[34] As randomized clinical trials were not required for FDA regulatory approval in 1972, the number of high-quality controlled trials of methotrexate is limited.

The Psoriasis Area and Severity Index (PASI) is commonly used to quantify the extent and severity of psoriasis. PASI 75 indicates a 75% or greater reduction in PASI scores from baseline and indicates excellent disease improvement.[35] A meta-analysis of published trials on methotrexate efficacy found that 45.2% of patients (n = 705) achieved PASI75 at 12 or 16 weeks of treatment, compared to 4.4% of patients for placebo.[36] Two large, high-quality controlled trials have compared methotrexate efficacy to those of the biologic agents infliximab and adalimumab, respectively.[37,38] The RESTORE1 trial conducted by Barker *et al* found that 42% of methotrexate-treated patients achieved PASI75 at 12 or 16 weeks of treatment, compared to 78% of infliximab-treated patients. The CHAMPION trial conducted by Saurat *et al* found that 35.5% of methotrexate-treated patients achieved PASI75 at 16 weeks of treatment, compared to 79.6% of adalimumab-treated patients. In sum, methotrexate has been shown to benefit patients with psoriasis, albeit to a lesser extent than biologics.

Methotrexate frequently causes abdominal discomfort, hepatotoxicity, and bone marrow toxicity.[1,36,39] Monitoring of complete blood counts, and liver and kidney function is required to ensure

patient safety. It is highly contraindicated for use in patients who are pregnant, due to possible miscarriage and/or congenital malformation.[40]

Systemic Agents: Cyclosporine

Cyclosporine received FDA approval for psoriasis in 1997. It acts by binding cyclophilin, which inhibits calcineurin and blocks proinflammatory signaling. Overall, cyclosporine results in reduced activation of T-cells. It is typically administered orally; however, it can also be administered parenterally.

A study by Peter *et al* found that 61% of patients with palmoplantar psoriasis treated with cyclosporine (n = 31) achieved PASI50 after 6 weeks of treatment.[41] A different study by Reitamo *et al* found that 89% of patients with palmoplantar psoriasis treated with cyclosporine (n = 19) had significantly reduced formation of new pustules, as compared to 26% of patients with placebo.[42] Interestingly, Ellis *et al* found that cyclosporine improved psoriasis in a dose-dependent fashion. After 8 weeks of fixed-dose therapy, 36, 65, and 80% of patients receiving 3, 5, and 7.5 mg of cyclosporine per kilogram per day, respectively, were rated as being clear or almost clear of psoriasis. Most studies on cyclosporine utilize dosing by weight. Shintani *et al* analyzed whether a fixed dose, 100 mg once daily or 50 mg twice daily, of cyclosporine can be used instead. There was no statistically significant difference in the percentage of patients achieving PASI75 and PASI90.[43] Altogether, cyclosporine has been shown to benefit patients with psoriasis.

The main side effects of cyclosporine include nephrotoxicity and hypertension.[44] A study by Markham *et al* found that patients treated with cyclosporine for an average of 4.5 years were found to have a serum creatinine level >30% above baseline, which did not return to normal after a decrease in dosage.[45] Therefore, monitoring of renal function levels, electrolytes, and blood pressure is required to ensure patient safety. In contrast to methotrexate, cyclosporine may be used in pregnant patients with caution.

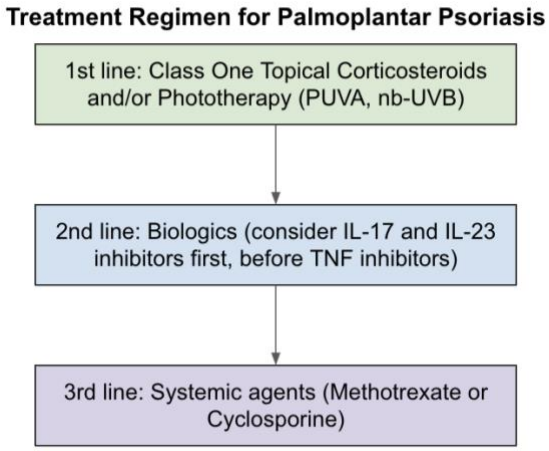

Figure 1: *Proposed treatment regimen for Palmoplantar Psoriasis.*

Discussion

Research shows that while super potent topical corticosteroids are employed as a first-line therapy for palmoplantar psoriasis, following common practice in treating psoriasis, it is not the most effective treatment for most patients. Despite its lowered efficacy, it remains an important early therapy to mitigate systemic side effects that may be elicited by second-, third-, and fourth-line therapies. They also serve as a scaffold for adjunctive therapies for recalcitrant cases. Studies analyzing efficacy of topical corticosteroids also require adjustment based on patient compliance, which can significantly alter the success of treatment and lead to unreliable data.

Phototherapy represents a strong option as a first- or second-line therapy. The two commonly used methods of delivering phototherapy, PUVA and nb-UVB, both prove effective in treating palmoplantar psoriasis as monotherapy and as adjuncts. While PUVA has proven to be more effective than nb-UVB in trials, it also has a higher risk of side effects.[12] The chemical adjuvants like psoralen and the subcutaneous penetration of UV-A increase cancer risk in patients. Consideration should be given to patients at higher risk of developing cancer when choosing between nb-UVB and PUVA. UVA-1 has proven more effective than nb-UVB and holds less cancer risk than PUVA due to the lack of chemical adjuvant need.[11] Finally, 308-nm excimer laser therapy represents a strong novel phototherapy method. Excimer laser allows for less surrounding skin involvement and boasts a very high efficacy rate when delivered in high dose.[14] Standardization of dosage when comparing phototherapies, as well as a lack of long-term side effect data on patients in the studies analyzed pose challenges in ruling a superior treatment. Some studies also mention a range of

wavelengths which makes direct comparison difficult to achieve. Continued research into targeted phototherapy is important for progressing this treatment to maximize the results, especially to reduce length of treatment to increase adherence, an important factor for treatment success.

Biologics are currently recommended as a third- or fourth-line therapy for the treatment of palmoplantar psoriasis due to their potential systemic side effects and high cost. Studies have shown that IL-23 and IL-17 inhibitors are effective in clearing symptoms due to their targeted effects. TH17 are thought to be largely responsible for the pathogenesis of palmoplantar psoriasis due to their elevated levels in effected tissue. Agents such as risankizumab, guselkumab, and tildrakizumab target IL-23, a cytokine which functions to maintain TH17 cells, have proven high efficacy with little adverse effects in trials.[21] Ixekizumab which targets IL-17, a cytokine released by TH17 cells, has also proven significant efficacy, even in low-dose targeted injections, although this was noted in a single case report.[25] Secukinumab is also an IL-17 inhibitor with strong positive results but has been shown to cause palmopolantar psoriasis in some cases.[24,26] TNF inhibitors have shown some efficacy in studies against palmoplantar psoriasis but have also been largely implicated as causative agents and thus should be reserved.[26] It is unclear from these studies how these biologics cause palmoplantar psoriasis. More research is needed to investigate the role of cytokines in palmoplantar psoriasis and the usage of biologic agents.

Systemic agents are indicated for severe, recalcitrant disease due to their significant side effects and limited efficacy. Methotrexate and cyclosporine have proven to be significantly less effective than biologics and appear to have more common adverse effects. However, the CHAMPION trial is limited in how the full effects of methotrexate may not have been achieved, possibly due to the short evaluation period or the titration process. This suggests that larger clinical trials with adjusted dosage for each treatment until efficacy is reached would be ideal to support one treatment over another. The RESTORE1 trial serves as an important direct comparison of infliximab and methotrexate. Despite the large amount of research discussing the side effects of systemic agents, the incidence and type of adverse effects were comparable. More infliximab patients discontinued due to adverse effects. However, a detailed statistical analysis was not performed on these aspects of the study. Further work is needed to provide a definitive picture of side effects and efficacy, via the direct comparison of corticosteroids, systemic agents, biologics, and light therapies. Cyclosporine appears to be more effective than methotrexate and safe to use in pregnancy, though the studies highlighting cyclosporine efficacy utilized smaller sample sizes which may impact the comparison. A larger scale study of cyclosporine efficacy is needed to explore its role in palmoplantar psoriasis treatment.

Conclusion

Superpotent topical corticosteroids and phototherapy agents serve as important first-line treatments in palmoplantar psoriasis. When recalcitrant, biologic agents have proven effective, but lack research, have high costs, and are associated with systemic adverse effects. More specifically, IL-17 and IL-23 inhibitors should be considered as first line agents, and TNF inhibitors should be used in reserve due to their potential for worsening symptoms. Systemic agents represent a last-line therapy due to their limited effectiveness and significant adverse effects.

References

1. Armstrong AW, Read C. Pathophysiology, Clinical Presentation, and Treatment of Psoriasis: A Review. JAMA 2020;323(19):1945-60
2. Miceli A, Schmieder, G. Palmoplantar Psoriasis. Mild to Moderate and Moderate to Severe Psoriasis (Set) 2019:145-56.
3. Chung J, Callis Duffin K, Takeshita J, et al. Palmoplantar psoriasis is associated with greater impairment of health-related quality of life compared with moderate to severe plaque psoriasis. J Am Acad Dermatol 2014;71(4):623-32
4. Callis Duffin K, Mason MA, Gordon K, et al. Characterization of Patients with Psoriasis in Challenging-to-Treat Body Areas in the Corrona Psoriasis Registry. Dermatology 2021;237(1):46-55
5. Lowes MA, Suarez-Farinas M, Krueger JG. Immunology of psoriasis. Annu Rev Immunol 2014;32:227-55
6. Spuls PI HS, Rivera L, Lebwohl M. Retrospective analysis of the treatment of psoriasis of the palms and soles. J Dermatolog Treat. 2003;14
7. Sanchez IM, Sorenson E, Levin E, et al. The Efficacy of Biologic Therapy for the Management of Palmoplantar Psoriasis and Palmoplantar Pustulosis: A Systematic Review. Dermatol Ther (Heidelb) 2017;7(4):425-46
8. Adışen E, Tekin O, Gülekon A, Gürer M. A retrospective analysis of treatment responses of palmoplantar psoriasis in 114 patients. Journal of the European Academy of Dermatology and Venereology 2009;23(7):814-19
9. Elmets CA, Korman NJ, Prater EF, et al. Joint AAD-NPF Guidelines of care for the management and treatment of psoriasis with topical therapy and alternative medicine modalities for psoriasis severity measures. J Am Acad Dermatol 2021;84(2):432-70
10. Orazio J, Jarrett S, Amaro-Ortiz A, et al. UV Radiation and the Skin. International Journal of Molecular Sciences 2013;14(6):12222-48.
11. Su LN, Ren J, Cheng S-m, et al. UVA1 vs. narrowband UVB phototherapy in the treatment of palmoplantar

pustulosis: a pilot randomized controlled study. Lasers in Medical Science 2017;32(8):1819-23
12. Sezer E, Erbil AH, Kurumlu Z, et al. Comparison of the efficacy of local narrowband ultraviolet B (NB-UVB) phototherapy versus psoralen plus ultraviolet A (PUVA) paint for palmoplantar psoriasis. The Journal of Dermatology 2007;34(7):435-40
13. Romani M, Biela G, Farr K, et al. Plantar Psoriasis: A Review of the Literature. Clin Podiatr Med Surg 2021;38(4):541-52
14. Peng C, Hu Y, Chen W, et al. A randomized prospective study of different dose regimens using the 308-nm excimer laser in the treatment of palmoplantar pustulosis. Dermatologic Therapy 2021;34(5):e15079
15. Nisticò SP, Saraceno R, Chiricozzi A, et al. UVA-1 Laser in the Treatment of Palmoplantar Pustular Psoriasis. Photomedicine and Laser Surgery 2013;31(9):434-38
16. Richer V, AlObaida S, Kharazmi P, et al. Old is gold? Retrospective evaluation of efficacy and safety of topical psoralen-ultraviolet A phototherapy for palmoplantar psoriasis and dermatitis. Br J Dermatol 2019;181(2):417-18
17. Al Muqrin AM, Alghamdi AA, AlShaalan ZM. Rapid Response of Palmoplantar Psoriasis to Risankizumab: A Case Report. Clin Cosmet Investig Dermatol 2022;15:2129-32
18. Morales-Múnera C, Vilarrasa E, Puig L. Efficacy of ustekinumab in refractory palmoplantar pustular psoriasis. British Journal of Dermatology 2013;168(4):820-24
19. Lillis JV, Guo CS, Lee JJ, et al. Increased IL-23 expression in palmoplantar psoriasis and hyperkeratotic hand dermatitis. Arch Dermatol 2010;146(8):918-9
20. Fukasawa T, Yoshizaki-Ogawa A, Enomoto A, et al. Involvement of Molecular Mechanisms between T/B Cells and IL-23: From Palmoplantar Pustulosis to Autoimmune Diseases. International Journal of Molecular Sciences 2022;23(15):8261.
21. Megna M, Tommasino N, Potestio L, et al. Real-world practice indirect comparison between guselkumab, risankizumab, and tildrakizumab: results from an Italian 28-week retrospective study. J Dermatolog Treat 2022;33(6):2813-20
22. Murakami M, Hagforsen E, Morhenn V, et al. Patients with palmoplantar pustulosis have increased IL-17 and IL-22 levels both in the lesion and serum. Experimental Dermatology 2011;20(10):845-47
23. Aboobacker S, Kurn H, Al Aboud AM. Secukinumab. StatPearls. Treasure Island (FL): StatPearls Publishing
24. Galluzzo M, Talamonti M, Atzori L, et al. Secukinumab for the treatment of palmoplantar psoriasis: a 2-year, multicenter, real-life observational study. Expert Opinion on Biological Therapy 2022;22(4):547-54
25. He F, Long F, Yin Z, et al. Local injection of low-dose ixekizumab for the treatment of palmoplantar pustular psoriasis. Int J Dermatol 2022;61(6):742-43
26. Lu JD, Lytvyn Y, Mufti A, et al. Biologic therapies associated with development of palmoplantar pustulosis and palmoplantar pustular psoriasis: a systematic review. International Journal of Dermatology;n/a(n/a)
27. Bae JM, Lee HH, Lee B-I, et al. Incidence of psoriasiform diseases secondary to tumour necrosis factor antagonists in patients with inflammatory bowel disease: a nationwide population-based cohort study. Alimentary Pharmacology & Therapeutics 2018;48(2):196-205
28. Gkalpakiotis S, Fridman M, Tivadar S. Adalimumab Biosimilar-Induced Severe Paradoxical Palmoplantar Pustulosis in a Patient with Psoriasis and Psoriatic Arthritis Successfully Treated with Ixekizumab. Dermatol Ther (Heidelb) 2022;12(2):605-09
29. Sarma N. Evidence and Suggested Therapeutic Approach in Psoriasis of Difficult-to-treat Areas: Palmoplantar Psoriasis, Nail Psoriasis, Scalp Psoriasis, and Intertriginous Psoriasis. Indian J Dermatol 2017;62(2):113-22
30. Heydendael VMR, Spuls PI, Opmeer BC, et al. Methotrexate versus Cyclosporine in Moderate-to-Severe Chronic Plaque Psoriasis. New England Journal of Medicine 2003;349(7):658-65
31. Matthews DA, Alden RA, Bolin JT, et al. Dihydrofolate Reductase: X-ray Structure of the Binary Complex with Methotrexate. Science 1977;197(4302):452-55
32. Saporito FC, Menter MA. Methotrexate and psoriasis in the era of new biologic agents. Journal of the American Academy of Dermatology 2004;50(2):301-09
33. Jeffes EW, 3rd, McCullough JL, Pittelkow MR, et al. Methotrexate therapy of psoriasis: differential sensitivity of proliferating lymphoid and epithelial cells to the cytotoxic and growth-inhibitory effects of methotrexate. J Invest Dermatol 1995;104(2):183-8
34. Menter A, Gelfand JM, Connor C, et al. Joint American Academy of Dermatology-National Psoriasis Foundation guidelines of care for the management of psoriasis with systemic nonbiologic therapies. J Am Acad Dermatol 2020;82(6):1445-86
35. Abrouk M, Nakamura M, Zhu TH, et al. The impact of PASI 75 and PASI 90 on quality of life in moderate to severe psoriasis patients. J Dermatolog Treat 2017;28(6):488-91
36. West J, Ogston S, Foerster J. Safety and Efficacy of Methotrexate in Psoriasis: A Meta-Analysis of Published Trials. PLoS One 2016;11(5):e0153740
37. Saurat JH, Stingl G, Dubertret L, et al. Efficacy and safety results from the randomized controlled comparative study of adalimumab vs. methotrexate vs. placebo in patients with psoriasis (CHAMPION). Br J Dermatol 2008;158(3):558-66
38. Barker J, Hoffmann M, Wozel G, et al. Efficacy and safety of infliximab vs. methotrexate in patients with moderate-to-severe plaque psoriasis: results of an open-label, active-controlled, randomized trial (RESTORE1). Br J Dermatol 2011;165(5):1109-17
39. Raposo I, Torres T. Palmoplantar Psoriasis and Palmoplantar Pustulosis: Current Treatment and Future Prospects. Am J Clin Dermatol 2016;17(4):349-58
40. Gotestam Skorpen C, Hoeltzenbein M, Tincani A, et al. The EULAR points to consider for use of antirheumatic drugs before pregnancy, and during pregnancy and lactation. Ann Rheum Dis 2016;75(5):795-810
41. Peter RU, Färber L, Weiβ J, et al. Low-dose cyclosporin A in palmoplantar psoriasis: evaluation of efficacy and safety. Journal of the European Academy of Dermatology and Venereology 1994;3(4):518-24
42. Reitamo S, Erkko P, Remitz A, et al. Cyclosporine in the Treatment of Palmoplantar Pustulosis: A Randomized, Double-blind, Placebo-Controlled Study. Archives of Dermatology 1993;129(10):1273-79
43. Shintani Y, Kaneko N, Furuhashi T, et al. Safety and efficacy of a fixed-dose cyclosporin microemulsion (100 mg) for the treatment of psoriasis. The Journal of Dermatology 2011;38(10):966-72
44. Maza A, Montaudié H, Sbidian E, et al. Oral cyclosporin in psoriasis: a systematic review on treatment modalities, risk of kidney toxicity and evidence for use in non-plaque psoriasis. Journal of the European Academy of Dermatology and Venereology 2011;25(s2):19-27

45. Markham T, Watson A, Rogers S. Adverse effects with long-term cyclosporin for severe psoriasis. Clin Exp Dermatol 2002;27(2):111-4

EXTREMITAS

Population-Based Medicine

Understanding how the Prevalence of Diabetic Foot Ulcers and Cardiac Autonomic Neuropathy Impacts Cardiovascular Mortality

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ABSTRACT

Objective: In a clinical setting, understanding how a diabetic foot ulcer may indicate a precipitating myocardial infarction may aid in improving overall quality of patient care. The purpose of this study is to perform a literature review on how the presence of a diabetic foot ulcer may be an early sign of a potential cardiac event in patients with a history of cardiac dysfunction.

