EXTREMITAS

JA



Vol. 9 April 2022



ELEVATING LIVES OF PATIENTS

BUILDING A FOUNDATION OF INTEGRATIVE PODIATRIC MEDICAL EDUCATION.

WWW.WESTERNU.EDU/PODIATRICMEDICINE

909.706.3933

EXTREMITAS Journal of Lower Limb Medicine

The Extremitas Editors' Choice Award

For the first time in Extremitas, student authors have the opportunity to earn a \$200 scholarship for their contribution to the journal. 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.

Congratulations to this year's winning authors, Harsh Varshney and Douglas Weng, for their research article titled *Podiatric Physician Perspective on the use of Cannabidiol (CBD) in the Treatment of Foot and Ankle Pathology*!



Harsh Varshney DPM Candidate 2024



Douglas Weng DPM Candidate 2024

Most But Not All Podiatric Residency Programs Offer Their Residents....

PRESENT Podiatric Residency Education Online!

PRESENT Podiatric Residency Education Online

This valuable service provides the online academics for the majority of the nation's podiatric residency programs.

One Lecture Each Week Per Resident Year

This extensive curriculum allows residents from programs all over the country to view the same standardized lectures each week.



Residency Education Summit East Teaneck Marriott, Teaneck, NJ August 12-14, 2022



MIDWEST

Residency Education Summit Midwest Hilton Chicago / Oak Brook Hills, IL September 9-11, 2022



Letter from the Editor in Chief

Dear Readers,

The continued efforts by healthcare professionals are finally flattening the curve of the COVID-19 pandemic. WesternU has adapted to these challenges over the past two years and is now able to participate in a hybrid curriculum. As WesternU looks forward to the future, we reflect on the sacrifices made by healthcare professionals for the countless hours spent fighting for patients. If the pandemic has taught us anything, it is the fact of how vital research is in the healthcare system. Extremitas continues to uphold the tradition of quality student research in light of these challenges.

This year's publication offers a great variety of subjects with a record number of non-podiatry student submissions, including some non-WesternU health professional students teaming up with WesternU students. The passion for research is showcased in this edition of Extremitas through the wide variety of research subjects ranging from pain management and treatment modalities to rare pathologies and original research.

I am beyond grateful to have had an excellent team of editors this year. Their determination and hard work made this edition of extremitas possible through rigorous editing and research analysis. The Extremitas publication would not exist without the research article submissions from the authors. As a reward for their hard work, authors were given the opportunity to be awarded the Extremitas Editor's Choice Award Scholarship voted on by our editing staff and Dr. Shapiro. Thank you to the authors and editors for all their efforts in contributing to this year's publication.

This year's publication would not be made possible without support from WesternU faculty and sponsors. I would like to thank Dean Satterfield for her continued support of Extremitas and her commitment to the WesternU CPM family. Thank you to Dr. Shapiro for continuing to guide this publication to its maximum potential year after year. I would like to thank our sponsors that graciously donated to this year's edition of Extremitas. Lastly, I would like to thank my beautiful and loving wife, McKenzie, for supporting me as this year's Editor in Chief.

It is with great pleasure to introduce the 9th volume of Extremitas: Journal of Lower Limb Medicine!

Sincerely,

Nathan Fischer Editor In Chief DPM Candidate 2023

2022 Editorial Team



ASSISTANT EDITOR *Elaine Chu* DPM Candidate 2024



ASSISTANT EDITOR *Vivian Chan* DPM Candidate 2024



ASSISTANT EDITOR *Harsh Varshney* DPM Candidate 2024



EDITOR *Jonathan Ibanez* DPM Candidate 2023





EDITOR EDITOR Alexander Carrillo-Kashani Sean Nguyen DPM Candidate 2023 DPM Candidate 2023



EDITOR *Ibrahim Abukhieran* DPM Candidate 2023



COVER DESIGNER *Gordon Yee* DPM Candidate 2023



SENIOR EDITOR *Aleksa Martin* DPM Candidate 2023



EDITOR IN CHIEF *Nathan Fischer* DPM Candidate 2023



SENIOR EDITOR *Michael Amedeo* DPM Candidate 2023



JOURNAL FACILITATOR **Dr. Jarrod Shapiro, DPM** WesternU Faculty

REFLECTIONS FROM THE TEAM

"Having the opportunity to be a part of the Extremitas editorial team for the past two years has been both an honor and one of my favorite experiences of podiatry school thus far. Thank you to Dr. Shapiro, our sponsors, and our awesome team of editors for making this journal possible each year."

Michael Amedeo, DPM Candidate 2023

"Working with the Extremitas editorial team for the past two years has been a rewarding and fulfilling experience. Thank you to our sponsors, our advisor Dr. Shapiro, and our university's knowledgeable librarians, all who helped us meet our goals with this edition."

Aleksa Martin, DPM Candidate 2023

"I feel grateful to have been a part of this years' Extremitas team. I am so proud of us for all the hard work and effort put in to make this journal great. Thank you to Dr. Shapiro, our sponsors, and most importantly, our authors and readers. I hope you enjoy this edition as much as we did."

Alexander Carrillo-Kashani, DPM Candidate 2023

"I am honored to be a part of the Extremitas team this year. It has been my greatest pleasure to work with this team of editors and our advisor, Dr. Shapiro. I am grateful to all those who entrusted their hard work to us. Finally, thank you to all the sponsors who made this year's issue possible."

Jonathan Ibanez, DPM Candidate 2023

"Being a part of this team has been a huge blessing and a life-changing opportunity that has further increased my passion for the field of podiatric medicine. It was a pleasure working with this amazing team and I am fortunate to be a part of this incredible experience. Thank you to everyone for making this all possible."

Ibrahim Abukhieran, DPM Candidate 2023

"Working with this talented group of individuals has been nothing short of amazing. Each member offered a unique point of view for a fruitful learning experience. Thank you to all the authors, sponsors, and leaders for making the publication of this journal possible."

Sean Nguyen, DPM Candidate 2023

"It has been a privilege to work with my fellow teammates on this year's journal. Medical research is crucial in the realm of medicine and I thank our sponsors and Dr. Shapiro for supporting this year's edition."

Vivian Chan, DPM Candidate 2024

"I am grateful for this opportunity to collaborate with such an outstanding team. It has been a privilege to further the podiatric field while cultivating my passion for research. A special thank you to the sponsors and Dr. Shapiro for having made this possible, and I hope the readers also find this year's journal to be informative and beneficial for clinical application."

Elaine Chu, DPM Candidate 2024

"It has been a pleasure to work alongside such a talented group of editors in promoting academic research and literature. Our sponsors, authors, and faculty advisor, Dr. Shapiro, receive the utmost applause for allowing us to continue our work. I am honored to welcome all to read the astounding articles in this year's publication."

Harsh Varshney, DPM Candidate 2024

Table of Contents

TREATMENT MODALITIES:

Co	DescriptionDescriptio
Co Hi	omparative Analysis of Iliotibial Band Release versus Corticosteroid Injection in otibial Band Syndrome Jacob Abjelina, B.S., Alex Dang, B.S., and Chanelle Mariano, B.S
Ef	ficacy of Stem Cell Therapy on Achilles Tendon Rupture Repair
A	Review of the Use of Platelet Rich Plasma in Treatment of Diabetic Foot Ulcers
Th of	ne Effectiveness of Nerve Growth Factor (NGF) Monoclonal Antibody for the Treatment Knee Osteoarthritis
Th	ne Effectiveness of Platelet-Rich Plasma Treatment of Plantar Fasciitis: A Literature Review 21 Gillian Mathews, B.S.
Th	ne Role of Hormesis in Polyphenol Dietary Treatments for Diabetic Neuropathy
A (the	Comparison of the Efficacy of Pharmacological, Physical, and Compression Therapy in e Treatment of Stasis Dermatitis: A Literature Review
In	travenous vs. Oral Antibiotics for Nonhematogenous Osteomyelitis: A Review
<u>POPI</u>	ULATION FOCUSED:
Th	ie Importance of Foot Hygiene and Proper Footwear for Preventing Disease

in Homeless Populations	7
Foot Pain and Plantar Pressure in Pregnancy: A Literature Review	10
Psychological Impact of Lower Limb Amputations on Patients with Diabetes	14