Methods: This literature review utilized articles including case series, randomized clinical trials, systemic reviews, and meta-analyses for the purpose of giving insight on how diabetic foot ulcers can be utilized as indication of cardiac dysfunction. Database search engines such as PubMed, ScienceDirect, and GoogleScholar were used to query. Query terms included "diabetic AND foot AND ulcers", "cardiovascular AND autonomic AND neuropathy", "(diabetic foot infection OR diabetic foot ulcer) AND myocardial AND infarctions", "cardiovascular AND autonomic neuropathy AND ischemia", "cardiovascular AND autonomic neuropathy AND mortality", "(diabetic foot infection OR diabetic foot ulcer) AND myocardial AND infarctions".

Results: Literature has shown that many complications arise as a result of diabetes such as ulceration, but cardiovascular dysfunction and mortality remains a relatively understudied aspect. All studies show a high prevalence of cardiovascular autonomic neuropathy in the diabetic population, especially in those comorbid with a diabetic foot ulcer.

Conclusion: Cardiac Autonomic Neuropathy (CAN) and Diabetic Foot Ulcers (DFUs) commonly co-exist, and the presence of either or both conditions significantly increase the risk of cardiovascular events and mortality. Hence, CAN and DFUs may represent an early predictive tool in preventing cardiovascular mortality in the diabetic patient population. However, currently there is not enough research proposing the mechanism between CAN and DFUs. Further research is warranted to properly understand their synergistic impact on cardiovascular outcomes.

Introduction

A diabetic foot ulcer, according to the International Working Group on the Diabetic Foot, is defined as a break in the skin of the foot that involves as a minimum, the epidermis and part of the dermis, in persons with currently or previously diagnosed diabetes mellitus.[1] Today, diabetic foot ulcers are responsible for more hospital admissions than any other diabetic complications.[2] The annual incidence of diabetic foot ulcers worldwide is between 9.1 million to 26.1 million, and around 15 to 25% of patients with diabetes mellitus will develop a diabetic foot ulcer during their lifetime.[3] Furthermore, the five-year mortality rate for a DFU was 30.5% in comparison to 31.0% for patients with cancer.[3] The high incidence of DFUs and their associated five-year mortality rates warrant a need for early identification for the causality of death in the diabetic patient population to provide early management and prevention of subsequent complications.

Patients with diabetic foot ulcers (DFUs) often present with comorbid neuropathic complications. A commonly overlooked result of diabetic neuropathy is Cardiac Autonomic Neuropathy (CAN), in which American Diabetic Association defined it as impairment of the autonomic nerve fibers that innervate the heart and the surrounding tissues.[4] It is strongly associated with a five-fold increase in risk of cardiovascular mortality, as well as other comorbidities, such as stroke, coronary artery disease, and silent myocardial ischemia (SMI).[5]

There is no widely accepted standard to test for CAN, and thus is currently diagnosed on the presence of abnormal cardiac autonomic reflexes and clinical symptoms.[6] These symptoms can be subclinical and range from resting tachycardia,

exercise intolerance, orthostatic hypotension, intraoperative cardiovascular instability, SMI, to even death.[5] While there is no unified treatment algorithm to treat CAN, it is imperative that early diagnosis to manage cardiovascular risk factors is paramount to improve patient outcomes.

Previous studies have found that a DFU is often a comorbidity with CAN.[7] The prevalence of CAN is high (62.8%) in patients with DFUs compared with 13.5% of those without a DFU.[7] Given the strong interplay between CAN and DFUs, it would be essential to analyze how incidence of cardiac dysfunction and mortality are influenced by CAN by itself and CAN in the presence of a DFU. This literature review will analyze the cardiac outcomes in patients with DFUs, CAN, or both to explore the potential interplay between them, as well as the possibility of using DFUs as an early predictive tool in preventing cardiovascular mortality in the diabetic patient population.

Methods

PubMed, ScienceDirect, and GoogleScholar were used to conduct a search of the literature to study how diabetic foot ulcers may be an indication of cardiac dysfunction. Keywords used included "diabetic AND foot AND ulcers", "cardiovascular AND autonomic AND neuropathy", "(diabetic foot infection OR diabetic foot ulcer) AND myocardial AND infarctions", "cardiovascular AND autonomic neuropathy AND ischemia", "cardiovascular AND autonomic neuropathy AND mortality". The results include case reports, prospective observational cohort studies, randomized clinical trials, systemic reviews, and meta-analyses for the years from 2010 until today. Inclusion criteria included patients with pre-existing diabetes with and without a diabetic foot ulcer, and diabetic peripheral neuropathy that presented with an acute cardiac event during their follow up. Exclusion criteria in this study included patients who had no history of the following listed: diabetes, diabetic peripheral neuropathy, diabetic foot ulcers, and cardiac-related mortality.

Results

Mortality of Cardiac Autonomic Neuropathy

Valensi et al. created a study that recruited 107 patients with no history of myocardial infarction of angina to determine the predictive value of silent myocardial ischemia (SMI) and cardiac autonomic neuropathy (CAN) in asymptomatic diabetic patients.[8] Of those 107 patients, 75 had CAN and SMI function tests performed on them. 2 groups of patients were subsequently created with a diagnosis of either SMI or CAN with 33 and 25 patients per group respectively. The 107 patients were followed for 3 to 7 years to track cardiac outcomes: 11 patients (10.3%) where 2 died, 5 non-fatal MI's, and 4 revascularizations. Univariate and multivariate analyses on patients with an MI, SMI or both were then performed to stratify variables associated with major cardiac events. They showed that when adjusting for SMI, there was a significant association between CAN and major cardiac events with an adjusted odds ratio of 4.30 (95% CI 1.07 - 17.31) (P = 0.04). SMI was found to be significantly independent from CAN as well according to the Kaplan-Meier method (P = 0.02). Similarly, a meta-analysis of 15 studies with 2900 total subjects by Brownrigg et al. found that the presence of CAN increased relative risk of mortality and SMI by 2.14 ($p < 0.0001$).[9]

Pop-Busui et al. analyzed the impact of the presence of CAN on mortality in 8,135 patients with type 2 diabetes at high-risk for CVD events that participated in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial, which is a randomized clinical trial assessing mortality outcomes from patients with CAN at baseline that were initiated on intensive (targeting a A1c level <6%) versus standard glycemia therapy (targeting a A1c level 7-7.9%). To assess CAN, they used 10-s resting electrograms to measure heart rate variability (HRV) and QT index (QTI) for presence of CAN. Patients were then followed up for a mean of 5 years. Analyses were created comparing CAN and non-CAN patients using chi-squared tests and two sample t tests. With the data collected, associations were established between CAN and mortality by performing proportional hazards analysis with a 95% confidence interval, CVD history, and adjustments for treatment group allocations. In a mean follow-up of 3.5 years, 329 deaths were recorded from all causes from the 8,351 patients. They discovered that patients with CAN had 1.55–2.14 times increased risk of mortality than those without CAN ($P < 0.02$).[10]

Study	Mortality Assessment		P value
Valensi et al.	Adjusted odds ratio	4.30	0.04
Brownwigg et al.	Relative risk	2.14	< 0.0001
Pop-Busui et al.	Adjusted hazard ratios	1.55–2.14	< 0.02

Table 1. *Summary of studies included to assess the impact of the presence of CAN on mortality*

Cardiac Autonomic Neuropathy and Diabetic Foot Ulcers

Yun et al. conducted a 13 years follow-up study to assess the risk factors that might influence the development of DFU in T2DM patients without diabetic polyneuropathy (DPN). A total of 449 out of 595 (75.4%) subjects completed a median 13.3 years of follow-up. At the follow-up, 22 (4.9%) patients developed a DFU. They also noted that patients with DFU had diabetes for a longer time period and received insulin treatment more often. Their follow up indicated that 139 men (31.0%) and 69 women (15.3%) had early and definite CAN. Overall the patients with CAN had more abnormalities and comorbidities than in patients without CAN. The patients with high CAN scores were older, had DM for a longer duration, had higher prevalence of diabetic retinopathy and high blood pressure, had higher fasting glucose and baseline HbA1c, and were more often treated with insulin. They found that patients with DFU had increased CAN scores; 5 (22.7%) patients with normal autonomic function, 7 (31.8%) patients with early CAN and 10 (45.5%) patients with definite CAN ($P < 0.001$). After adjusting for possible confounding factors, a Cox hazard regression analysis revealed that the presence of CAN results in a 4.5-fold increased risk of DFUs compared with those who had normal autonomic function.[11]

Another similar but smaller sample size study by Menon et al. reported on the prevalence of CAN in patients with T2DM at high risk for DFUs. The study grouped 74 diabetic patients into categories 1, 2, and 3 based on criteria made by the Foot Care Interest Group and cardiovascular autonomic reflex tests. The patients with one abnormal test were defined as probable CAN and with two abnormal tests as definite CAN. Patients with a postural fall in blood pressure (BP) in the presence of another abnormal test were deemed to have advanced CAN. They found that the prevalence of possible CAN was 31% (23/74), and definite CAN was 66.2% (49/74) (P = 0.06). The occurrence of advanced CAN was seen with 10 patients. Although no statistically significant difference was observed in the presence of probable vs definite CAN in three risk categories for foot ulcers, there were only 2 patients (2/74 = 2.7%) did not have abnormal test.[12]

In a cross-sectional case-control study conducted by Wadhera et al.**,** 246 out of 530 diabetic patients screened were analyzed to determine if age and disease duration affect the prevalence of CAN in patients with foot complications. 246 out of 530 patients with DM that were screened for CAN using CAN assessment (automated CANS-analyser) were included in the study. Subjects were further categorized into 3 groups: +Diabetic foot complications (N=82; Charcot foot n=42 + DFU n=40) was group A; +DPN/-foot complications (n=82) was group B; and -DPN/-foot complications (n=82) was group C. Sub-group analysis showed that CAN was prevalent in 75.6% of the DFU group compared to 57.9% in those without DFU (p < 0.001).[13]

Study	n	% + DFUs	% + DFUs and CAN	P value
Yun et al.	449	22.7	45.5	< 0.001
Menon et al.	74	2.7	66.2	NS*
Wadhera et al.	246	57.9	75.6	< 0.001

**Study only showed p=0.06 between DFU with probable CAN vs definite CAN*

Table 2. *High prevalence of CAN in patients with DFUs*

Mortality of Diabetic Foot Ulcers

A study conducted by Pinto et al. compared the prevalence of main CV events and mortality in 102 DM patients with a DFU and 123 DM patients without a DFU. The prevalence of cardiovascular risk factors, and incidence of newly diagnosed cardiovascular complications on a 5 year follow up were assessed via student t tests for non-paired data to compare means, F-test to compare variances, and the Beherens-Welch test with Satterwaite approximation to provide inferential statistical data. Hazard ratios, univariate cox regression and multivariate regression analyses were then conducted on the prior calculated statistics, to compare risk factors and their attribution to cardiovascular mortality. It was noted that patients with a foot ulcer had a high prevalence of previous CAD, TIA, ischemic stroke, PAD, and diabetic retinopathy compared to diabetic patients without foot ulceration. At the 5-year follow-up, patients with DFU yielded a higher incidence of new-onset CV events, as well as 13.7% deaths compared to 8.1% in non-DFU ($p<0.05$). Its analysis revealed DFU presence as the highest hazard ratio (11.40) as compared to the absence of DFU (8.67) ($p < 0.01$).[14]

In addition, Brownrigg et al. conducted a random-effects meta-analysis on 8 studies to determine to what extent a DFU is associated with CVD and all-cause mortality. Their analyses included data from 17,830 diabetic patients and their outcomes after follow-up. Pooled data from a total of 81,116 person-years of follow-up resulted in 3,619 deaths from any cause. Calculated crude event rates for all-cause deaths the DFU vs. diabetes-only populations were 99.9 vs. 41.6 per 1,000 person-years respectively. Brownrigg et al. also analyzed the crude event rate for fatal MI in the DFU and diabetes-only populations to discover 4.6 vs. 3.8 respectively as well. The relative risk for MI was found to be 2.22 with a 95% confidence interval.[9]

Similarly, a systematic review performed by Jupiter et al. assessed the likelihood of mortality in patients with DFU. In one of the many studies systematically reviewed by Jupiter et al, they found that mortality over a 6 year period was 10.5% among 3632 non-diabetic individuals, 35.2% in 1229 diabetic individuals without a history of ulceration and 49% in 155 diabetic individuals with a history of ulcerations. Overall, patients with no ulceration history had a 12.7% 6-year mortality rate. To further evaluate the impact of DFUs on mortality rates, Jupiter et al. analyzed another study that reported differences in mortality rates before and after an aggressive CVD risk policy was implemented at a Diabetic Foot Clinic in the Royal Infirmary of Edinburgh in 2001. Policy changes forced all patients to be screened for CV risk factors including BP and serum cholesterol. A1C, total cholesterol, and serum creatinine results were taken from the year of ulceration. Patients were then recommended to receive an antiplatelet agent, statin therapy, ACE inhibitors or angiotensin receptor blockers (ARB) for patients with hypertension (HTN) or β-blockers. for patients with CVD or uncontrolled BP despite ACE inhibition. Patients were allocated into 2 cohorts: The first cohort included patients referred before the policy change and the second cohort being the patients referred after the policy change in 2001. Cohort 1 included 404 patients with 52% with ulceration and 70% with type II diabetes. Cohort 2 had 251 patients with 48% with ulceration and 77% with type II diabetes. Data was then collected over a 5 year period recording deaths following acute onset of diabetic-related ulcers. Five year mortality rates were significantly higher in cohort 1 (48%) in comparison to cohort 2 (26.8%).[15]

Study	*Mortality Assessment*	*DM*	*DM + DFUs*	*P value*
Pinto et al.	5-yr mortality rate	8.1 %	13.7 %	< 0.05
Brownwigg et al.	Pooled Relative Risk	1	1.89	0.01
Jupiter et al.	5-yr mortality rate	NS*	40 %*	NS*

* Collective 5 yr mortality was reported to represent the results from all the reviewed studies. Therefore, the p value and 5-yr mortality rate of DM were not stated in the article

Table 3. *Summary of studies reviewed to assess mortality of patients with vs without DFUs*

Discussion

From the studies reviewed, there is a consensus that overall patients with DFU or CAN

have a high prevalence of cardiovascular comorbidities and mortality. DFUs occur in about 25% of patients with diabetes and is a severe complication that can lead to 2-fold increased risk of all-cause mortality.[3,16] Pinto et al. particularly found that patients with DFUs have a worse cardiovascular risk profile than those without DFUs. Correspondingly, DFU populations were reported to have a higher prevalence of major CV risk factors, such as hypercholesterolemia, LDL plasma levels >300 mg/dL, and microalbuminuria/ proteinuria.[14] Those risk factors contribute to the development of atherosclerosis. Other studies suggest that autonomic neuropathy may have downstream physiological effects that further the development of atherosclerosis.[17] Since subclinical atherosclerosis is known to be a risk marker of CV morbidity, it could contribute to a greater association of DFU with CV morbidity and mortality.

CAN in patients with DM has been shown to be associated with two to five-fold increased mortality risk.[5,18] One of the presentations of CAN is silent myocardial ischemia (SMI). Valensi et al. and Pop-Busui et al. observed that patients with DM and CAN have a significantly greater incidence of cardiovascular events, one of which is silent myocardial ischemia (SMI). SMI is consistently found in all CAN patients and can easily go unnoticed because patients do not experience typical anginal symptoms, which further contributes to mortality. The studies suggest that the presence of CAN alone serves as a strong predictor for SMI and subsequent cardiovascular events and mortality.[8,10] Many other studies analyzed have shown the presence of CAN strongly predicts the development of silent myocardial ischemia and its subsequent cardiovascular events and mortality. A proposed mechanism on how CAN can lead to cardiac dysfunction is via the impairment of the vagus nerve, which supplies parasympathetic innervation to the heart.[17] If severe enough, CAN can progress to complete cardiac denervation, which results in a major cardiovascular dysfunction or death.[16]

CAN often coexists with diabetic peripheral neuropathy (DPN) and other risk factors that all contribute to the development of DFUs.[9] While there is not enough evidence to illustrate the exact physiological mechanism on how CAN and DFUs affect one another, their prevalence in the diabetic population is significant. Yun et al. found that greater than two thirds of their studied population with CAN developed DFU independent of other main factors, such as DPN.[11] This indicates that CAN itself may be a risk factor for future DFU development.

As independent risk factors, DFU and CAN are both associated with increased risk of cardiovascular disease and mortality.[8,9,10,14,15] However, there is not enough evidence showing reliable data on patient outcomes in the presence of both DFU and CAN. Farrow et al. attempted to compare these risks and discovered an insignificant increased mortality rate, but the lack of significance may be attributed to a type II error due to a small sample size (N = 47). Therefore, individuals with both DFUs and CAN may still have a greater mortality risk in comparison to patients with only one condition, but this is still disputed due to insufficient data and poor understanding of their mechanisms.

As with all literature review, there are limitations that are related to the available data and may affect the overall determination. In particular, two of the reviewed studies *Valensi et al.* and *Menon et al.* are limited by its small sample sizes which make it difficult to establish a statistically significant association between CAN and DFU. Another notable study is *Pinto et al.*, which of its mortality rate (13.7%) is much lower compared with the other reviewed studies. However, it is not entirely clear of its difference. While many of our reviewed studies adjusted for possible confounding factors, we still cannot fully exclude the potential impact of confounding due to the inherited limitations of study designs. Furthermore, the clinical and methodological heterogeneities in the above reviewed studies make the interpretation difficult. The patients selected for the studies had various demographics and comorbidities which limits the generalizability of the study. The design for the above reviewed studies include case control, prospective cohort study, clinical trials, systemic review, and meta-analysis. Despite each study's drawbacks and strengths, different study designs may not be directly comparable.

Conclusion

The main purpose of this literature review is to analyze the cardiac outcomes in patients with DFUs, CAN, or both conditions to explore the

potential interplay between them. Based on literature results, CAN and DFUs commonly co-exist, and the presence of either or both conditions significantly increase the risk of cardiovascular events and mortality. Hence, CAN and DFUs may represent an early predictive tool in preventing cardiovascular mortality in the diabetic patient population. Much data exists regarding the prevalence of each condition and their downstream effects on the heart. As such, they show great promise in guiding future studies once the correlation between CAN and DFUs become well understood. However, currently there is not enough research proposing the mechanism between CAN and DFUs. Further research is warranted to properly understand their synergistic impact on cardiovascular outcomes.