SURGERY AND SPORTS MEDICINE:

Treatment and Impact of Accessory Navicular Syndrome in an Athlete and Non-Athlete Populations
Savannah Santiago, B.S. and Hadia Bharoocha, B.S.
Outcomes of Operative vs. Nonoperative Management of Displaced, Intra-Articular Calcaneus Fractures: A Current Review
Compare and Contrast Keller Arthroplasty versus Arthrodesis for Hallux Rigidus 58 Alex Dang, B.S., Rahul Natarajan, B.S., and Harsh Varshney, B.S.
Retrospective Comparison of Tarsal Coalition Resection versus Arthrodesis
Kirschner Wire Fixation versus Implants for Proximal Interphalangeal Joint Arthrodesis 67 Jonathan Ibanez, B.S., Alex Dang, B.S., and Rahul Natarajan, B.S.
Pes Planus: Prevalence, Complications, and Treatment in Athletes
RARE PATHOLOGY:
Klippel-Trenaunay Syndrome: a review of management and treatment of lower extremity vascular malformations
Unmasking Acral Lentiginous Melanoma
PAIN MANAGEMENT:
Comparing and contrasting peripheral nerve blocks and spinal anesthesia in lower extremity surgery
Comparing Local Perioperative Methods and Antibiotic Prophylaxis in SurgicalSite Infection PreventionSravani Sai Alla, B.S., Jessica Trujillo Landeros-Arnold, B.S., and Anushka Sunil Ramnani, B.S.
Examining the Overall Efficacy of the Addition of an Interspace Between the Popliteal Artery and Capsule of the Posterior Knee (iPACK) Block to an Adductor Canal Block in the Setting of Major Knee Surgery, a General Review

ORIGINAL RESEARCH AND CASE STUDY:

Evaluation of Similarities and Discrepancies in International Podiatry9 Jacob Abjelina, B.S. and Chanelle Mariano, B.S.	6
Podiatric Physician Perspective on the use of Cannabidiol (CBD) in the Treatment of Foot and Ankle Pathology	02
Harsh Varshney, B.S. and Douglas Weng, B.S. Atypical Presentation of a Plantar Ganglion Cyst: A Case Study 10	08
Jonathan Ibanez, B.S., Michael Amedeo, B.S., and Tanisha Minasian, B.A.	

Comparative Analysis of Tinea Pedis Treatments

Daniel Ahdoot, B.S. and Sean Lee, M.S., B.A.

ABSTRACT

Objective: To perform a literature review on relevant studies regarding the efficacy of different tinea pedis treatments, and to compare various antifungal treatments, including novel fungicides to a common ergosterol synthesis inhibitor allylamine, Terbinafine.

Methods: Relevant research found through PubMed, Google Scholar, and Western University Pumerantz Library database. Key words like "tinea pedis treatment" and "athlete's foot" were used to find relevant literature.

Results: Terbinafine resolved tinea pedis at a higher percentage than placebo treatments. While clotrimazole showed promising results, terbinafine was shown to have greater efficacy (negative direct and culture mycology, as well as two or less symptoms of tinea pedis) when compared to clotrimazole. Moreover, terbinafine yielded better results in treating tinea pedis than griseofulvin.

Conclusion: Terbinafine appears to be the most effective drug for tinea pedis treatment. Cream treatments are more heavily researched and are the preferred treatment type, but oral treatment may be effective as well. Hydrogel may be added to cream treatment to improve efficacy.