References

1. Netten JJ, Bus SA, Apelqvist J, et al. Definitions and criteria for diabetic foot disease. *Diabetes/Metabolism Research and Reviews.* 2020;36(S1).
2. Oliver TI, Mutluoglu M. Diabetic Foot Ulcer. PubMed. Published August 19, 2021.
3. Armstrong DG, Boulton AJM, Bus SA. Diabetic Foot Ulcers and Their Recurrence. Ingelfinger JR, ed. *New England Journal of Medicine.* 2017;376(24):2367-2375.
4. Standards of Medical Care in Diabetes—2017 : Summary of Revisions. *Diabetes Care*. 2016;40(Supplement 1):S4-S5.
5. Serhiyenko VA, Serhiyenko AA. Cardiac autonomic neuropathy: Risk factors, diagnosis and treatment. *World Journal of Diabetes*. 2018;9(1):1-24.
6. Agashe S, Petak S. Cardiac Autonomic Neuropathy in Diabetes Mellitus. *Methodist DeBakey cardiovascular journal*. 2018;14(4):251-256.
7. McFadden JP, Corrall RJM, O'Brien IAD. Autonomic and sensory nerve function in diabetic foot ulceration. *Clinical and Experimental Dermatology.* 1991;16(3):193-196.
8. Valensi P, Sachs RN, Harfouche B, et al. Predictive Value of Cardiac Autonomic Neuropathy in Diabetic Patients With or Without Silent Myocardial Ischemia. *Diabetes Care*. 2001;24(2):339-343.
9. Brownrigg JRW, Davey J, Holt PJ, et al. The association of ulceration of the foot with cardiovascular and all-cause mortality in patients with diabetes: a meta-analysis. *Diabetologia*. 2012;55(11):2906-2912.
10. Pop-Busui R, Evans GW, Gerstein HC, et al. Effects of cardiac autonomic dysfunction on mortality risk in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial. *Diabetes Care*. 2010;33(7):1578-1584
11. Yun JS, Cha SA, Lim TS, et al. Cardiovascular Autonomic Dysfunction Predicts Diabetic Foot Ulcers in Patients With Type 2 Diabetes Without Diabetic Polyneuropathy. *Medicine*. 2016;95(12):e3128.
12. Menon A, Dixit A, Garg M, Girish R. Cardiac autonomic neuropathy in patients with Type 2 diabetes mellitus at high risk for foot ulcers. *Indian Journal of Endocrinology and Metabolism*. 2017;21(2):282.
13. Wadhera S, Rastogi A, Dutta P, Gupta A, Bhadada SK. Age and Disease Duration Independent Cardiac Autonomic Neuropathy in Patients with Diabetic Foot Complications: Case-Control Study. *Indian Journal of Endocrinology and Metabolism*. 2022;26(4):362-371.
14. Pinto A, Tuttolomondo A, Di Raimondo D, et al. Cardiovascular risk profile and morbidity in subjects affected by type 2 diabetes mellitus with and without diabetic foot. *Metabolism*. 2008;57(5):676-682.
15. Jupiter DC, Thorud JC, Buckley CJ, Shibuya N. The impact of foot ulceration and amputation on mortality in diabetic patients. I: From ulceration to death, a systematic review. *International Wound Journal.* 2015;13(5):892-903.
16. Rubio JA, Jiménez S, Lázaro-Martínez JL. Mortality in Patients with Diabetic Foot Ulcers: Causes, Risk Factors, and Their Association with Evolution and Severity of Ulcer. *Journal of Clinical Medicine*. 2020;9(9):3009.
17. Basra R, Papanas N, Farrow F, Karalliedde J, Vas P. Diabetic Foot Ulcers and Cardiac Autonomic Neuropathy. *Clinical Therapeutics*. 2021;44(2).
18. Vinik AI, Ziegler D. Diabetic Cardiovascular Autonomic Neuropathy. *Circulation*. 2007;115(3):387-397.
19. Farrow F, Fountoulakis N, Cummins K, et al. Cardiac Autonomic Neuropathy is Associated with Improved Diabetic Foot Ulcer Healing: A Single Centre Prospective Cohort Study. *Experimental and Clinical Endocrinology & Diabetes.* 2020;129(12):895-898.

Correlation Between Poor Glycemic Control in Type 2 Diabetic Patients and Subsequent Diagnosis of Dementia

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ABSTRACT

Objective: Diabetes mellitus (DM) is a metabolic disorder resulting from defects in the insulin secretion or action pathways. A chronic complication of diabetes can be cognitive decline and dementia. As healthcare professionals, it is important to be cognizant of our patients' comorbidities, especially those that affect our patient's mental status and consequently their ability to care for themselves. The objective of this paper is to provide a literature review on the correlation between poor glycemic control in type 2 diabetic patients and the risk of subsequently being diagnosed with dementia.

Methods: Multiple peer-reviewed journal databases were used to collect literature. These databases included ScienceDirect, Google Scholar, and EBSCOHost. Keywords included "glycemic index", "dementia risks", and "uncontrolled diabetes".

Results: Studies were identified based on inclusion and exclusion criteria. The studies examined focused on the relationship between poor glucose control and increased risk of dementia.

Conclusion: The results from this paper present a clear correlation between poor glycemic control and cognitive decline in patients. Cognitive well-being is an integral aspect in the management and prognosis of patient care and, thus, must be well-studied.

Introduction

Diabetes mellitus (DM) is a metabolic disorder resulting from defects in the insulin secretion or action pathways resulting in high blood glucose concentration. The International Diabetes Federation has estimated that over 451 million people worldwide have diabetes with an estimated increase to over 693 million by 2045.[1] With an increase in the number of diabetic patients, there is likely to be an increase in the number of systemic pathological complications. One of the most prevalent complications in patients with diabetes is diabetic foot ulcers (DFU). Thus, patients diagnosed with diabetes are referred to podiatric specialists to assist in their care. Additionally, a growing body of literature has reported that patients with diabetes present with increased risk of developing cognitive impairment and subsequent dementia.[2]

The regulation of insulin throughout the body plays a crucial aspect in the proper maintenance of many physiological processes. Insulin acts in the brain to stimulate the growth of neuronal cells and maintains protection against apoptosis and oxidative stress. With the dysregulation of insulin, the body can present in a hyperglycemic state. Elevated glucose levels lead to the overproduction of advanced glycation end products (AGE) which, in turn, cause oxidative damage and neuronal injury.[3,4] In addition, patients with diabetic mellitus can present with insulin resistance which further contributes to an accumulation of beta-amyloid protein.[3,4] This protein competitively binds to insulin to decompose enzymes and hyperphosphorylated tau proteins. These pathophysiological mechanisms contribute to cognitive decline and dementia.

Literature has suggested that up to one-third of all dementia cases may be attributable to modifiable risk factors.[5] One of those risk factors includes type 2 diabetes (T2DM), which accounts for 3.2% of cases of dementia. Cognitive decline and dementia can have detrimental outcomes on our patients. Thus, it is important to understand the link between poor glycemic control and dementia. The objective of this paper is to provide a literature review on the correlation between poor glycemic control in type 2 diabetic patients and the risk of subsequent diagnosis of dementia.

Methods

Journal articles pertaining to hyperglycemia, dementia, and T2DM were reviewed from peer-reviewed journals. These journals were obtained from the databases of: Google Scholar, ScienceDirect, and EBSCOHost. Keywords included "hyperglycemia", "uncontrolled diabetes", "blood sugar control", and "dementia". The types of studies evaluated included retrospective and prospective cohort studies, case reports, literature reviews, and randomized control trials. In order for a study to be included, it needed to compare the relationship between glucose levels in patients and subsequent cognitive decline in patients.

Results

The prospective, community-based cohort study by Crane et al included 2067 dementia-free members of the Group Health Cooperative in Washington State. All participants were over the age of 65 and follow up occurred at two year intervals in order to identify cases of dementia. The Cognitive Abilities Screening Instrument was used to assess cognitive function and diagnose dementia. A total of 35,264 clinical measurements of glucose and 10,208 measurements of glycated hemoglobin levels were drawn from two groups of patients: one group of patients diagnosed with diabetes and another group of patients not diagnosed with diabetes. The purpose of this study was to effectively assess the correlation between glucose levels and risk of dementia. In the five years leading into the study, the median glucose for non-diabetics was 101 mg per deciliter and the median for the diabetic population was 175 mg per deciliter. Through a median follow-up of 6.8 years, a total of 524 patients had developed dementia. 450 of the 1724 non-diabetic patients (26.1%) developed dementia versus 74 of 343 diabetic patients (21.6%) developed dementia.[7] A smaller portion had dementia which was mostly attributed to vascular disease. The study used stratified Cog regression models with empirical standard errors to examine the relation between glucose level and incidence of dementia. In the non-diabetic group, the adjusted hazard ratio for dementia was 1.18 (95% CI, p=0.01).[7] Among the diabetic population, the adjusted hazard ratio for dementia was 1.40 (95% CI, p=0.002).[7]

Koh et al conducted a cross-sectional survey study with data drawn from 2018 Korea Community Health Survey. The goal of this study was to study the association between blood glucose control and subjective cognitive decline. The study included 18,789 individuals over the age of 50 with diabetes. Furthermore, cognitive decline was measured using the cognitive decline module of the Behavioral Risk Factor Surveillance System. 2,311 (12.3%) of individuals had reported uncontrolled blood glucose levels. 13,580 (72.3%) reported no subjective cognitive decline whereas 5,209 (27.7%) reported subjective cognitive decline.[3] The rate of subjective cognitive decline was higher among patients with uncontrolled blood glucose levels. 34.5% reported cognitive decline in diabetic patients with uncontrolled blood glucose versus 26.8% reported cognitive decline in patients with controlled blood glucose.[3] A multivariable logistic regression analysis was used to analyze the data. Patients with uncontrolled blood glucose levels had a higher risk of subjective cognitive decline with an odds ratio of 1.22 (95% CI).

Christman et. al in a 2011 prospective cohort study looked to see if there was any correlation between diabetic hyperglycemia and change in cognitive decline. This study included 8,958 patients, 516 of which were diabetic and the remaining 8,442 were not.[8] The study analyzed the correlation and association of baseline changes in hemoglobin A1c with a 6 year change in cognition. The cognitive changes were measured via use of the digital symbol substitution test (DSST), the delayed word recall test (DWRT) and the word fluency test (WFT). Adjusted logistic models were then computed based on age, sex, education, lifestyle and metabolic factors. Overall there was a mean HbA1c of 8.5 in the diabetic individuals and 5.5 in the non diabetic individuals (normal A1c being below 5.7).[8] The results showed that there was a correlation between diagnosis of diabetes, determined by elevated hgA1c, and cognitive decline on the DSST (p=0.002) but not the other measurements of cognitive decline (DWRT and WFT).[8] When the results were stratified for all individuals the study suggested that hyperglycemia measured by HbA1c did not add any additional predictive power for cognitive decline. The study further determined that in the diabetic population (HbA1c > 6.5), HbA1c was not independently associated with a risk of dementia.

A prospective cohort study by Amidei et al looked at whether a younger age of diabetic diagnosis

demonstrated a stronger association with incidence of dementia. This was a population based study in the United Kingdom that was established in 1985-88 and continued through with the last followup being the end of March in 2019. The study calculated the hazard ratio (HR) of dementia in participants with and without diabetes. It was found that in patients with dementia that the onset of diabetes was 2.12 years earlier for 10 years [95% CI 1.5, 3.0] and for diabetes onset 6-10 years earlier it was 1.49 years earlier in the diabetic group [95% CI 0.95, 2.32].[3] This trend continued with dementia onset 5 years earlier or less with a 1.11 year onset difference [95% CI 0.70, 1.76].[3] This data was then compiled and a linear trend test with the p value set to less than .001 was run. The linear trend test indicated a graded association between age of onset of type II DM and dementia. Overall the data spanning 35-75 years of age of diabetic onset demonstrated that for every 5 years of earlier onset of DM was significantly associated with a higher hazard of dementia. However, late onset diabetes demonstrated no statistically significant difference in onset of dementia. The study further looked at the association between the FINDISC score (Finnish Diabetic Risk Score) and the correlation between prediabetes or normal fasting glucose and it demonstrated that there was a lack of robust association or statistically significant data.

In 2019, Wium-Andersen et al conducted a prospective cohort study to determine the risk of dementia in patients with T1 or T2 DM and in individuals with HbA1c of ≥ 48 mmol/mol (6.5%). They included 4 different cohorts: (1) a nationwide, register based cohort with all diabetes cases registered in the National Diabetes Register (NDR, 2011) and a matched reference population, (2) the Glostrop cohorts (2011), (3) the ADDITION cohort (2000), and (4) the Copenhagen Aging and Midlife Biobank (CAMB, 2014). The NDR cohort included 127, 369 persons with T2D and 20,664 patients with T1D. The Glostrup cohort included 16,780 patients, the ADDITION study 26,536 patients and finally, the CAMB cohort included 5,408 individuals. In all cohorts, diabetes was defined as having a HbA1c of 48 mmol/mol and in CAMB, diabetes was also defined by self-reported diabetes. The paper's hypotheses were tested using Cox proportional hazard regression models with age as the underlying time scale and multiple regression models to estimate the correlation between HbA1 level and cognitive performance. T2DM was associated with increased risk of all cause dementia (HR 1.22 [95% CI 1.17, 1.6]) . The rates were slightly lower for Alzheimer's dementia (HR 1.06, [95% CI .99, 1.14]) and slightly higher for vascular (HR 1.12, [95% CI 1.00, 1,27]) and other dementias (HR 1.30, [95% CI 1.24, 1.36]). Furthermore, in the Glostrup cohorts, HbA1c of 48 mmol/mol was associated with increased risk of dementia (HR 1.94 [95% CI 1.10, 3.44]). In ADDITION, HbA1c was not correlated with dementia risk. In the CAMB cohort, individuals with DM had lower cognitive performance scores as compared to individuals without DM (p=.004). These hazard ratios and p value were adjusted for multiple variables including but not limited to age, sex, marital status, and education.

Celi-Morales et al conducted a prospective cohort study in 2022 to examine to what extent T2D is associated with dementia subtypes and whether these associations are affected by glycemic control. In this study, 378,299 patients with T2D and1,866,022 age and sex matched control subjects were studies thought the Swedish National Diabetes Register. Patients were registered from January 1, 1998 and followed until (1)December 31, 2012, (2)the ICD diagnosis of dementia or (3)death. The mean age for both groups was 64 years, and 55% were men. The association between T2D and dementia outcomes was evaluated using Cox proportional hazards regression model with attained age as the time scale. Compared with controls, patients with T2D had a 34% higher risk for vascular dementia with a hazard ratio of 1.34 [95% CI 1.28, 1.41] and a 10% higher risk of non-vascular dementia with a hazard ratio of 1.10 [95% CI 1.07, 1.13]. These results were independent of sex, income, education, country of birth and existing CVD. However, the risk of Alzheimer's disease was 6% lower in patients with T2D with a hazard ratio of 0.94 [95% CI 0.9, 0.99]. To evaluate how these associations differ by glycemic control, a Cox proportional hazards regression analysis was conducted by categories of HbA1c concentration. The groups were <53, 53-64, 65-75, 76-86, and 86+ mmol/mol. The study concluded that compared with patients with T2D with better glycemic control, those with HbA1c levels higher than 53 mmol/mol (7%)

have a higher risk of vascular and non-vascular dementia, with risk increasing by about 1.3% and 0.9% per 1 mmol/mol higher HbA1c, respectively.

Discussion

The focus of this literature review was to study the correlation between poor glycemic control in individuals with type II DM and the subsequent diagnosis of dementia. The pathophysiology of hyperglycemia and insulin resistance caused by type II DM provide a foundation for understanding the mechanism by which patients undergo cognitive decline. These potential mechanisms are attributed to hyperglycemia, insulin resistance, advanced glycation end products, and protein aggregation in the brain tissue.[9]

The prospective study by Crane et al used a Bayesian model to obtain a time-varying estimate of glucose levels in order to assess the risk of new onset dementia.[6] The long-term follow up study design allowed the researchers to measure glucose levels at set intervals in order to ascertain the correlation between the variables. In both the diabetic and non-diabetic population, there were statistically significant findings that elevated glucose levels increase risk of dementia. The data suggests that the increasingly abnormal levels of glucose may have deleterious effects in the brain. The survey study conducted by Koh et al provides further evidence to the notion that poorly controlled glucose levels in the diabetic population increases the risk of cognitive decline. It is important to understand the physiological process involved within this correlation to fully grasp the concept. Increasingly abnormal glucose levels have been shown to contribute to microvascular disease of the central nervous system which may be the cause of this correlation.[3] Another school of thought may be that fact that hyperglycemia contributes to insulin resistance, which leads to the accumulation of beta-amyloid.[3] An inference is that both of these pathways are at play in contributing the the correlation at hand. This study was able to account for socioeconomic and demographic factors to provide for a more diverse population pool. The limitation to this study was the subjective nature of its survey process. Given that this was a cross-sectional survey study, a certain level of recall bias may have come into play as well. This subjective study does continue to provide a framework for further objective research studies.

Furthermore, the prospective cohort study by Chirstman et. al utilized HgA1c levels to look at risk of cognitive decline in the Atherosclerosis risk in communities (ARIC) study. This study used adjusted logistic regression models and measured cognitive decline via three different cognition exams (DSST, DWRT, WFT).[7] Overall only one of the exams (the DSST) showed any evidence of elevated HbA1c showing correlation with cognitive decline with insignificant correlation for the other two. The lack of significant association between DM and cognitive decline on either the WFT or DWRT may possibly be due to the short duration of follow-up, which was not as large of a factor in the DSST. The DSST only showed the cognitive domain of executive and processing speed aspects of cognitive decline. It is a timed test of of translation of numbers to symbols using a key and is timed for 90 seconds. This exam did not require follow up to visualize ability to recall after a passed period of time like the DWRT and WFT. The results were also stratified to consider potential covariants. This was achieved by making two models with adjustments. The first model included adjustments for age, race, sex, education, income and center. The second model included adjustments for smoking, drinking, BMI, blood pressure and total cholesterol. The benefit of the use of the two model system helped adjust the data to help focus the data on HgA1c alone and not other potential influences. Some of the other strengths of this study are the large sample size and use of multiple cognitive assessment exams. This specific study may provide a greater level of insight due to the variable being measured. HgA1c is a measure of average blood sugar level of three months whereas merely measuring fasting glucose is a short-term marker. Another benefit of this study is that most of the studies assessing the potential correlation between HbA1c and cognitive function have been limited to just analyzing the correlation between patients with diabetes. In contrast, this study was community based and included persons with and without diabetes. However, there were some limitations to the study. These limitations include lack of data on hypoglycemia, the lack of multiple HgA1c measurements over a period of time for the same patient, proper insulin or drug regimen

adherence information, and examination of other potential influences and risk factors.

The longitudinal study by Amidei et al provides further evidence to the idea that uncontrolled diabetes can contribute to onset of cognitive decline and dementia. This study was unique in that it found a significant association between younger age of diabetes diagnosis with higher hazard ratio of dementia.[5] Although this study had a different specific setup, it factors into the overall objective being reviewed. This study, like the others, was not without its set of limitations. The most prevalent was that this study did not use glycated hemoglobin as a marker to evaluate diabetes. An inference that could be made is that those that are diagnosed with diabetes at a younger age may be more likely to have uncontrolled glucose levels. The study also only looked at the glycemic risk factor that diabetes poses in association with cognitive decline. With diabetes being such a multifactorial disease there are many other non-glycemic risk factors by which diabetes could correlate with cognitive decline. This would consequently contribute to the findings from the prior studies mentioned.