Introduction

Tinea pedis (commonly known as 'athlete's foot') involves cutaneous fungal infection originating from dermatophyte infection, leading to keratin degradation.¹ It has been reported that as much as 70% of the population is infected with athlete's foot at some point in their lives.² It is not a life-threatening condition, but improper treatment can lead to persistent discomfort and itching, ultimately resulting in more serious issues such as fissures and radiation to other parts of the body.¹ In addition, tinea pedis is highly contagious and inadequate treatment can cause allergic diseases and secondary bacterial infections.³ due to its similarity with other dermatophyte infections; previous literature had reported that tinea pedis was a condition resulting from a rare infection by the organism involved in tinea capitis, but this equivocation led to misdiagnosis and insufficient treatment for tinea pedis.4,5

Treatment for tinea pedis has improved since the 1950s when topical interventions (cream, sprays, lotions) were the only available option.⁶ Medications for tinea pedis aim to inhibit ergosterol synthesis, which is a necessary component of fungal cell membranes.⁷ Patients are usually recommended to continue topical treatment for 1-4 weeks, but compliance throughout the whole treatment period is an issue, decreasing the efficacy of the treatment.⁸ Antifungal oral treatments have been introduced as an alternative to topical drugs, although they are generally reserved for chronic conditions or when topical drugs fail. They may provide a more convenient and potentially more potent treatment option, but may also have undesirable adverse effect.⁶ The treatments being compared to terbinafine include clotrimazole, griseofulvin, itraconazole, and fluconazole. The indications for terbinafine include dermal mycosis, onychomycosis due to dermatophyte, and tinea capitis.⁹ Clotrimazole's indications are candidal vulvovaginitis, candidiasis (topical), oropharyngeal candidiasis (prophylaxis), and pityriasis versicolor.¹⁰Griseofulvin has a number of indications, including onychomycosis due to dermatophyte, tinea barbae, tinea capitis, tinea corporis, tinea cruris, and tinea pedis.¹¹ Itraconazole has many indications, such as aspergillosis, blastomycosis, candidiasis of the esophagus due to HIV infection, disseminated histoplasmosis, non meningeal disseminated histoplasmosis due to an HIV infection, HIV induced oropharyngeal candidiasis, onychomycosis due to dermatophyte, oropharyngeal candidiasis, and pulmonary histoplasmosis.¹² A wide range of indications for fluconazole involve candidiasis (prophylaxis), candidal vulvovaginitis, candidiasis, candidiasis of the esophagus, candidiasis of urogenital site, cryptococcal meningitis, and oropharyngeal candidiasis.13

This review will evaluate different treatments for tinea pedis with their benefits and potential drawbacks. By synthesizing results from various studies, this review will aim to compare the effectiveness of terbinafine to other tinea pedis therapies, as well as document any challenges and adverse effects deriving from the treatment.

Methods

Relevant research was found using PubMed, Google Scholar, and the Western University Pumerantz Library database. Keywords such as "tinea pedis treatment" and "athlete's foot" were used when searching for literature. Research chosen was not limited to a timeframe, but more recent literature (within five years) was preferred over older literature. Literature that studied other foot conditions was excluded, so the scope of this review was strictly on tinea pedis. Eight sources were gathered from this search to evaluate the efficacy of current and novel antifungal treatments.

Results

A novel topical single-dose formulation of terbinafine film-forming solution (FFS) showed that after six weeks, groups treated with terbinafine 1%, 5%, and 10% FFS were 66%, 70%, and 61% effective, respectively, while the placebo was only 18% effective.¹⁴ Effective treatment rate was calculated based on direct and culture mycology along with minimal signs and symptoms, recording two or less with mild symptoms.

Another study used microscopy and mycological cultures while assessing clinical signs, symptoms, and adverse events to measure the potency of a 1% terbinafine film-forming solution (FFS) compared to a placebo. The results showed that those treated with 1% terbinafine FFS had an effective treatment rate of 63%, a clinical cure rate of 30%, a mycological cure rate of 86%, a negative microscopy rate of 90%, and a negative mycological culture rate of 90%, while the placebo had rates of 6%, 12%, 24%, and 27% respectively ($p \le 0.001$) after six weeks.¹⁵

To measure the efficacy of terbinafine compared to clotrimazole, negative results on microscopy and culture were recorded to calculate the mycological cure rate. Treatment efficacy was then determined by looking at both the mycological cure rate as well as the severity of signs and symptoms. Measurements were taken on the first, second, third, fourth, and sixth weeks. Terbinafine treatment's mycological cure rate was found to be 93.5% after four weeks, while the cure rate for the clotrimazole treatment was 73.1% (p = 0.0001). In the sixth week, the mycological cure rate for terbinafine increased to 97.2% and 83.7% for clotrimazole (p = 0.001). The effective treatment rate for terbinafine at week four was 89.7% and 58.7% for clotrimazole (p = 0.0001). In the sixth week, the effective treatment rate for terbinafine was maintained at 89.7%, while the rate for clotrimazole increased to 73.1% (p = 0.002).¹⁶

To examine the effectiveness of oral therapies against tinea pedis, fifteen randomized controlled trials of oral treatments involving clinically diagnosed participants (confirmed by microscopy and dermatophyte growth in culture) were studied. Under independent study selection, two review authors assessed the risk of bias and extracted data. Two trials comparing terbinafine (ergosterol synthesis inhibitor)

and griseofulvin (fungal mitotic inhibitor) in 71 participants resulted in a pooled risk ratio (RR) of 2.26 with a confidence interval (CI) of 95%, indicating a preference for terbinafine. Two other trials comparing terbinafine and itraconazole (ergosterol synthesis inhibitor) to a placebo demonstrated that both terbinafine and itraconazole were effective when compared to the placebo, with the 31 participants who used terbinafine having a pooled RR of 24.54 with a 95% CI, and the 72 participants who used itraconazole yielding a pooled RR of 6.67 with a CI of 95%. The trials set up to analyze the difference in efficacy between terbinafine and itraconazole, fluconazole (ergosterol synthesis inhibitor) and itraconazole, fluconazole and ketoconazole (ergosterol synthesis inhibitor), and griseofulvin and ketoconazole showed no significant differences between the drugs. The results of this study pointed to terbinafine being a more effective oral treatment method for fungal infections of the skin of the foot than griseofulvin. Additionally, all of the drugs were shown to cause some type of adverse effect, gastrointestinal effects being the most prominent.6

Discussion

Based on the research explored, tinea pedis can be treated effectively with different interventions. Terbinafine appears to be the most common method of treatment, and has repeatedly been shown to be effective when compared with placebo cases.^{14,15} In addition, terbinafine cure rates were significantly higher when compared clotrimazole to treatment.¹⁶ Interestingly, one study did note that there was no significant difference in efficacy when terbinafine treatment was compared to other drugs that treat tinea pedis; however, the authors did mention that terbinafine may be more effective than griseofulvin.⁶ Therefore, other drugs such as itraconazole and fluconazole may be effective alternative options for tinea pedis treatment, and terbinafine does not have to be relied upon as the sole treatment option.

Another aspect of treatment to be considered is the efficacy of different methods of applying the treatment. Comparing terbinafine and clotrimazole creams as the methods of treatment, terbinafine was found to be more effective.¹⁶ Terbinafine compared to placebo treatments was also more effective.¹⁵ It is unsurprising that there is more research on cream treatments than oral treatments due to cream treatments being the only available option before the 1950s as mentioned before.⁶ With cream treatments requiring compliance throughout the treatment period, oral methods may therefore improve treatment efficacy due to its ease of treatment application, especially for people who have difficulty reaching the area of infection. However, it may be wiser to reserve oral treatments for more severe cases of tinea pedis or when cream treatments do not work due to side effects.⁶ Further research that directly compares oral and cream treatments for the same type of drug can help when weighing the potential costs and benefits of each treatment type.

Terbinafine may be the most effective current treatment option for tinea pedis. However, exploring the efficacy of other drugs and therapies in treating tinea pedis is essential for cases in which terbinafine may prove futile. Additionally, there is the potential to combine terbinafine with other drugs, in hopes of increasing potency of treatment.

The research referenced as well as this study as a whole had some limitations. One limitation is that many of the studies referenced did not mention severity of infection for the patients chosen. Patients with more severe cases of tinea pedis may have had decreased efficacy from treatment, and those with less severe cases may have had their symptoms resolved quicker. If a treatment type had a disproportionate amount of less/more severe patients, this would skew results. Another limitation was that fungal elements may remain present in skin without causing any noticeable signs or symptoms.¹⁵ The criteria for efficacy in many of the papers referenced included patients showing two or less symptoms. It is therefore possible that patients may have reported no symptoms, but were actually not cured, making efficacy percentages higher as a result.