Overall, the population-based cohort studies conducted by Wium-Andersen et al and Celis-Morales et al showed an association between uncontrolled HbA1C levels (6.5% and 7%, respectively) and lower cognitive performance as well as increased dementia risk. Wium-Andersen et al showed that the highest risk (up to a 30% increase) was for dementia diagnosed before age 65. The salient contribution that both author groups contributed to this topic was their aim to distinguish between which dementia subtypes are more influenced by T2D and poor glycemic control. Wium-Andersen et al reported an increased risk in T2D for: all cause dementia, vascular dementia, other cause dementia with the smallest risk for Alzheimer's dementia. Similarly, Celis-Morales et al reported patients with T2D had a higher risk for vascular dementia, non-vascular dementia and a negligible risk for Alzheimer's disease. Wium-Andersen et al proposed that providers may be utilizing a general ICD code for dementia in their reporting, leading to Alzheimer's diagnosis being hidden in the "other dementia" category. This is certainly something to consider.

Interestingly, in the ADDITION cohort (Wium et al), HbA1c was not correlated with dementia. The authors propose that this may be because the study participants were part of an intervention study receiving intensive care including educational classes with doctors and nurses. They received discussions on treatment regimens, lifestyle modifications and more controlled treatment of risk factors including blood pressure and cholesterol levels. While this may have skewed the data, it alludes to the idea that strict metabolic control lowers the risk of dementia in patients with diabetes. However, a gap in the literature remains on this specific evaluation. Celis-Morales et al is the most recent publication thus far that has evaluated HA1c ranges and their relationship with dementia. Their latest evidence supports a dose-response association between HbA1c concentration and dementia risk in patients with T2D. They observed that patients with HbA1c levels higher than 53 mmol/mol (7%) have a higher risk of vascular and non-vascular dementia, with risk increasing by about 1.3% and 0.9% per 1 mmol/mol higher HbA1c, respectively.

Due to its nature as an observational study, the findings by Celis-Morales et al have limitations. It is possible that there are residual confounding factors due to unmeasured variables such as hereditary factors, comorbidities (psychiatric disease), physical activity, alcohol intake and dietary differences. Evidently, additional studies must be conducted to further evaluate an association between HA1c ranges and the subsequent diagnosis of dementia. Nevertheless, the articles discussed above provide a solid framework that highlights the importance of educating our patients on tight glycemic control to decrease their risk of neurological diseases.

A limitation of this literature review was the presence of confounders within the individual studies that were not directly addressed. Some of these confounders include smoking status, exercise, and blood pressure measurements.[7] Given the study design in this literature review, a causal relationship cannot be established. However, correlation and odds ratios were able to be computed.

Conclusion

The results from this paper present a statistically significant correlation between poorly

controlled glucose levels and subsequent diagnosis of dementia. The underlying pathophysiological processes can be used to explain this correlation. As podiatric physicians, many of our patients have underlying glucose abnormalities. Our patients' hyperglycemic state presents with systemic wide complications including neurological impairment. When a patient develops neurological deficits, they are not as capable of caring for themselves and not able to appropriately monitor lower extremity changes. As such, it is important to understand the pathophysiology behind the correlation between poor glycemic control and cognitive imbalance in order to aid their overall treatment. Future studies should continue to investigate what other pathophysiological changes are seen in the presence of uncontrolled glucose control.

References

1. Negash W., Assefa T., Sahiledengle B., et al Prevalence of diabetic foot ulcer and foot self-care practice, and associated factors in adult patients with diabetes in south-east Ethiopia. *Journal of International Medical Research*. 2022; 50(10)
2. Ma F., Wu T., Mia, R., Zhan, W., Huang, G. Conversion of Mild Cognitive Impairment to Dementia Among Subjects with Diabetes: A Population-Based Study of Incidence and Risk Factors with Five Years of Follow-Up. *Journal of Alzheimers Disease.* 2015*;* 43: 1441-1449
3. Koh D-H, Rho Y-J, Lee SY, Kim K-N, Ju YJ. Association between Blood Glucose Control and Subjective Cognitive Decline in Korean Patients with Diabetes Aged over 50 Years. *International Journal of Environmental Research and Public Health*. 2022; 19(12):7267-77.
4. Ledesma, M.D., Boney, P., Colaco, C., Avila, J. Analysis of Microtubule-Associated Protein Tau Glycation in Paired Helical Filaments. *The Journal of B*iological Chemistry. 1994; 269(26): 21614-21619
5. Livingston, G., Huntly, J., Sommerland A., Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. *The Lancet Commisions. 2020;* 396: 413-446.
6. Amidei, C.B., et al Association Between Age of Diabetes Onset and Subsequent Risk of Dementia. *Journal of the American Medical Association*. 2021; 325(16): 1640-1659.
7. Crane, P.K., Walker, R., Hubbard, R.A., et al Glucose levels and risk of dementia. *New England Journal of Medicine.* 2013; 369: 540-548
8. Christman, AL, Matsushita, K., Gottesman, RF, et al Glycated haemoglobin and cognitive decline: the Atherosclerosis Risk in Communities (ARIC) study. *Diabetologia*. 2011; 54(7):1645–52.
9. Wium-Andersen, I.K., Rugby, K., Jorgensen, M.B., et al Risk of dementia and cognitive dysfunction in individuals with diabetes or elevated blood glucose. *Epidemiology and Psychiatric Sciences. 2019;* 29(43): 109.
10. Celis-Morales, C.S., et al Type 2 Diabetes, Glycemic Control, and Their Association with Dementia and its Major Subtypes: Findings from the Swedish National Diabetes Register. *Diabetes Care. 2022;* 45: 634-641

Anxiety and Depression in Individuals with Diabetic Foot Ulcers

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ABSTRACT

Objective: To investigate how diabetic foot ulcers are associated with anxiety and depression in patients.

Methods: A PubMed and Google Scholar search was conducted on studies simultaneously investigating both anxiety and depression in patients with diabetic foot ulcers. Key search terms include: "diabetes", "diabetic foot ulcers", "psychological impact, diabetic foot ulcers", "anxiety and depression, diabetic foot ulcers" and "mental health, diabetic foot ulcers."

Results: Patients with diabetic foot ulcers face a multitude of issues that can exacerbate depression and anxiety, such as older age, duration of ulcer, increased risks of recurrence, physical impairment, and diminished quality of life.

Conclusion: While different psychosocial factors have varying degrees of association to mental health in patients with diabetic foot ulcers, there is a high prevalence of anxiety and depression in the populations studied.

Introduction

Diabetes mellitus is one of the most common chronic diseases worldwide, with the prevalence estimated to reach as high as 592 million by the year 2035.[1] The disease process disrupts the normal functions of multiple organ systems, which cumulates into one of its most serious complications: diabetic foot ulcers (DFU). Only two thirds of ulcers will heal within a median time of six months and the recurrence of foot ulcers within twelve months is seen in 60% of patients.[2] If an ulcer were to deteriorate into a gangrene or a severe infection, patients are at a high risk for amputation. Mortality following an amputation is statistically grim, ranging from 39 to 80% at five years. Once amputated, 30-50% of these patients will undergo an amputation on the contralateral leg in three years' time.[2] These statistics and the escalating prevalence of diabetes therefore make DFU a considerable threat to public health.

Along with the physical symptoms of DFU, these chronic disturbances interrupt patients' sleep, debilitate their mobility, and interfere with emotional wellness, ranging from feelings of alienation and inadequacy to anxiety and depression.[3] In particular, general anxiety disorder includes symptoms of restlessness, excessive worry, sleep disturbances, and concentration difficulties. Depression is characterized by anhedonia, changes in appetite, psychomotor slowing, lack of energy, trouble concentrating, feeling of worthlessness, and thoughts of suicide.[4]

Previous studies have demonstrated that although psychosocial symptoms occur in response to foot ulceration, the presence of anxiety and depression itself is found to be associated with delays in healing.[4,5] Furthermore, it has been found that diabetic patients are almost twice as likely to suffer from anxiety and depression than the general public.[6] There is also a twofold increased risk of developing diabetic foot ulcers in patients diagnosed with depression compared to those who were not.[7] Moreover, patients are at a threefold increased risk of mortality within 18 months of their first presenting foot ulcer.[8] Despite their relevance to diabetes as a chronic disease, anxiety and depression are recognized and appropriately treated in fewer than 25% of diabetic patients.[9] Therefore, this paper aims to examine the association between patients with DFU and anxiety and depression.

Methods

A PubMed and Google Scholar search was conducted with the keywords "diabetes" "diabetic foot ulcers" "psychological impact, diabetic foot ulcers" "anxiety and depression, diabetic foot ulcers" and "mental health, diabetic foot ulcers". Included studies identified patients with DFU and quantified their levels of anxiety and depression. The exclusion criteria restricted non-English-language publications, articles individually investigating anxiety or depression in patients with DFU, and studies that were published before 2010.

Results

In 2018, Ahmad et al. published a cross-sectional study to determine the prevalence rates of anxiety and depression and to explore the associated risk factors seen in diabetic foot patients.[4] This study was conducted over seven months on all adult patients with diabetic foot ulcers attending the Diabetic Foot Clinic in the National Center for Diabetes, Endocrine, and Genetics in Amman, Jordan. With the exclusion of pregnant, lactating, intellectually disabled patients, there were 260 patients included in the study.[4] Self-administered questionnaires were composed of three sections. The first part collected sociodemographic data, including age, gender, education level, family monthly income, marital status, and smoking status. The second part quantified the level of anxiety using a version of the Generalized Anxiety Disorder Scale (GAD-7); seven items were included, each of which was scored from zero to three. Cutoff scores of five, ten, and fifteen represented mild, moderate, and severe anxiety respectively.[4] The third part of the study included a Patient Health Questionnaire, which was used to evaluate depression using the Diagnostic and Statistical Manual of Mental Disorder, Fourth Edition (DSM- IV). It similarly scored each of the nine DSM-IV criteria for depression from zero to three points, with scores of five, ten, fifteen, and twenty representing mild, moderate, moderately severe, and severe depression respectively.[4] Major depression would be diagnosed if five out of nine symptom criteria had been present for the past two weeks. Minor depression would be diagnosed if two to four depressive symptoms had been present for the past two weeks. Finally, medical charts were used to gather data on patients' comorbidities, HbA1c level, weight, and height. [4]

First addressing the prevalence of depression, it was found that 39.6% of patients reported depressive episodes. The data analysis concluded that women, patients with longer than seven months of foot ulcer duration, and patients with three chronic concurrent diseases had statistically higher rates of depression than other groups (p=0.01, 0.00, 0.00 respectively).[4] As stated prior, depression was found to be 2.45 times more common compared to men (p=0.01). Current smokers were found to be 2.51 times more common compared to nonsmokers (p=0.01). Patients with foot ulcer durations surpassing seven months were 12.62 times more likely to have depressive episodes than those who have had foot ulcer durations for fewer than seven months (p=0.00).[4] Patients with greater than three comorbidities were found to be 3.25 times more depressed than those with less than three comorbidities.[4]

Regarding the prevalence of anxiety, 37.7% of patients reported suffering from anxiety.[4] Further analysis reported that patients with an ulcer over seven months in duration, diabetes for >10 years, and HbA1c of over 7%, as well as three chronic diseases were significantly and statistically more anxious than patients without (p=0.01, 0.02, 0.00, 0.00 respectively).[4] More specifically, the risk of anxiety in patients with longstanding diabetes (>10 years) is 2.69 times compared to patients who have had diabetes for <10 years. In addition, patients with three or more chronic diseases are 4.82 times more likely to have anxiety when compared to other patients who have less than three chronic diseases. Patients with HbA1c levels of >7% were found to be 2.51 times more likely to have anxiety than patients with a HbA1c <7%.[4]

In 2020, Polikandrioti et al. published a cross-sectional study to explore the impact of anxiety and depression in DFU patients.[10] In this study, 180 DFU patients were chosen to be part of the study, taking place at an outpatient clinic in Attica, Greece for eight months. Criteria for inclusion included: adults with type 2 diabetes mellitus who attended follow-up visits during the study period and ability to read and write Greek fluently.[10] Exclusion criteria for this study were: history of mental illness, traumatic ulcer, or patients that were severely ill and unable to communicate during the study period. Each interview was conducted for all patients as they waited for clinic follow-ups and lasted about 15 minutes.[10] The patients completed a Self-rating Depression/Anxiety Scale-Zung (SDS/SAS) survey.[10] Results of this survey demonstrated that the patients had moderate levels of anxiety and depression, in addition to high levels of perceived social support from their significant others or families and friends.[10] Specifically, patients with increased social support had 1.52 fewer points in the level of depression. Additionally, a one-point increase in patients' anxiety score correlated to a 0.71 increase in their depression score.[10]

The categories of participants who reported a statistically significant association with depression were older (p=.001), single/divorced (p=.019), had comorbidity, and smoked. In addition, patients who

were living alone reported more feelings of depression, experienced social isolation, and faced more issues with self-care.[10] The study also found that the more anxious a patient was, the more depressed they felt as well (p = .001). Finally, DFU patients are more likely to have depression and anxiety when compared to diabetic patients free of foot complications.[10]

The 2016 paper by Pedras et al. examined the relationship between anxiety, depression, and functionality and their impact on the quality of life in patients with DFU.[11] This cross-sectional study was conducted over two years in six hospitals in Portugal and enrolled 202 adult participants with type II diabetes mellitus and DFU who required a lower limb amputation.[11] Those with dementia or a psychiatric disorder were excluded. The patients' sociomedical information was collected using four main instruments. The first questionnaire gathered sociodemographic and clinical data; the second scale assessed psychological morbidity on a Portuguese-adapted version of the Hospital Anxiety and Depression Scale (HADS); the third quantified the functional level for activities of daily living using the Barthel Index; the fourth instrument evaluated the quality of life by the physical component score (PCS) and the mental component score (MCS) using Short-Form Health Survey 36.[11]

Focusing on the psychosocial findings of this paper, it was found that the proportion of participants with clinical symptoms of anxiety and depression symptoms was 59.9% and 37.6% respectively. Regarding the functionality level, only 18.3% showed independence while 62.4% reported a mild level of dependency, 14.9% severe dependency, and 4.5% total dependency.[11]

Regarding MCS, there were significant positive correlations with type of foot ($r = .168$) and functionality ($r = .498$). However, there were significant negative associations between MCS and gender ($r = -.294$), age ($r = -.191$), number of hospitalizations over the past year ($r = -.194$), presence of pain ($r = -.224$), depression ($r = -.720$), and anxiety symptoms ($r = -.498$)[11]. Furthermore, the regression analysis depicted that while functionality positively predicted MCS, anxiety and depression were negative predictors.[11]

Regarding PCS, there were also significant positive correlations with type of foot ($r = .255$) and functionality ($r = .606$), as well as significant negative associations with gender ($r = -.254$), age ($r = -.307$), number of hospitalizations in the last year ($r = -.273$), presence of pain ($r = -.469$), ulcer duration ($r = -.151$), depression ($r = -.502$), and anxiety symptoms ($r = -.267$).[11]

The following table summarizes the significant correlations of demographic and clinical variables to MCS and PCS respectively:

	MCS	PCS
Type of foot	0.168	0.255
Functionality	0.498	0.606
Gender	-0.294	-0.254
Age	-0.191	-0.307
Number of past year hospitalizations	-0.194	-0.273
Pain	-0.224	-0.469
Ulcer duration	—	-0.151
Depression	-0.720	-0.502
Anxiety	-0.498	-0.267

Contrary to PCS, none of the demographic and clinical variables were significant predictors of MCS. However, lower anxiety and depression and high functionality significantly predicted MCS.[11]

Discussion

Ahmad et al., Polikandroti et al., and Pedras et al. were all cross-sectional studies that explored depression and anxiety in patients with diabetic foot infections.[4,10,11] In the three studies, it was mentioned that DFU patients collectively face a multitude of issues that have the ability to exacerbate depression and anxiety, such as increased risks of recurrence, diminished quality of life, uncertainty, physical impairment, and fears of mortality.[12] In Ahmad et al. and Polikandroti et al., it was found that patients with depression were more likely to have up to three comorbidities and be current smokers.[4,10] Ahmad et al. found more cases of depression in patients that were <50 years of age, while Polikandroti et al. found depression to be more prevalent in the age group of <60 years.[4,10] Meanwhile, Pedras et al. found age to be

negatively associated with MCS but did not stratify the age groups or assess smoking status in association with anxiety or depression.[11] This suggests that despite a higher prevalence of depression in patients younger than 60 years old, older age is associated with lower quality of life in the mental component assessment. It is difficult to assess the correlation between age and depression based on these three studies alone, but this surprising finding warrants further investigation into whether depression in patients with diabetic foot ulcers is necessarily linked to perceived lower quality of life.

In Polikandroti et al., it was found that single or divorced patients were more depressed, while Ahmad et al. found that marital status was not significantly associated with an increase risk of depression; instead, it found that other variables such as age, gender, smoking status, foot ulceration duration, and comorbidity were positively associated with depression.[4, 10] Polikandroti et al. found other variables had more impact on depression, including age, education, and job status.[10] These factors might be closely attributed to the social isolation, lack of emotional support, and challenges with self-care.

Meanwhile, Pedras et al. noted a significant correlation in symptoms of depression and anxiety to both MCS and PCS - the two components of Health-Related Quality of Life (HRQoL).[11] The two symptoms also predicted MCS, according to a regression analysis. Additionally for both MCS and PCS, researchers found positive relationships to type of foot and functionality, but negative relationships to gender, age, number of hospitalizations in the last year, and presence of pain.[11] PCS was also found to be negatively associated with ulcer duration.[11]

The interplay between sociodemographic, clinical, and psychological variables complicates the pathology of DFU. While the three papers highlight different factors' varying degrees of association to mental health in patients with DFU, there is a commonality in the high prevalence of anxiety and depression in the populations studied. This is a concerning finding, given that clinically depressed DFU patients actually require more structured surveillance, as these patients are most at risk for delaying treatment care or failing to comply with wound care appointments. Therefore, non-adherence to treatment should be noted as a marker of depression, which may easily go undiagnosed,[12] and not as patients lacking accountability. With the added concern for anxiety and depression symptoms adversely affecting the HRQoL, it could become a vicious cycle of despair and dysfunction in the patients' everyday lives, emphasizing the need for early identifications of and interventions in highest risk patients.[11]

Regarding the types of surveys and instruments used, Ahmad et al. collected data from self-administered questionnaires as well as patient medical charts for comorbidities.[4] The questionnaire had three parts: sociodemographic data, anxiety disorder using the GAD-7, and depression survey based on the DSM-IV criteria for assessing depression in primary care. Between the three studies, Admad et al. performed a more clinical evaluation of mental health with the use of psychological manuals that defined anxiety and depression.[4] In contrast, both Polikandroti et al. and Pedras et al. combined the psychological assessment of anxiety and depression into one scale.[10, 11] In doing so, the authors effectively categorized the two mental health conditions under one umbrella term of "mood disorder," leading to an imprecise distinction between two very different disorders. This problem becomes even more prominent when considering the following combined score cut-offs and their respective categories.

Polikandroti et al. used a "Self-rating Anxiety/Depression Scale (SAS/SDS)- Zung" scale, which consisted of 20 questions for anxiety and 20 questions regarding depression.[10] Scores were added up as each question was given four points, with a >11 points indicating severe levels of anxiety/depression.[10] Similarly, Pedras et al. used the Portuguese-adapted version of "Hospital Anxiety and Depression Scale (HADS)," which consisted of seven items each for anxiety and depression.[11] With each item scored from zero to three, the score for each scale ranged from zero to 21, with higher scores indicating higher levels of anxiety and depression. In the Portuguese validation, the cutoff is 11 points for the presence of clinical depressive and anxiety symptoms or a mood disorder.[11] In Polikandroti et al., the questionnaires were given weekly, allowing for more accurate tracking of week to week progress, while Admad et al. and Pedras et al. conducted one larger survey that took place at one time period.[4, 10, 11]

The former methodology provides a longitudinal insight into the patients' anxiety/depression symptoms

over time, while the latter two's cross sectional data does not highlight such a development as clearly.

There were several limitations in our study. Firstly, the studies included in this literature review were conducted in three different locations: Jordan, Greece, and Portugal. Thus, the results may not be applicable to the DFU patient population in the United States. Secondly, the studies included in this literature review are all cross-sectional and not longitudinal, which limit the ability to investigate definitive causal relationships between anxiety, depression, and patients with DFU. Third, all three studies used self-reported surveys to describe symptoms of anxiety and depression, which are therefore not assessed clinically by a professional. Finally, studies before 2010 and those that examined anxiety and depression individually were not considered for this review, which limited older and broader mental health data from being assessed. While there was not as much literature on anxiety, there was a number of articles on depression in DFU patients published post-2010, which would have provided a more in-depth investigation on this topic.

Conclusion

Physicians, by virtue of medical training, are knowledgeable on the management of diabetes and its associated complications. However, not enough attention is paid to the mental health burden that accompanies the development of a diabetic foot ulcer. Between the three papers in this review, there was a high prevalence of anxiety and depression in patients with DFU. It was also found that certain factors could exacerbate these psychological symptoms, such as older age, duration of ulcer, increased risks of recurrence, physical impairment, and diminished quality of life, among others.

Overall, depression and anxiety may be correlated with low motivation, cognitive impairment, and reduced energy which ultimately impact the ability of individuals to care for themselves.[13, 14] Beyond treating the DFU, there should be a greater focus on accompanying psychological support to reduce the odds of such symptoms from occurring in the first place. Having a deeper understanding of the association between DFU patients and anxiety and depression would thus allow for better planning of interventional strategies that desperately need to be addressed for these chronic patients.

References

1. Guariguata L, Whiting DR, Hambleton I, Beagley J, Linnenkamp U, Shaw JE. Global estimates of diabetes prevalence for 2013 and projections for 2035. *Diabetes Res Clin Pract*. 2014;103(2):137-149.
2. Pearson S, Nash T, Ireland V. Depression symptoms in people with diabetes attending outpatient podiatry clinics for the treatment of foot ulcers. *J Foot Ankle Res*. 2014;7(1):47. Published 2014 Nov 25.
3. Herber OR, Schnepp W, Rieger MA. A systematic review on the impact of leg ulceration on patients' quality of life. *Health Qual Life Outcomes*. 2007;5:44. Published 2007 Jul 25.
4. Ahmad A, Abujbara M, Jaddou H, Younes NA, Ajlouni K. Anxiety and Depression Among Adult Patients With Diabetic Foot: Prevalence and Associated Factors. *J Clin Med Res*. 2018;10(5):411-418.
5. Monami M, Longo R, Desideri CM, Masotti G, Marchionni N, Mannucci E. The diabetic person beyond a foot ulcer: healing, recurrence, and depressive symptoms. *J Am Podiatr Med Assoc*. 2008;98(2):130-136.
6. Roy T, Lloyd CE. Epidemiology of depression and diabetes: a systematic review. *J Affect Disord*. 2012;142 Suppl:S8-S21.
7. Williams LH, Rutter CM, Katon WJ, et al. Depression and incident diabetic foot ulcers: a prospective cohort study. *Am J Med*. 2010;123(8):748-754.e3.
8. Ismail K, Winkley K, Stahl D, Chalder T, Edmonds M. A cohort study of people with diabetes and their first foot ulcer: the role of depression on mortality. *Diabetes Care*. 2007;30(6):1473-1479.
9. Rubin RR, Ciechanowski P, Egede LE, Lin EH, Lustman PJ. Recognizing and treating depression in patients with diabetes. *Curr Diab Rep*. 2004;4(2):119-125.
10. Polikandrioti M, Vasilopoulos G, Koutelekos I, et al. Depression in diabetic foot ulcer: Associated factors and the impact of perceived social support and anxiety on depression. *Int Wound J*. 2020;17(4):900-909.
11. Pedras S, Carvalho R, Pereira MG. Predictors of quality of life in patients with diabetic foot ulcer: The role of anxiety, depression, and functionality. *J Health Psychol*. 2018;23(11):1488-1498.
12. Coffey L, Mahon C, Gallagher P. Perceptions and experiences of diabetic foot ulceration and foot care in people with diabetes: A qualitative meta-synthesis. *Int Wound J*. 2019;16(1):183-210.
13. Grenard JL, Munjas BA, Adams JL, et al. Depression and medication adherence in the treatment of chronic diseases in the United States: a meta-analysis. *J Gen Intern Med*. 2011;26(10):1175-1182.
14. Salomé GM, Blanes L, Ferreira LM. Assessment of depressive symptoms in people with diabetes mellitus and foot ulcers. *Rev Col Bras Cir*. 2011;38(5):327-333.

The Importance of Cognitive Functioning on Geriatric Mobility

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ABSTRACT

Objective: The goal of this study is to determine whether cognitive functioning should be considered when assessing the risk of falling in geriatric populations.

Methods: A Google Scholar and Pubmed search was conducted on empirical studies investigating the relationship between geriatric mobility and cognitive functioning.

Results: Research demonstrated that there is a significant link between cognitive functioning and geriatric mobility.

Conclusion: While structural deformities should remain at the forefront of podiatric assessments with geriatrics, cognitive functioning should be taken into greater consideration. Taking this greater systems approach would shed light on better diagnostic etiologies, more effective treatment plans, and even the probability of predicting future impairments.

Introduction

America's large population of geriatrics (≥65 years) will nearly double in the next three decades, from 48 million to 88 million by 2050.[1] This highlights the importance of developing more comprehensive care for preserving geriatric health. Mobility is one of the core concerns of geriatric health. It refers to the ability to move one's body freely and efficiently, and it encompasses a variety of factors (e.g., muscle strength, range of motion, and endurance capacity). Having intact mobility is essential for maintaining social roles, independence, quality of life, and most importantly, safety.

It is common for mobility to decline with age. Mobility used to be thought of as an automatic process, but recent research demonstrates that it is a complex function that includes multiple cognitive processes.[2] For instance, walking requires intact attention and executive function (i.e., higher-level processes that enable us to plan, organize thoughts, initiate and maintain complex tasks, adapt to changing contingencies, shift attention from one stimulus to another etc.).[2] Mobility impairments have been associated with normal age-related cognitive decline which generally refers to typical mild decline in thinking abilities (i.e., the brain's ability to maintain attention, process information, understand and express language, learn and remember information, conduct complex tasks, etc.) that normally occur during aging.[3] It is normal for healthy geriatrics to experience impairments relative to their cognitive abilities as younger adults. The effect that cognitive decline may have on mobility-related injuries (e.g., injuries from falls) is important to consider for healthy geriatric populations.

There is a subpopulation of geriatrics whose cognitive decline may make them even more susceptible to mobility-related injuries. A greater risk for mobility-related injuries has been associated with the presence of age-related diseases (i.e., illnesses and conditions that occur more frequently in individuals as they get older) that affect cognitive functioning.[4] Some of the most common age-related diseases that affect cognitive functions necessary for mobility include mild cognitive impairment and dementia. Mild cognitive impairment (MCI) is a neurocognitive disorder associated with impairments to cognition that is not significant enough to interfere with activities of daily living (ADLs). In some circumstances, it may occur as a transitional stage between normal aging and dementia. Dementia is not a specific disease, but rather a general term for impaired ability to remember, think, or make decisions that interfere with ADLs. Alzheimer's disease is the most common type of dementia. Though dementia mostly affects older adults and geriatrics, it is not a part of normal aging.[4]

The current field of podiatry is primarily concerned with physical markers to assess geriatric health. The causes of faulty mobility are often attributed to physical deformities or structural weaknesses. This often leads to clinicians overlooking the integral part that cognitive functioning plays in mobility. For geriatrics who have age-related cognitive decline or more severe impairments such as MCI or dementia, their performance on tests of cognitive functioning (particularly for attention and executive functioning) may give physicians better insight into patients' mobile abilities. It may also lead physicians to have better discernment of impairment, leading to more effective treatment plans, safety procedures, and overall better health outcomes for geriatric patients. The purpose of this article is to evaluate whether cognitive function should be taken into greater consideration when providing podiatric exams for geriatric patients.

Methods

A Google Scholar and Pubmed search was conducted with the keywords "mobility", "gait", "velocity", "cognitive function", "older adults", "geriatrics", "cognitive impairment" for papers published within the last few decades. A literature review was conducted to determine the link between mobility and cognitive functioning. Exclusion criteria restricted non-English publications. Inclusion criteria consisted of elderly greater than or equal to 60 years old.

Results

Mobility and Cognitive Functioning in Healthy Geriatrics

A study by Gleason et al examined how normal age-related cognitive decline may be associated with decreased mobility and an increased risk of falls.[5] Researchers conducted a randomized controlled trial with 175 healthy geriatrics with an average age of 80.4 years (*SD* = 7.7) who lived independently and had normal age-related decline. Baseline data (e.g., demographic information, ADLs, history of impaired vision or use of an ambulation assistive device, comorbid conditions, medications, exercise, etc.) was gathered. Pre- and post-assessments of cognitive functioning were measured using the Mini Mental State Exam (MMSE) and mobility impairments were measured by calculating fall rates over one year. The rate of falls was defined as a person coming to rest inadvertently on the ground or other lower level. Exclusion included falls that resulted from a sustained violent blow or epileptic seizure. Results were analyzed using a univariate analysis and demonstrated that the rate of falls increased with each unit decreased in MMSE score down to at least 22 (rate ratio [*RR*]: 1.25, *95% CI:* 1.09–1.45, $p<0.01$).[5] Using stepwise multivariate regression, the association between MMSE score and falls rate were still statistically significant after controlling for other factors, such as the ability to perform activities of daily living, use of an assistive device, current exercise, and arthritis, (*RR*: 1.20, *95% C*I 1.03–1.40, $p<0.05$).[5] Lower scores on the MMSE were associated with an increased rate of falls.

Mobility and Mild Cognitive Impairment

A study by Delbaere et al investigated how MCI may be associated with decreased mobility and increased risk of falls.[6] Researchers conducted a prospective cohort study with 419 geriatrics with an average age of 77.8 years (*SD* = 4.6). A comprehensive neuropsychological test battery based on 11 test measures across four cognitive domains (i.e., attention/processing speed, memory, language, and executive functioning) were administered to examine cognitive functioning. The Physiological Profile Assessment was used to assess five domains of physiologic functioning (i.e., visual contrast sensitivity, proprioception, quadriceps strength, simple reaction time, and postural sway). 342 participants were classified as having normal age-related cognitive impairment and 77 were classified as having MCI. After a one-year follow-up, people who had at least one injurious fall or at least two non-injurious falls during a 12-month follow-up period were defined as fallers. Participants with MCI performed worse than those without MCI in measures of general health and balance. When comparing participants with and without MCI using analyses of covariance while controlling for age and years of education, there was a significant between-group difference in general health ($F[1, 415] = 6.30$, $p<0.01$), physiologic fall risk ($F[1, 415] = 3.70$, $p<0.05$), and postural sway ($F[1, 415] = 3.78$, $p<0.05$) in addition to differences in neuropsychological performance.[6] Participants with MCI performed significantly worse on tests of cognitive functioning compared to participants without MCI. Group differences were seen for attention/processing speed ($F[1, 415] = 70.99$, $p<0.001$), language ($F[1, 415] = 109.75$, $p<0.001$), executive functioning ($F[1, 415] = 126.40$, $p<0.001$), and memory ($F[1, 415] = 60.81$, $p<0.001$). Logistic regression analyses demonstrated that fall risk was significantly greater in people with MCI (odds ratio [*OR*]: 1.72, *95% CI*: 1.03–2.89).[6] This association was mainly apparent when the analysis was restricted to those with nonamnestic MCI (*OR*: 1.98, *95% CI*: 1.11–3.53), where the relationship was primarily explained by impaired executive functioning (*OR*: 1.27, *95% CI*: 1.02–1.59).[6]

Velocity as a Predictor For Cognitive Decline

Research demonstrated that the relationship between mobility and cognitive function may also have a temporal element. In a study by Alfaro-Acha et al, researchers examined whether reduced gait velocity is a significant predictor for cognitive decline over a seven-year period.[7] Participants included 2,070 noninstitutionalized geriatrics with the average age of 71.7 years (*SD* = 5.7). Cognitive functioning was assessed using the MMSE. To assess mobility, gait velocity was measured by timing how long it took participants to walk eight-feet and rounding to the nearest second. Participants included those with an MMSE score of 21 or greater and the ability to complete an eight-foot walk time test at baseline. A follow-up was conducted after seven years. Results were analyzed using general linear mixed models and suggested that participants with the slowest eight-foot walk time had a significantly greater rate of cognitive decline over seven years (estimate=-0.32, SE=0.08;

p<.001) than subjects with the fastest eight-foot walk time.[7] This association remained statistically significant after controlling for potential confounding factors. Additionally, slow eight-foot walk time in older geriatrics without cognitive impairment at baseline was an independent predictor of MMSE score decline over a seven-year period. Slow eight-foot walk time may be an early marker for older adults in a predementia state who may benefit from early-intervention programs to prevent or slow cognitive decline.[7] Mobility and cognition are not only related, but changes in velocity may be seen long before any cognitive changes are typically detected.

Dual Task Paradigm

A study by Montero-Odasso et al determined whether a dual task may predict dementia progression in older adults with MCI.[8] As previously mentioned, the most important cognitive functions required for mobility are attention and executive functioning. The link between mobility and these cognitive functions is commonly assessed by using the dual-task paradigm. Dual tasking utilizes the executive function ability to perform two tasks simultaneously. This requires the individual to allocate and shift attention between the tasks.

The study included 112 community-dwelling geriatrics with a mean age of 76.0 years (*SD* = 6.9) and a diagnosis of MCI. Participants were followed up for 6 years.[8] To assess cognitive functioning the MMSE and Montreal Cognitive Assessment (MOCA) were administered. Gait velocity was recorded under single-task and 3 separate dual-task conditions using an electronic walkway. Dual-task gait cost was defined as the percentage change between single- and dual-task gait velocities: ([single-task gait velocity – dual-task gait velocity]/single-task gait velocity) × 100. Cox proportional hazard models were used to estimate the association between the risk of progression to dementia and the independent variables, adjusted for age, sex, education, comorbidities, and cognition. Slow single-task gait velocity (<0.8 m/second) was not associated with progression to dementia (hazard ratio [*HR*], 3.41; *95% CI*, 0.99-11.71; p=.05) while high dual-task gait cost while counting backward (*HR*, 3.79; *95% CI*, 1.57-9.15; p<.003) and naming animals (*HR*, 2.41; *95% CI*, 1.04-5.59; p< .04) were associated with dementia progression (incidence rate, 155 per 1000 person-years).[8] Dual-task gait was associated with progression to dementia in patients with MCI.

Discussion

Research demonstrated that impaired mobility in geriatric patients is highly prevalent and has a significant impact on independence, social roles, quality of life, and safety. A review of the literature has demonstrated that impairments in cognitive functioning, especially attention in executive functioning, are associated with greater mobility impairments and safety risks. In a study by Gleason et al, decreased cognitive functioning was associated with a higher fall risk in geriatric populations with normal age-related decline.[5] These findings may suggest that subtle cognitive deficits reflected in MMSE may be indicative of the risk for falls. This study had some limitations. First, there was a relatively small number of subjects with MMSE scores ranging from 22 to 26. Despite this small sample size, there was a significant association between MMSE score and rate of falls for MMSE scores from 22 to 26. Regardless, further evaluation with larger sample sizes and more detailed array of cognitive tests are needed to corroborate these findings. Secondly, these findings may lack generalizability to geriatrics without a recent history of falls or unable to seek intervention because the participants were part of an at-risk cohort, residing in one geographic area, and self-selected to enroll in an intervention study. Strengths of this study included the systematic, monthly tracking of falls prospectively and the derivation of community-based falls rate, adjusting for a number of days subjects spent in the community. The findings of this study are consistent with similar results from previous studies suggesting that healthy geriatrics may experience normal age-related cognitive decline that contributes to an increase in mobility-related safety issues, such as an increased risk of falling.[3]

Secondly, having MCI was associated with greater mobility impairments. In the study by Delbaere et al, findings suggested that MCI, in particular the nonamnestic type, is predictive of falls independent from physiologic fall risk, poor general health, and medication use.[6] This suggests that increased fall risk in people with MCI relates to fall risk factors that are specific to cognitive impairment. When investigating the individual domains within the nonamnestic MCI subtype, researchers found that impaired executive functioning showed the strongest association. Limitations to this study include the finding that having an amnestic subtype of MCI was not related to future falls might be influenced by recall bias. These participants may have been more likely to forget that they had fallen if they did not immediately record it on their fall calendars, especially when a fall did not involve injuries. The strengths of this study included the large sample size, validated assessments of fall events and cognitive function, and the MCI classification based on recent international criteria. It is common for cognitive functioning, especially domains necessary for intact mobility, to worsen with age. These declines in cognitive function and attention

are also associated with increased risk of falling and pose great safety concerns. The findings of this study are consistent with results from previous studies suggesting that when more severe cognitive impairment is added on top of normal age-related decline, the risk of falls significantly increases.[4, 5, 6]

Furthermore, mobility performance may be used to predict cognitive impairments and safety concerns. In a study by Alfaro-Acha et al, researchers found that slower gait velocity (i.e., slower times on the eight-foot walk test) was a significant predictor for long-term cognitive decline (i.e., MMSE score after a seven-year period.[7] This study was limited to self-reports of medical conditions. However, previous research has reported high validity for self-reported medical conditions confirmed by physician diagnosis.[8] Additionally, the study included subjects who were re-interviewed, potentially biasing the subject pool to including healthier individuals. This could have led to an underestimation of the effect of eight-foot walk time on the onset of decline in cognitive functioning, particularly those with greater cognitive impairments. Strengths included a large, well-defined community sample, the prospective design, the seven-year period of follow-up, and the use of mixed models (i.e., an analytic approach that allows the use of available data and evaluates time-dependent effects). Slow eight-foot walk time may be an early marker for older adults in a pre-dementia state who may benefit from early-intervention programs to prevent or slow cognitive decline. It may also be useful for predicting a significant increase in risk for falls.