Conclusion

Terbinafine appears to be the most effective drug for tinea pedis treatment. Other drugs such as clotrimazole and itraconazole may also be used as less-effective alternative treatments. Cream treatments are the predominant treatment option due to the wealth of literature on them. However, oral treatments may show to be effective as well with more evidence and research.

References

- 1. Crawford F. Athlete's Foot. *Clinical Evidence*. 2009;07:1712.
- Rippon JW. (1988). Dermatophytosis and dermatomycosis. In: Medical mycology: the pathogenic fungi and the pathogenic actinomycetes. Philadelphia: WB Saunders.
- Ilkit M, Durdu M. Tinea pedis: The etiology and global epidemiology of a common fungal infection. *Critical Reviews of Microbiology*. 2015; 41(3):374-388.
- Whitfield A. (1908). A note on some unusual cases of trichophytic infection. Lancet 172:237–8.
- Merlin K, Kilkenny M, Plunkett A, Marks R. (1999). The prevalence of common skin conditions in Australian

school students: 4 Tinea pedis. Br J Dermatol 140:897-901.

- Bell-Syer SEM, Khan SM, & Torgerson DJ. Oral treatments for fungal infections of the skin of the foot (Review). *The Cochrane Database of Systematic Reviews*. 2012, 10:1-50.
- Makola NF, Magongwa NM, Matsaung B, Schellack G, & Shellack N. Managing athlete's foot. *South African Family Practice*. 2018; 60(5):37-41.
- Tosti A, Hay R, Arenas-Guzman R. Patients at risk of onychomycosis- risk factor identification and active prevention. *Journal of European Academic Dermatology Venereol.* 2005; 19(1):13–16.
- Terbinafine. In: IBM Micromedex
 BRUGDEX® (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://wwwmicromedexsolutions-com.proxy.westernu.edu/ (cited: 02/10/22).
- Clotrimazole. In: IBM Micromedex

 PRUGDEX®
 (electronic version). IBM Watson Health, Greenwood
 Village, Colorado, USA. Available at: https://www micromedexsolutions-com.proxy.westernu.edu/ (cited:
 02/10/22).
- Griseofulvin.. In: IBM Micromedex

 PRUGDEX®
 (electronic version). IBM Watson Health, Greenwood
 Village, Colorado, USA. Available at: https://www micromedexsolutions-com.proxy.westernu.edu/ (cited:
 02/10/22).
- Itraconazole. In: IBM Micromedex

 PRUGDEX®
 (electronic version). IBM Watson Health, Greenwood
 Village, Colorado, USA. Available at: https://www micromedexsolutions-com.proxy.westernu.edu/ (cited:
 02/10/22).
- Chauvin MF, Viguie-Vaillant C, Kienzler JL, & Larnier, C. Novel, Single-Dose, Topical Treatment of Tinea Pedis Using Terbinafine: Results of a Dose-Finding Clinical Trial. *Mycoses*. 2007; 51, 1-6.
- Li RY, Wang AP, Xu JH, Xi LY, Fu MH, Zhu M, Li XQ, Lai W, Liu WD, Lu XY, & Gong ZQ. Efficacy and safety of 1% terbinafine film-forming solution in chinese patients with tinea pedis: a randomized, double-blind, placebo-controlled, multicenter, parallel-group study. *Clinical Drug Investigations*. 2014; 34:223-230.
- Evans EGV, Dodman B, Williamson DM, Brown GJ, & Bowen RG. Comparison of terbinafine and clotrimazole in treating tinea pedis. *British Medical Journal*. 1993; 307:645-64

Comparative Analysis of Iliotibial Band Release versus Corticosteroid Injection in Iliotibial Band Syndrome

Jacob Abjelina, B.S., Alex Dang, B.S., and Chanelle Mariano, B.S.

ABSTRACT

Objective: To summarize the current research on the evaluation and management of iliotibial band syndrome in runners.