Lastly, mobility performance on tests requiring intact executive functioning also predicted cognitive decline. A study by Montero-Odasso et al determined whether a dual task may predict dementia progression in older adults with MCI.[8] The findings suggested that dual-task gait testing could be used to predict whether individuals with MCI will progress towards dementia. Difficulties on dual tasks that measured executive functioning were associated with an increased risk of progression to dementia. These findings could be easily translated to the clinical setting owing to the simplicity, noninvasive nature, and low cost of dual-task gait assessment. The sensitivity analysis showed that dual-task gait was comparable with cognitive testing to predict incident dementia, and adjustments for baseline cognition only partially attenuated the associations when modeled as a dichotomous variable, suggesting that dual-task gait test is providing extra information not captured by cognitive testing. Quantitative techniques were used to measure velocity, which can be a limitation to wide clinical applicability. However, dual-task gait velocity can be simply measured using a stopwatch, and dual-task gait cost can be easily calculated. Although predictive validity might be improved by considering cognitive errors on dual tasking, that would make it more difficult to apply in clinics. The strengths of this study included a well-characterized MCI cohort with a long period of follow-up and with biannual assessments to adequately monitor the time to progression to dementia. Researchers used a validated dual-task protocol on quantitative gait analysis and standardized assignment of dementia diagnoses blinded to gait categories, with robust analyses adjusting for a number of important covariates.

Dual-task gait testing is easy to administer and may be used by clinicians to decide on further biomarker testing, preventive strategies, and follow-up planning in patients with MCI. An assessment question is whether there is a need for a dual-task test to predict falls or if it is sufficient to use a challenging single task that examines attention and executive function. Further research is needed to investigate how complex the tasks must be in order to be able to discern impairment is another factor that should be considered since there is no certainty on different levels of complexity within dual-task tests predicting different levels of cognitive impairment in older adults.

The etiology of issues with gait is often multifactorial, and while the role of cognitive functioning in mobility has been established, it is often overlooked as a concern. Primarily focusing on structural deformities in podiatric assessments is adequate, but having a better understanding of this relationship will allow physicians to take a greater systems approach to podiatric care. Taking patients' cognitive function into greater account may lead physicians to have better discernment of etiologies when it comes to patients' individual mobility issues. When specific causes of illness and impairment are pinpointed, this can lead to more effective treatment plans and overall better health outcomes for patients. Additionally, having a better understanding of the physical and psychological dynamic of mobility may also be helpful if patients have various pathologies that impair attention and executive functioning. While mild cognitive impairment and various forms of dementia are common in geriatrics, similar principles may apply to other pathologies that impair these domains of cognitive functioning. Other conditions that are common but often overlooked are benign paroxysmal positional vertigo, bilateral vestibular hypofunction, apractic gait in vascular encephalopathy or normal pressure hydrocephalus, and early-stage neurodegenerative disorders (e.g., progressive supranuclear palsy or downbeat nystagmus). Therefore, without an understanding of cognition's role in mobility, important etiological considerations may be easily overlooked when conducting

assessments. As a result, podiatric assessments specifically for geriatric populations should include some clinical tests for these deficits.

Additionally, understanding the link between mobility and cognition may allow physicians to use podiatric information as a warning sign for other pathologies. As previously stated, one of the common age-related changes in gait is reduced velocity, which was found to be an indicator of increased fall risk.[8] Changes in gait velocity can occur up to 12 years before signs of cognitive impairment become evident.[5] Slow gait speed was found to predict declines in MMSE scores over a seven-year follow-up period.[9] This indicates that mobility assessment can be beneficial in the early detection of cognitive impairment.

Lastly, some clinicians may be concerned about the time and resource restraints involved with considering cognitive function when assessing patients. Some dual task tests that measure the link between cognitive functioning and mobility involve costly materials and complex methodology (e.g., force platforms and electronic walkways). These resources may be difficult to implement across average clinical settings. However, research demonstrates that brief tests that utilize low-cost materials may still garner useful results in discerning this link, predicting further cognitive decline, and predicting the risk of falls. Therefore, utilizing dual task tests may be realistically implemented into clinical exams for geriatric patients.

Conclusion

The growing population of geriatrics highlight the importance for more comprehensive care for preserving geriatric health. Mobility is one of the core concerns of geriatric health and impairments may lead to significant safety concerns. The current field of podiatry often overlooks the role cognitive impairment may play in mobility and the risk for mobility-related injuries. Considering how cognitive impairments (e.g., from age-related cognitive decline, MCI, or dementia) impact mobility may lead physicians to have more comprehensive assessments, more effective treatment plans / safety procedures, and overall better health outcomes for geriatric patients. Implementing tests that measure this relationship (e.g., eight-foot walk test and a dual-task test) may be cost and time efficient. These considerations will allow for more comprehensive and thorough geriatric assessment of mobility and greater holistic care.

References

1. Cire B. World's older population grows dramatically. *National Institutes of Health*. Published March 28, 2016.
2. Zijlstra W, Aminian K. Mobility assessment in older people: new possibilities and challenges. *European Journal of Ageing*. 2007;4: 3–12.
3. Muir SW, Gopaul K, Montero-Odasso MM. The role of cognitive impairment in fall risk among older adults: a systematic review and meta-analysis. *Age and Ageing*. 2012;41: 299–308.
4. Montero-Odasso M, Verghese J, Beauchet O, Hausdorff JM. Gait and cognition: a complementary approach to understanding brain function and the risk of falling. *Journal of the American Geriatrics Society*. 2012;60: 2127–2136.
5. Gleason CE, Gangnon RE, Fischer BL, Mahoney JE. Increased risk for falling associated with subtle cognitive impairment: secondary analysis of a randomized clinical trial. *Dementia and Geriatric Cognitive Disorders*. 2009;27(6): 557–563.
6. Delbaere K, Kochan NA, Close JCT, et al. Mild cognitive impairment as a predictor of falls in community-dwelling older people. *The American Journal of Geriatric Psychiatry*. 2012;20(10): 845–853.
7. Alfaro-Acha A, Al Snih S, Raji MA, Markides KS, Ottenbacher KJ. Does 8-foot walk time predict cognitive decline in older Mexican Americans? *Journal of the American Geriatrics Society*. 2007;55: 245–251.
8. Montero-Odasso MM, Sarquis-Adamson Y, Speechley M, Borrie MJ, Hachinski VC, Wells J, Muir-Hunter S. Association of dual-task gait with incident dementia in mild cognitive impairment. *JAMA Neurology*. 2017;74(7): 857.
9. Okura Y, Urban LH, Mahoney DW, Jacobsen SJ, Rodeheffer RJ. Agreement between self-report questionnaires and medical record data was substantial for diabetes, hypertension, myocardial infarction and stroke but not for heart failure. *J Clin Epidemiol*. 2004;57:1096–1103.

EXTREMITAS

Original Research

Osteoid Osteoma of the Talar Neck: A Case Report

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ABSTRACT

Objective: We report our experience in diagnosing and treating an osteoid osteoma in the talar neck. This case report illustrates the successful surgical treatment of this condition and also discusses reasons why this pathology frequently has a delayed diagnosis.

Case Report: This article describes the workup of a 22-year-old patient with a 3-year history of persistent ankle pain who underwent arthroscopic evaluation and open excision of an osteoid osteoma of the talar neck with subsequent bone grafting.

Discussion: The difficulty in diagnosing osteoid osteoma of the small bones of the feet is widely recognized. Subperiosteal osteoid osteomas are difficult to diagnose because of their unique radiographic appearance. These types of osteoid osteomas lack the periosteal response with sclerotic bone which is typically present. The clinical picture of this diagnosis can vary but usually includes no traumatic onset of pain, intermittent pain, pain that worsens at night, and pain relieved by NSAIDs or Aspirin, in an adolescent and young adult population. Advanced imaging should be considered if the pain does not subside with standard treatments.

Conclusion: This article reports our experience in the diagnosis and successful operative excision of an osteoid osteoma of the talar neck. This article serves as an educational tool for providers to help reduce the time to diagnosis for future patients.

Introduction

Osteoid osteomas are benign bone tumors that constitute 10%-14% of all benign bone tumors, 2%-10% of which are found in the talus.[1] This benign lesion was first described by Jaffee in 1935. Cases of osteoid osteomas with talar involvement have rarely been reported in American literature. An osteoid osteoma is most commonly seen in adolescents and young adults and most often occurs in the femur and tibia. Classically, the pain manifests as indolent pain that worsens at night and is generally relieved by salicylates and non-steroidal anti-inflammatory drugs. [1] Diagnosis is usually made with confirmatory imaging such as plain radiographs, or computed tomography which can detect osteoid osteomas with a 96% sensitivity.[1] The bone tumor is usually less than 1.5cm in size that does not grow and the pathophysiology is not well understood. These cases are difficult to diagnose, which can lead to a delay in treatment. The average time from the onset of symptoms to the correct diagnosis is about 2.5 years. [3] This article describes the workup of a patient with a 3-year history of persistent ankle pain who underwent arthroscopic evaluation and open excision of an osteoid osteoma of the talar neck. The purpose of this article is to report our experience in the diagnosis and treatment of osteoid osteomas of the talar neck with the goal of reducing the time to diagnosis for future patients.

Case History

The patient, a 22-year-old Hispanic female, presented to her primary care physician with a 2-year history of right ankle pain thought to be secondary to a previous ankle sprain. Initially, the patient's ankle was swollen, and she was not able to bear weight. Since then she had returned intermittent pain, exacerbated in the last month. On her initial visit with a primary care physician, right ankle radiographs *(Fig.1A,1B)* were ordered and the patient was given a prescription for Ibuprofen. The patient followed up 2 months later, reporting persistent pain and minimal swelling; ibuprofen helped relieve some of the pain. At this point, an MRI of the right ankle was ordered. MRI reading dictated the following, "severe trabecular bone edema of the talus, involving the body of the talus and talar neck and to a lesser extent the talar head, most likely related to a stress fracture. Large ankle effusion", *(Fig. 2A, 2B,2C)*. The patient was instructed to limit activity and utilize an ankle

brace at work and continue NSAIDs; a stress fracture of the right ankle was the given diagnosis. The patient was then referred to orthopedic surgery.

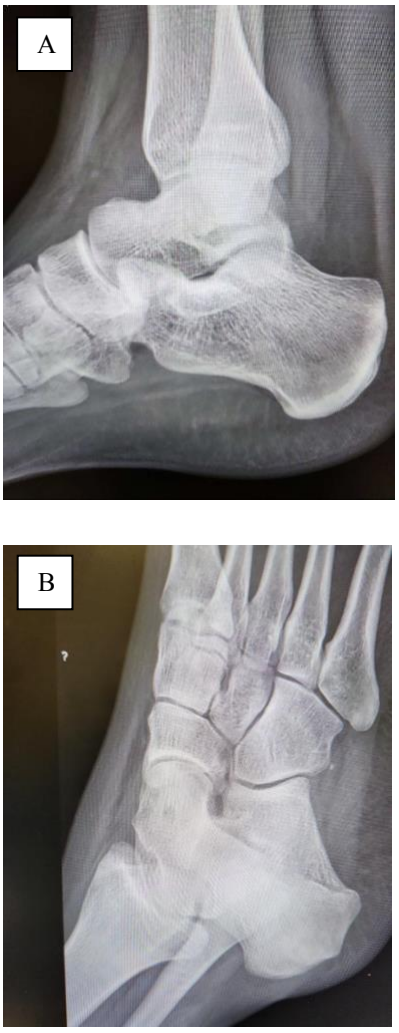


Figure 1A,1B. Radiographs of the right ankle.

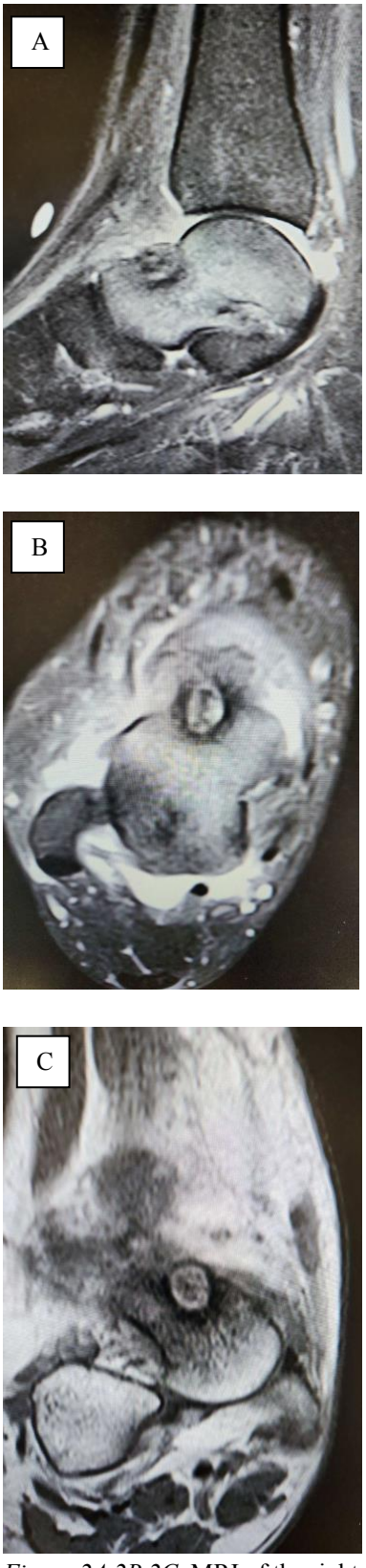
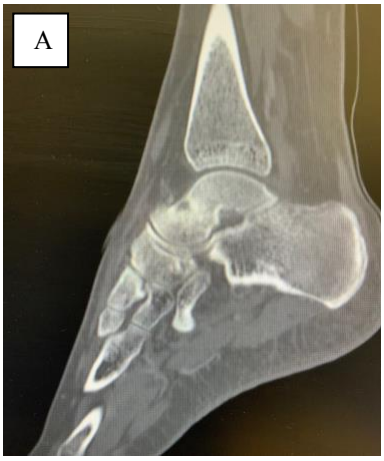


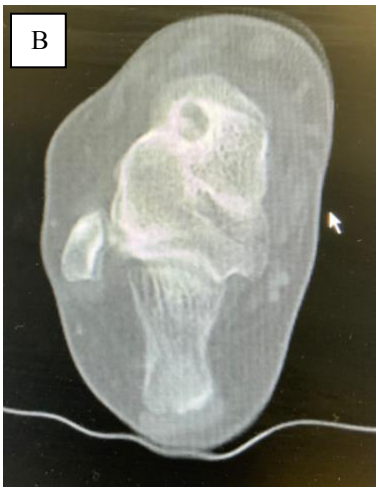
Figure 2A,2B,2C. MRI of the right ankle- sagittal, coronal, and axial; respectively.

The patient was seen by orthopedic surgery 4 months after her initial visit with her PCP. On physical exam, the patient had pain with dorsiflexion of the ankle and generalized tenderness at the tibiotalar joint. The patient was placed in a CAM boot with crutches. The patient followed up 2 months later reporting that she was not improving in the CAM boot; physical therapy was ordered. The patient once again followed up 2 months after that reporting she was not contacted by physical therapy and did not attend any sessions; the patient was cleared to gradually discontinue the CAM boot. Another two months passed by, and the patient was seen by their primary care provider who placed the patient on workplace accommodations and restrictions due to her occupation as a restaurant server who is constantly on their feet. The patient was prescribed lidocaine patches and was referred to pain management. A week and a half after this visit, the patient was again seen by orthopedics at which time she reported that her pain did not subside with physical therapy and was getting worse. She could not walk and mostly ambulated with a wheelchair or crutches. At that point, the patient had been off work for 3 weeks. The patient was once again cleared to gradually discontinue her CAM boot, given home ROM exercises, and was referred to podiatric surgery.

A month later, the patient was seen by author JP for an initial consultation. Upon physical examination, the patient had tenderness to palpation of the medial and lateral gutters, EHL tendon, EDL tendon, and TA at the level of the ankle joint as well as limited range of motion of the ankle: 15 degrees of dorsiflexion and 25 degrees of plantarflexion. The patient was instructed to stop physical therapy and instructed to bring her MRI images with her as they were not available in her chart. The patient returned one month later, JP evaluated the MRI images and concluded the following, “Excess fluid in the ankle joint, edema of the talus noted, increased signal intensity of the dorsal talar neck, suspected osteoid osteoma”. Based on history, physical exam, and imaging; the diagnosis of osteoid osteoma was made. At this time, surgical intervention was discussed for ankle arthroscopy, ostectomy of the talar neck, with bone graft, likely full open resection of the osteoid osteoma. A diagnostic ankle block was performed; 3ccs (1cc Dexamethasone phosphate and 2cc 1% Lidocaine) were injected into the ankle joint. The patient experienced immediate relief of 80% of her pain with the injection. A CT of the right ankle was ordered to evaluate the talus and aid in preoperative planning.

One month later the patient presented for her preoperative visit. On her preoperative visit, the patient reported she experienced 80-90% pain relief for 2 days after the ankle injection. The surgical procedure was discussed, and the patient consented to surgical intervention. The CT report dictated, “Round lucent lesion with sclerotic borders measuring approximately 1 cm in the dorsal talar neck. There appears to be a small sclerotic nidus. No overlying soft tissue edema can be seen. Findings for benign osteoid osteoma”, *(Figure 3A,3B,3C)*. The largest diameter of the nidus measured by computerized tomography preoperatively was 1cm in diameter, consistent with typical findings of an osteoid osteoma. The osteoid osteoma in this case was a juxta-articular, subperiosteal type. A few days after the pre-op visit, the patient was evaluated by pain management who prescribed Gabapentin 300mg qHS in addition to her acetaminophen and ibuprofen PRN. One month later, a surgical procedure was performed without complications. The patient was placed in a tall CAM boot, non-weight bearing protocol for 4 weeks. At 4 weeks physical therapy was initiated with ankle range of motion and protected weight bearing was permitted. She transitioned out of the CAM boot at 6 weeks. She was not allowed to return to high-impact activities for 3 months from the date of surgery. From the initial visit at the hospital with a primary care provider to the day surgical intervention, the patient was seen by multiple providers for a total of 14 months.





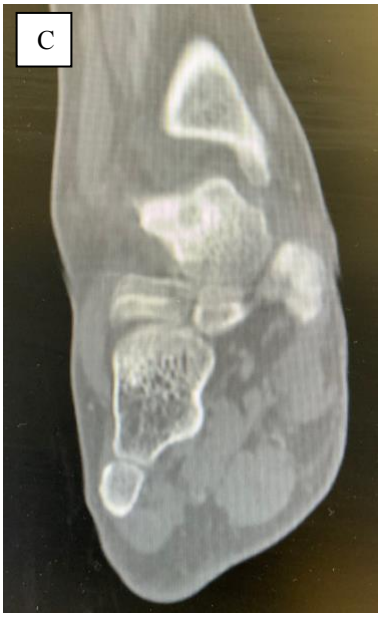


Figure 3A,3B,3C. CT of the right ankle- sagittal, coronal, and axial; respectively.

Operative Technique

The patient was brought to the operating room and placed on the operating table in a supine position with a thigh holder. Anesthesia was initiated, and following adequate sedation, a local anesthetic block of 20 cc of 0.25% marcaine with epinephrine was administered intra-articularly within the ankle joint. Anteromedial and anterolateral portals were formed and 2.7mm arthroscopic instrumentation was used. The camera was inserted and significant chronic synovitis and capsular adhesions were appreciated, particularly of the anterior lateral ankle. An arthroscopic shaver was used to release the adhesions and remove the synovitis assisted with joint flush with NSS. Visual inspection of the joint revealed an improved appearance of the joint space. The scope was removed, and the portals were closed with 3-0 nylon *(Figure 4)*.

Attention was then directed to the right anterior ankle. A 5 cm longitudinal anterior ankle incision was performed in the interval between the tibialis anterior and extensor hallucis tendons. Careful dissection was performed down to the talus bone, and care was taken to avoid neurovascular structures and tendons. The bone lesion was visualized over the dorsolateral talar neck; a soft hemorrhagic bone tumor was noted *(Figure 5)*. The lesion was curetted out *(Figure 6)* and bone tissue was sent for pathology *(Figure 7)*. The defect in the talus measured approximately 1.0x1.0x1.0 cm. Subchondral drilling was performed with a 1.6mm k-wire *(Figure 8)* and a 3mm round burr; bone allograft was used to backfill the lesion *(Figure 9A, 9B)*. The incision was closed in a standard layered fashion *(Figure 10)*. A lateral ankle radiograph was taken at the conclusion of the case to confirm adequate bone allograft placement *(Figure 11)*.

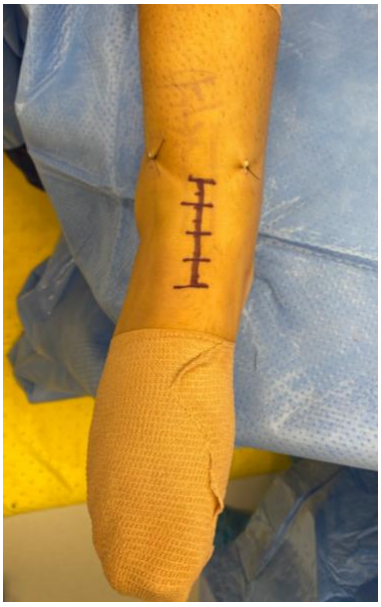


Figure 4. The two arthroscopy portals were closed with 3-0 nylon.

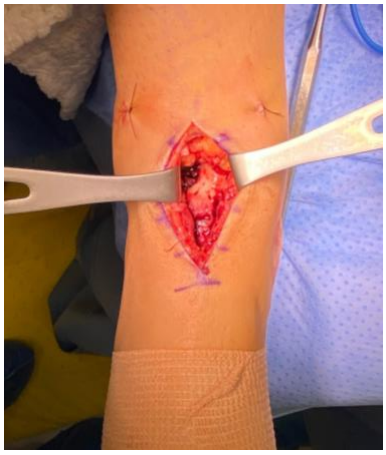


Figure 5. The bone lesion was visualized over the dorsolateral talar neck; a soft hemorrhagic bone tumor was noted.

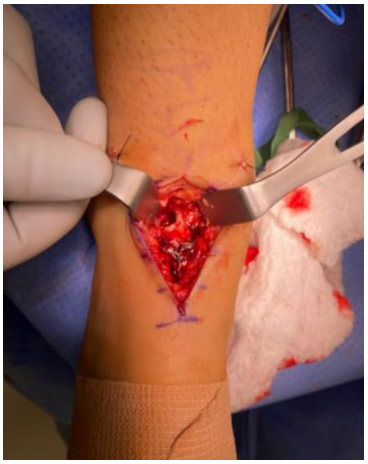


Figure 6. The lesion was curetted out.

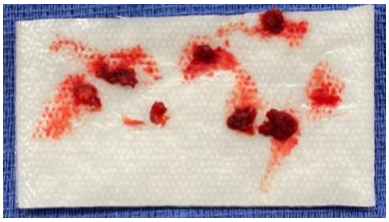


Figure 7. The bone tissue was sent for pathology.

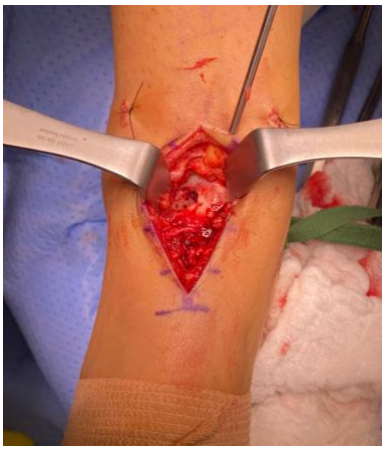


Figure 8. Subchondral drilling was performed with a 1.6mm k-wire.

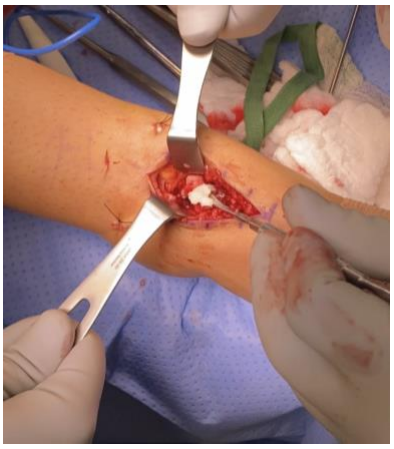


Figure 9A. Bone allograft was used to backfill the lesion.

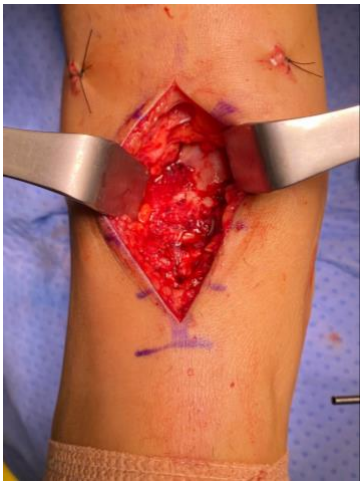


Figure 9B. Bone allograft was used to backfill the lesion. The finished step is shown above.

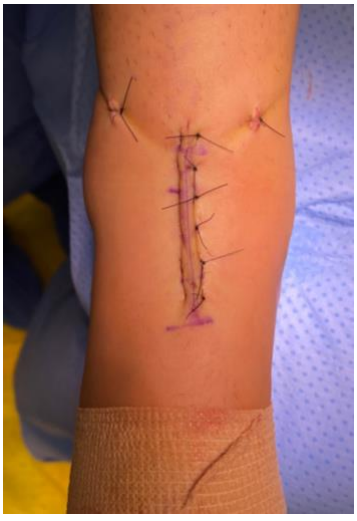


Figure 10. The incision was closed in a standard layered fashion

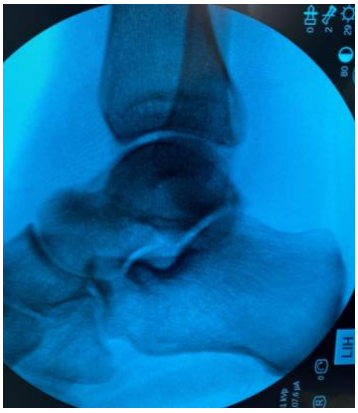


Figure 11. A lateral ankle radiograph was taken at the conclusion of the case to confirm adequate bone allograft placement.

Discussion

The difficulty in diagnosing osteoid osteoma of the small bones of the feet is widely recognized. The problem is especially difficult in the ankle due to the elaborate composition of the joint; encompassing ligament, tendons, capsules, and intricately shaped bones. For this reason, plain radiographs are often not enough to come to the correct diagnosis. In 1966, Ediken et al classified different types of osteoid osteomas into three types- cortical, cancellous, and subperiosteal. In this case, the osteoid osteoma was subperiosteal and juxta-articular. Subperiosteal osteoid osteomas are difficult to diagnose because they are unique radiographically. This is because the typical periosteal response with sclerotic bone is usually not present. This feature was present in our patient's original radiographic imaging and is one of the reasons that it was treated conservatively without a definitive diagnosis for so long. In addition, if the lesion is not fully developed, it may lead to an uncertain diagnosis in lesions that are cancellous or intra-articular in nature.

Another difficulty with this tumor is that the radiographic appearance of this particular osteoid osteoma location (talar neck) can resemble the appearance of an osteophyte, indicating a diagnosis of impingement syndromes and leading a medical professional down the wrong treatment path. This is especially true with the juxta- or intra-articular lesions, which can mimic ankle sprains, arthritis, sinus tarsi syndrome, or tarsal tunnel syndrome. Additional tests like CT are necessary for localizing

the nidus, aiding in preoperative planning. In our patient, a CT was not ordered until it was needed for preoperative planning. Had the imagining been ordered after her MRI showed nonspecific bony changes, her diagnosis would likely have been made at an earlier time period.

The clinical picture of this diagnosis can vary but usually includes no traumatic onset of pain, intermittent pain, pain that worsens at night, and pain relieved by NSAIDs or Aspirin, in an adolescent and young adult population. These key characteristics emphasize the importance of taking a detailed history and physical exam to diagnose a patient rather than diagnosing based on what is seen on imaging. In this case report, a final and accurate diagnosis was made by combining findings from the history (positive for young adult, pain relieved by NSAIDS), physical examination (positive for mild swelling, tenderness to palpation, and limited range of motion), and subsequent CT (positive for- a round lucent lesion with sclerotic borders measuring <1.5 cm in diameter). As literature has shown, even with key signs and symptoms, this diagnosis is easily overlooked in the ankle as the average time from onset of symptoms to correct diagnosis is about 2.5 years.[3] In this patient, multiple conservative treatments were implemented for long periods of time which delayed her diagnosis.

Additionally, a point to learn from this case is the importance of obtaining advanced imaging in a timely manner. The patient underwent an MRI of the ankle, but due to the frequently nonspecific findings of an osteoid osteoma on MRI, the lesion was mistaken for a stress fracture of the bone and treated as such for many weeks.[4]

From the initial visit to the day of surgical intervention, the patient was seen by multiple providers for a total of 14 months. In addition to the time that the patient had not yet sought out medical treatment, this sums up a total of 3 years the patient experienced intermittent then worsening pain. It is imperative that physicians take time to learn about complex diagnoses such as this to be able to identify and provide timely treatment to patients.

The literature shows that the surgical treatment of osteoid osteoma has very high success rates, ranging from 88%-100%. [9] In our patient, at the 4-week postoperative visit, she stated that she could sleep at night for the first time in years due to her improvement in pain.

Conclusion

Osteoid osteomas are difficult to diagnose due to signs and symptoms that overlap with other diagnoses and nonspecific findings on plain film. This article reports our experience in diagnosing and treating an osteoid osteoma of the talar neck as an educational tool to reduce the time to diagnosis for future patients.

Conflicts of Interest

The authors report no conflicts of interest in relation to this study.

References

1. Jordan RW, Koç T, Chapman AW, Taylor HP. Osteoid osteoma of the foot and ankle--A systematic review. Foot Ankle Surg. 2015;21(4):228-234.
2. Jaffe Hl. "Osteoid-Osteoma:: A Benign osteoblastic tumor composed of osteoid and atypical bone. Arch Surg. 1935;31(5):709–728.
3. Snow SW, Sobel M, DiCarlo EF, Thompson FM, Deland JT. Chronic ankle pain caused by osteoid osteoma of the neck of the Talus. Foot & Ankle International. 1997;18(2):98-101.
4. Franceschi F, Marinozzi A, Papalia R, Longo UG, Gualdi G, Denaro E. Intra- and juxta-articular osteoid osteoma: a diagnostic challenge : misdiagnosis and successful treatment: a report of four cases. Arch Orthop Trauma Surg. 2006;126(10):660-667. doi:10.1007/s00402-006-0203-9
5. Ge SM, Marwan Y, Abduljabbar FH, Morelli M, Turcotte RE. Arthroscopic management of intra- and juxta-articular osteoid osteoma of the upper extremity: a systematic review of the literature. Eur J Orthop Surg Traumatol. 2020;30(8):1333-1344.
6. Dubuc JE, Docquier PL, Schubert T, Galant C, Malghem J. Diagnosis failure led to the recurrence of an intra-articular osteoid osteoma at the talus neck after arthroscopic excision. Foot Ankle Surg. 2014;20(3):e40-e42.
7. Chuang SY, Wang SJ, Au MK, Huang GS. Osteoid osteoma in the talar neck: a report of two cases. Foot Ankle Int. 1998;19(1):44-47.
8. Resnick RB, Jarolem KL, Sheskier SC, Desai P, Cisa J. Arthroscopic removal of an osteoid osteoma of the talus: a case report. Foot Ankle Int. 1995;16(4):212-215.
9. Tepelenis, Kostas et al. "Osteoid Osteoma: An Updated Review of Epidemiology, Pathogenesis, Clinical Presentation, Radiological Features, and Treatment Option." *In vivo (Athens, Greece)* vol. 35,4 (2021): 1929-1938. doi:10.21873/invivo.12459

Gender Disparities in Financial Relationships between Podiatric Physicians

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ABSTRACT

Objective: Studies across multiple physician specialties have continued to demonstrate gender-based discrepancies in financial compensation. This study aims to determine if gender disparities exist in industry relationships with podiatric medicine physicians.

Methods: This retrospective study obtained publicly accessible data from the Centers for Medicare and Medicaid Services (CMS), at https://openpaymentsdata.cms.gov/. Data was gathered for payments made to podiatric physicians from industry in 2019 and 2020. Data was limited to payment under royalties or licensing and consulting fees. Name, gender, state of active practice and years of experience were gathered via professional sites such as https://www.topnpi.com. The total number of payments and amounts were analyzed and compared between gender, state of active practice (CA, IL, ME, NE, NH, OK, FL, NY), and years of experience. Multilinear regression models were used to determine predictors of higher payment amounts.

Results: The study included 256 practicing podiatrists, 81.25% were men and 18.75% were women. The majority of the total payment amount $5,390,697.12 (94.82%) was made to men, while only $294,290.24 (5.18%) was made to women. In California and Nebraska, men had more years of experience (p=.006, p=.022). In California and Florida, men received a higher total number of payments (CA: 2019, p=.011, FL: 2020, p=.015). In Illinois, men were paid higher consulting fees than women (2019, p = .001). There was no predictive association between gender, state or years of experience to higher payment amounts (2019,2020).

Conclusion: Gender, state, and years of experience were not predictors of higher payment amounts from industry. However, men do show a gross higher total number of payments in every state. As there is an increasing number of women podiatric medical students matriculating, this does mark a historic and persistent discrepancy in the hiring process favoring male podiatric physicians in regard to industry relationships.

Introduction

In the last few years there have been efforts to increase transparency of relationships, in particular, financial relationships between physicians and the industry. This is of notable concern as these ties may influence a physician to act in their best interest as opposed to the best interest of the patient. With new laws having changed the way certain forms of payment are distributed, such as not allowing gifts as a form of payment, payment for consulting services and royalties continue. These changes have allowed for information to gather which finds physicians' decisions of care are influenced by financial factors.[2,3,4] Disclosures include royalties and licensing, total payments, and number of payments.[2,3] A recent study identified an association between industry payments and physician prescribing, this being one of many others, most of them being to orthopaedic surgeons being paid by royalties and licensing[2]. Higher proportion of male otolaryngologists and neurosurgeons receive industry payments in contrast to their female peers while those same men typically saw higher amounts as well[4].

Discord such as these must be routinely discussed among our profession, to promulgate efforts to eliminate these biases. Legislature has been put into place that has terminated the ability of physicians to receive industry payment as gifts (Physician Payment Sunshine Act). However, there are no stringent rules on payment in the form of "consulting services" and "royalties". Recent studies have demonstrated that most payments were paid to a minority of physicians of the particular specialty but also that the majority of the number and sum of payments were dispersed to male physicians.

Podiatric Medicine is a historically male populated specialty. Of the 18,000 currently practicing DPM licensed physicians, only 5,148 are female. With this legacy, comes ingrained bias and faulty assumptions on what women are capable of doing in spite of their equal qualification and experience. Female physicians continue to face barriers to closing the gender gap. They have lower academic standings and fewer publications, receive less awards/grants, are underrepresented in leadership positions, have a lower incidence pursuing surgical specialties, and receive lower compensation[3].

This discrepancy largely contributes to the pervasive wage gap, difference in leadership roles, academic position, overall professional exposure and likely, an inconsistency in industry payments. Increased acknowledgement of this gender gap is essential to the growth of the medical community as a whole. Multiple studies across an amalgam of physician specialties have continued to demonstrate gender based discrepancies not only in financial compensation but leadership roles and academic positions as well. This study aims to determine if gender disparities exist in industry relationships with podiatric medicine physicians as seen in other fields of medicine. Currently, there is no available literature to describe gender based disparities or trends in this field. We hypothesize that men receive a higher proportion of royalties and consulting fees than women, adjusting for the number of men and women in the field of Podiatric medicine. Our aim is to analyze discrepancies in genders with respect to location of active practice, and years of experience.

Methods

Data collected for this retrospective study was gathered via publicly accessible data from the Centers for Medicare and Medicaid Services (CMS), at https://openpaymentsdata.cms.gov/. for payments made to podiatric physicians from industry from 2019-2020 specifically, payment under royalties, licensing and consulting fees. Name, gender, active practice location and years of experience were collected via https://www.topnpi.com/. The total number of payments and amounts were analyzed and compared between gender, location of active practice, and years of experience. Non-parametric multivariable linear regression and Mann-Whitney U test models were used to determine predictors of total payments, number of payments and mean of payments utilizing SPSS.

Results

The study included 256 practicing podiatrists from CA, IL, ME, NE, NH, OK, FL, and NY; 81.25% were men and 18.75% were women. In 2019 and 2020, there were 4,785 separate (study specific) payments reported from industry to 284 podiatric physicians, for a total of $5,684,987.36. The majority of the total payment amount ($5,390,697.12) (94.82%) was made to men, while only ($294,290.24) (5.18%) percent was made to women.

The median payment for royalties or licensing paid to men was $7,958.065 (n=54), while only 2 women were paid money in royalties or licensing. Both in the state of Florida, one was paid a total of $10,934.80 and the other $18. Women in the remaining states (California, Illinois, Maine, Nebraska, New Hampshire, Oklahoma, and New York) as well as men in Maine, Nebraska, New Hampshire, New York (2019 only) were not paid in royalties or licensing. Mann Whitney U tests could not be run for gender discrepancies in royalties or license for California, Illinois, Maine, Nebraska, New Hampshire, Oklahoma and New York (2019,2020) due to lack of available data. In Florida, there was no statistical significance between the total amount of royalties or licensing paid to men and women (p=1.000, p=.308).

The median payment for consulting fees paid to men was $3,950 (n=176) and women was $1,500 (n=28). Women in Maine, Nebraska, New Hampshire, Oklahoma (2020) as well as men in New Hampshire (2020) were not paid for consulting services. Mann Whitney U tests could not be run for gender discrepancies in consulting fees for Nebraska, Maine, New Hampshire, and Oklahoma (2019, 2020) due to lack of available data. In Illinois, men were paid higher consulting fees than women (2019, p = .001). All other tests were not statistically significant (CA: p=.605, p=.825, IL: p=.211 (2020), FL: p=.862, p= .650, NY: p=.209, p=.571)

The median pay for services other than counseling was $1,000 (n=132) for men and $124.99 (n=28) for women. Mann Whitney U tests could not be run for gender discrepancies in services other than consulting fees for California (2020), Nebraska (2020), Maine (2019, 2020), New Hampshire (2019, 2020), and Oklahoma (2019, 2020) due to lack of available data. All other tests were not statistically significant (CA: p=.388, IL: p=.275, p=.500, FL: p=.182, p=.684, NE: p=.429, NY: p=.250, p=.571)

The median pay for the total amount of payment for men was $3,800 (n=285) and women was $869.02 (n=50). Mann Whitney U tests could not be run for gender discrepancies in total amount of payments for Nebraska (2020), Maine, New Hampshire and Oklahoma due to lack of available data. In Maine, women did not receive any payments from industry (2019, 2020) as well as Nebraska and Oklahoma (2020). No tests were significant in this category.

Men received 4,301 single payments (84.61%) compared with 733 single payments to women (15.39%). In regards to the total number of payments, the median for men was 6 (n=277) and women 2 (n=53). In California and Florida, men received a higher total number of payments (CA: 2019, p=.011, FL:2020, p=.015). All other tests were not statistically significant.

Lastly, a multilinear regression model was conducted to evaluate if gender, state or years of

experience could predict higher payment amounts. Maine, Nebraska, New Hampshire and Oklahoma were not included due to a lack of sufficient data. In 2019, gender, state and years of experience were not predictors of higher payments (p=.126, p=.850, p=.646). In 2020, gender and years of experience did not predict higher payment amounts (p=.634, p=.228). The significance value for the state was .022, which satisfies the threshold of statistical significance. However, since the test only included 4 states, we do not feel it is an adequate representation of trends in the United States. A study including a larger number of states would be a more adequate representation.

California		
	2019	2020
Years of Experience	p= 0.006*	
Royalty/Licensing	Not enough data	Not enough data
Consulting Fee	p=0.605	p=0.825
Other Services	p=0.635	Not enough data
Total Amount of Payment	p=0.388	p=0.913
Total Number of Payments	p=0.011*	p=0.640

Figure 1: This table illustrates the results of the Mann-Whitney U test conducted for each parameter in California; an asterisk indicates statistically significant values.

Illinois		
	2019	2020
Years of Experience	p=0.087	
Royalty/Licensing	Not Enough data	Not Enough data
Consulting fee	p=.001*	p=0.211
Other Services	p=0.275	p=0.500
Total Amount of Payment	p=0.37	p=0.705
Total Number of Payments	p=.0837	p=0.488

Figure 2: This table illustrates the results of the Mann-Whitney U test conducted for each parameter in Illinois; an asterisk indicates statistically significant values.

Florida		
	2019	2020
Years of Experience	p=0.263	
Royalty/Licensing	P=1.000	P=0.308
Consulting fee	p=0.862	p=0.650
Other Services	p=0.182	p=0.684
Total Amount of Payment	p=0.538	p=0.822
Total Number of Payments	p=0.750	p=0.015

Figure 3: This table illustrates the results of the Mann-Whitney U test conducted for each parameter in Florida; an asterisk indicates statistically significant values.

Nebraska		
	2019	2020
Years of Experience	p=0.022*	
Royalty/Licensing	Not Enough data	Not Enough data

Consulting Fee	Not Enough data	Not Enough data
Other Services	p=0.429	Not Enough data
Total Amount of Payment	p=0.273	Not Enough data
Total Number of Payments	p=0.436	Not Enough data

Figure 4: This table illustrates the results of the Mann-Whitney U test conducted for each parameter in Nebraska; an asterisk indicates statistically significant values.

New York		
	2019	2020
Years of Experience	p=0.107	
Royalty/Licensing	Not Enough Data	Not Enough Data
Consulting fee	p=0.209	p=0.731
Other Services	p=0.250	p=0.571
Total Amount of Payment	p=0.261	p=0.405
Total Number of Payments	p=0.837	p=1.000

Figure 5: This table illustrates the results of the Mann-Whitney U test conducted for each parameter in New York; an asterisk indicates statistically significant values.

Maine, New Hampshire, Oklahoma
Not enough data

Figure 6: There was not enough data available to run statistical analysis for states Maine, New Hampshire and Oklahoma.

Discussion

Podiatric Medicine is a historically male-dominated specialty. Of the 18,000 currently practicing DPM-licensed physicians, only 28.6% are female. However, an increase in female podiatric physicians and female physicians overall, within the last 50 years, has improved representation throughout the field. [3] Nevertheless, there are obstacles unique to female physicians which are evident across multiple professions, particularly in regard to financial compensation. In addition to deficits in financial compensation females in podiatric medicine receive less awards, publications, and experience more gender discrimination and sexual harassment.[2] These factors contribute to explain the data outcomes in this research. These discrepancies shed a light on the need to improve the professional atmosphere for females in podiatric medicine. The fewer number of females compared to their male counterparts creates a vacuum in leadership for women in the field, which impedes gender equality.[8] These findings allow those in the hiring process to hire more men based on "availability" alone and continue to perpetuate a discrepancy in pay between genders.

The finding that women are hired less in positions of influence and more so in supportive roles brings into question, the reasons for these kinds of hiring practices. Future research inquiring into hiring criteria for podiatric physicians is needed to evaluate if there are intrinsic gender biases during resume searches and interviews. Along with hiring criteria, there can also be a perception bias of the ability to perform the job for physical reasons, one of the most obvious being that a surgical specialty is physically demanding and those hiring could be operating under the false pretense that woman are faster to fatigue or incapable of dealing with the physical rigor of surgery compared to their male counterparts. In addition, there may be a classic patriarchal notion that women will be preoccupied with home life and not capable of performing to their best capacity at work.

As the ratio of men to women in podiatric medicine continues to be drastic, despite recent improvements promoting equity and inclusion. A survey conducted by Brower *et al* found females experienced gender discrimination at a rate of 73.1% versus males at 5.8% and sexual harassment, 41.6% for females and 5.1% for males.[2] This also called into light that if individuals are being harassed or assaulted then they may be more likely to accept lower pay and less likely to mention it as a reason for lower pay.[6] Women also experience roles by bias. In previous years a majority of women were hired as support staff, not as physicians which is reflected in their current pay.[7] Data collected in our research displayed women get paid less frequently than men

and another confound would be the time taken off for maternity leave also the slow increase in hours upon returning from leave.[5]

The many gender-based difficulties faced by female podiatric physicians contributed to the results of the data collected in this research. In addition to those factors, other research attributes affected our data such as the number of years and states selected. The largest states with practicing physicians were accounted for (CA, FL, IL) however many other states would be necessary to strengthen the research. Also, the number of years could be expanded from two years to three or more years to account for any potential outlier information or worldwide events. This research aimed to find if gender-based disparities existed within podiatric medicine. The data indicates that there are instances in which males have a benefit over female physicians, however, this 256-person sample size does not allow for that relationship to be definitive. The strength of this data was the use of geographic location as a variable which allowed trends and statistics that otherwise may have been overlooked to be acknowledged. This paper aims to inspire further research and primary literature on the topic. This will require transparency in the reporting of income, which is still considered a faux pas in many instances. Nevertheless, these findings open the door to revealing biased gender discrepancies in financial compensation in the field of podiatric medicine.

Conclusion

Gender, state, and years of experience were not predictors of higher payment amounts from industry. However, men do show a gross higher total number of payments in every state. As there is an increasing number of women podiatric medical students matriculating, this does mark a historic and persistent discrepancy in the hiring process favoring male podiatric physicians in regard to industry relationships.

References

1. American Association of Colleges of Podiatric Medicine Statistics (2016) Available at https://www.aacpm.org/statistics/. Accessed April 27, 2022.
2. Brower BA, Butterworth ML, Crawford ME, Jennings MM, Tan Z, Moore JD, Suzuki S, Carpenter BB. The Podiatric Medical Profession: A Gender Comparison. *J Foot Ankle Surg*. 2020 Sep-Oct;59(5):997-1007.
3. Brower, B. A., Jennings, M. M., Butterworth, M. L., & Crawford, M. E. (2019). Women in Podiatry and Medicine. Clinics in podiatric medicine and surgery, 36(4), 707–716.
4. Mitchell AP, Trivedi NU, Gennarelli RL, Chimonas S, Tabatabai SM, Goldberg J, Diaz LA Jr, Korenstein D. Are Financial Payments From the Pharmaceutical Industry Associated With Physician Prescribing? ; A Systematic Review. Ann Intern Med. 2020 Nov 24.Epub ahead of print.
5. Rangel EL, Smink DS, Castillo-Angeles M (2018) Pregnancy and Motherhood During Surgical Training. *JAMA Surg* (2018); Vol.153(7), pp 644-652(2018). PMID: 29562068
6. Walton MM (2019). Sexual equality, discrimination and harassment in medicine: it's time to act. Medical journal of Australia (Aug 2015), pp167-169.
7. Ward, L (2008) Female Faculty in Male-Dominated Fields: Law, Medicine and Engineering. New Directions for Higher education, 143, pp.63-72.
8. Yedidia MJ, Bickel J (2001) Why aren't there more women leaders in academic medicine? The views of clinical department chairs. Academic Medicine (May 2001), 76, Issue 5, pp.435-465.

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This could be an indication of small fiber peripheral neuropathy[1] (SFPN), a condition that can be definitively confirmed with a quick, in-office punch biopsy procedure and epidermal nerve fiber density (ENFD) analysis.

"For the early detection of small fiber peripheral neuropathy, ENFD analysis is the best objective tool," says Dr. Wayne L. Bakotic, ENFD Medical Director at BakoDx. "The ENFD diagnostic test allows for the confirmation of SFPN, the assessment of the degree and severity, and determination of effective treatment."

This in-office procedure is a minimally invasive, 3mm punch biopsy of the distal leg (10cm proximal to the lateral malleolus). It typically takes about five minutes, with little to no post-procedure care. The ENFD test is reimbursable by most insurance companies.

During ENFD analysis, a specially trained pathologist calculates the density per unit area and quantifies the tiny myelinated A-delta and unmyelinated C fibers within the epidermis. This highly specific and sensitive testing method allows clinicians to definitively diagnose suspected SFPN.

Neuropathy is complex

While peripheral neuropathy affects about 20 million adults in the U.S.[2], it is often misdiagnosed with large fiber neuropathy due to its complex array of symptoms, both somatic and autonomic. Patients with SFPN will often have normal reflexes, muscle strength and electromyography (EMG) and nerve conduction velocity (NCV) test results.

SFPN usually affects the hands and/or feet in a stocking or glove-like pattern.[3] A patient may present with symptoms that range from burning and tingling, to coolness and numbness. This form of neuropathy often occurs secondary to diseases such as diabetes mellitus or it may be an indication of other autoimmune disorders.

Other patient presentations may include:

- Restless leg syndrome

[1] Hovaguimian A, Gibbons CH. Diagnosis and treatment of pain in small-fiber neuropathy. Curr Pain Headache Rep. 2011 Jun;15(3):193-200. doi: 10.1007/s11916-011-0181-7. PMID: 21286866; PMCID: PMC3086960.
[2] Peripheral Neuropathy Fact Sheet | National Institute of Neurological Disorders and Stroke. Ninds.nih.gov. https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Peripheral-Neuropathy-Fact-Sheet. Published 2020. Accessed August 20, 2020.
[3] Cascio MA, Mukhdomi T. Small Fiber Neuropathy. In: StatPearls. Treasure Island (FL): StatPearls Publishing; May 23, 2022..

- Abnormalities in sweating (hyperhidrosis)
- Inability to sweat normally (anhidrosis)

But because these presentations are not always SFPN, identifying the precise form of neuropathy allows for the most effective treatment method.

ENFD test benefits

ENFD is a powerful tool that provides the most objective method of documenting and monitoring the progression of SFPN. Early ENFD testing may also reveal degenerative changes, so that patients are placed on preventative therapies prior to the onset of symptoms.

Once the diagnosis of SFPN is confirmed, there are several medical treatments that may provide relief, depending on the type of nerve damage. Therapy to treat the symptoms and underlying causes of the neuropathy could include diet/lifestyle modifications, supplements, or topical medications. However, because SFPN has many causes, no product works for everyone.

Studies show that dietary supplements, such as NeuRx-TF, containing Alpha-Lipoic Acid[4] (600mg daily) and Benfotiamine[5] (600mg daily) may be helpful in some cases to diminish symptoms of neuropathy and improve epidermal nerve health. Investigators also have noted a benefit to using combination therapy that includes L-methylfolate, methylcobalamin and pyridoxal 5'-phosphate[6].

ENFD retesting at future intervals, between six-to-12 months, may also help to assess the disease progression or regression and the therapy effectiveness over time. An accurate and definitive diagnosis of SFPN provides improved patient care and allows for appropriate neuropathy management.

"My patients have seen a drastic improvement in their quality of life through providing ENFD analysis and subsequent treatment," said Lilly Khavari, DPM, a Texas-based physician-owner. "Your patients will love you for offering this test."

For more information on how to perform an ENFD procedure, request your complimentary ENFD test kits and an in-service, visit bakodx.com/enfd.

DID YOU KNOW?

Conditions associated with Small Fiber Peripheral Neuropathy

• Metabolic (diabetes mellitus, metabolic syndrome, hyperlipidemia)
• Inherited (Fabry's disease, Tangier's disease, familial amyloid polyneuropathy)
• Toxic (chemotherapy, alcoholism, solvent exposure)
• Autoimmune (Sjögren's syndrome, vasculitis/polyarteritis nodosa)
• Amyloidosis (non-inherited forms of amyloidosis, e.g. lymphoma or plasma cell dyscrasias)
• Infectious (HIV, hepatitis C, Lyme disease)
• Idiopathic (For a relatively large percentage of cases, there is no identifiable cause of SFPN)

[4] Ziegler D, Low PA, Litchy WJ, et al. Efficacy and safety of antioxidant treatment with α-lipoic acid over 4 years in diabetic polyneuropathy: the NATHAN 1 trial. *Diabetes Care*. 2011;34(9):2054-2060. doi:10.2337/dc11-0503
[5] Luong KV, Nguyen LT. The impact of thiamine treatment in the diabetes mellitus. *J Clin Med Res*. 2012;4(3):153-160. doi:10.4021/jocmr890w
[6] Walker MJ Jr, Morris LM, Cheng D. Improvement of cutaneous sensitivity in diabetic peripheral neuropathy with combination L-methylfolate, methylcobalamin, and pyridoxal 5'-phosphate. Rev Neurol Dis. 2010;7(4):132-139.

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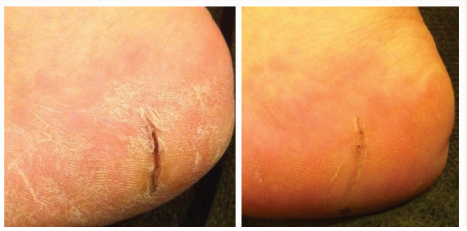

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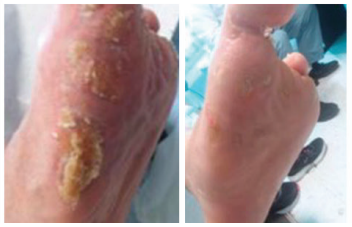

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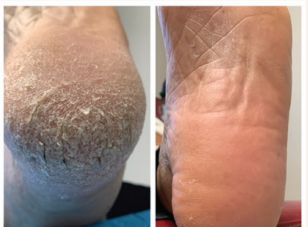

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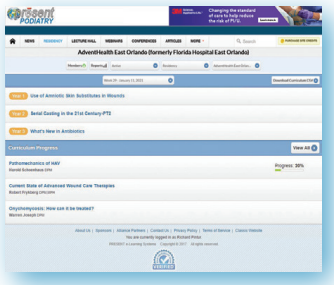

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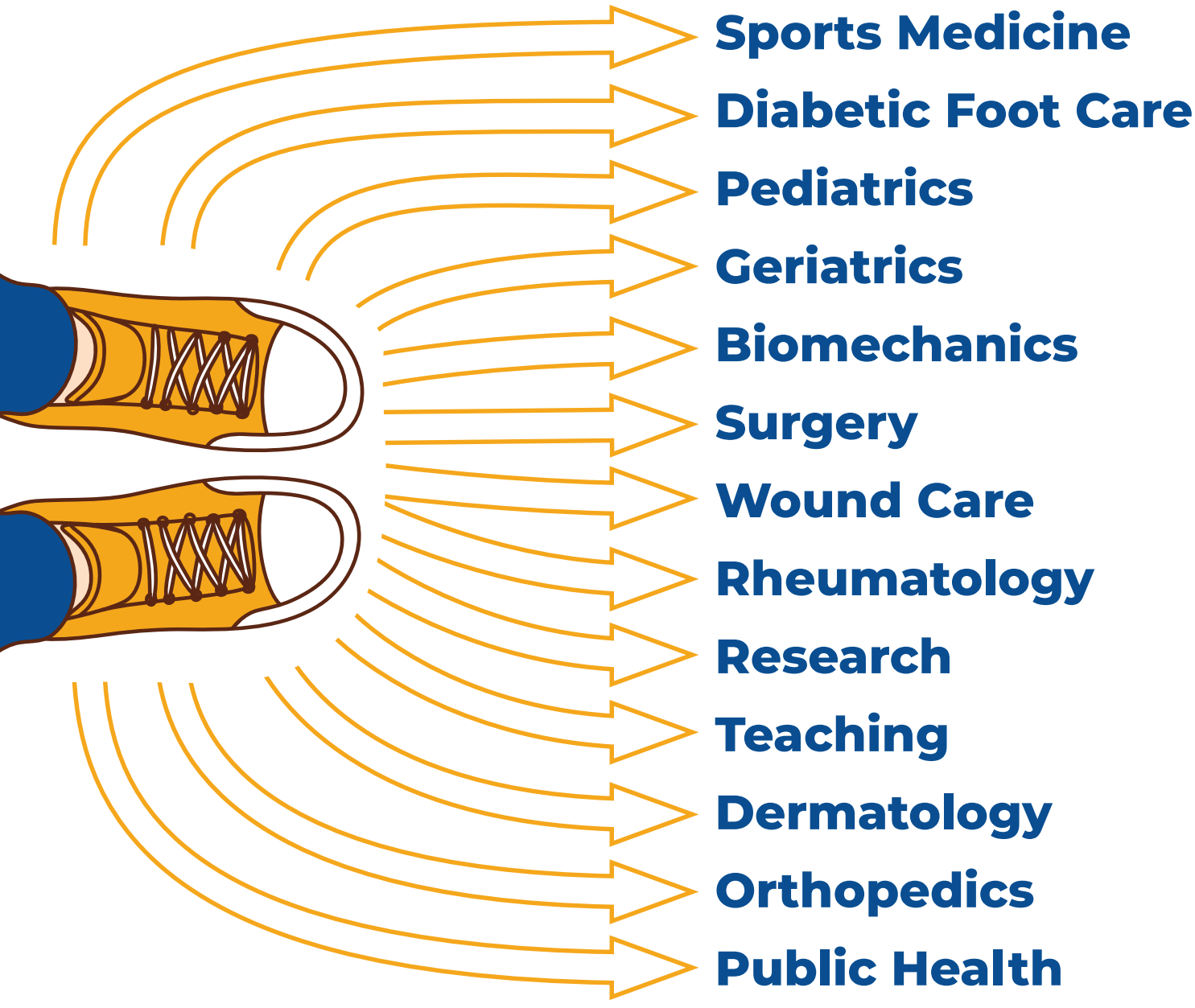

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