Methods: A literature review on relevant research articles pertaining to iliotibial band release versus corticosteroids injection in iliotibial band syndrome was conducted using Pubmed and Google Scholars databases. Additionally, search terms such as: "iliotibial band surgery," "iliotibial band treatment," and "iliotibial band syndrome" were used. **Results:** There was a decrease in visual analogue scale (VAS) score in 53.9% of the population that underwent corticosteroid injections. Additionally, the standard of error (SEM) score went down from 197 to 140. In the group that underwent the surgical intervention through IT band release, the majority of the patients returned to prior activity within 7 weeks. Postoperatively, the Tegner score was 6 and the Lysholm score was 93.

Conclusion: Recent studies indicate that while corticosteroid injections achieve pain relief, the high recurrence rate leads patients to seek surgical intervention through IT band release. However, future studies should include a bigger sample size and longer follow-up to fully appreciate the efficacy of either treatment.

Introduction

The iliotibial band is a thick band of fascia that originates from the external iliac crest and inserts on the lateral condyle of the tibia. Repetitive flexion and extension of the knee leads to iliotibial band syndrome. Iliotibial band syndrome is a common injury in athletes, especially runners, resulting in pain at the lateral aspect of the knee. This pain may radiate proximally or distally to the joint line and depending on the severity, may subside with cessation of activity.¹ There are several etiologies proposed for iliotibial band syndrome such as friction of the fascia against the lateral condyle of the femur or compression of the band under the tissues layers of the fat and skin. However, the most common etiology agreed upon is chronic inflammation due to overuse during activities that require repetitive flexion and extension of the knee.²

Iliotibial band syndrome is a clinical diagnosis that can usually be made through a thorough history and physical. For inconclusive cases, an MRI may be used to image and confirm iliotibial band syndrome. The most common chief complaint amongst patients of iliotibial band syndrome is lateral knee pain worsened with activity.

Conservative treatments often include a stretching protocol, physical therapy, bedrest, and corticosteroid injections. Many athletes achieve symptomatic relief with conservative treatment, however in some refractory cases, surgical intervention is needed.² Although several interventions have been proposed in the treatment of iliotibial band syndrome, it is unclear which of the available techniques results in the best outcomes for

the patient. There is a lack of studies comparing the results of conservative treatment such as corticosteroid injections and surgical treatment such as an iliotibial band release. The purpose of this review is to compare and contrast corticosteroid injections and an iliotibial band release to better outline the pros and cons of each procedure.

Methods

A search for relevant research articles regarding iliotibial band syndrome pathology and treatment were conducted through the PubMed and Google Scholar databases. Search terms and keywords included: "iliotibial band surgery," "iliotibial band treatment," and "iliotibial band syndrome." Articles of case studies involving specific patient groups of iliotibial band syndrome cases were collected. Inclusion criterias include VAS score, SEM score, patients at least 18 years old, and patients with IT band syndrome confirmed by imaging modalities. Exclusion criterias include blogs, opinion articles, patients less than 18 years old, and patients with unrelated knee pain.

Results

Conservative Treatment

Strauss et al. summarized a randomized controlled trial by Gunter et al. on 18 patients with iliotibial band syndrome. In the control group, patients were injected with two mL of one percent lidocaine and in the experimental group, patients were given a mixture of one mL of one percent lidocaine plus one mL of methylprednisolone. The mean standard error of measurement (SEM) was used to measure pain score during treadmill running at day 0, day 7, and day 14 after injection. The lower the SEM score, the lower the pain level the patient experienced. If the patient experienced no pain, then the lowest possible score would be 0. Both groups were instructed to rest and apply ice for a minimum of 20 minutes daily to the area between visits. At day 0, the control group had an average score of 197, while the experimental group had a score of 222. The score went down to 178 for the control group, and 140 for the experimental group. At day 14, both groups experienced another decrease where the control was now 157 and 103 for the experimental group. After day 14, neither group reported any pain.^{2,3}

Beals and Flanigan reviewed a similar randomized controlled trial to assess the corticosteroid injection as a conservative treatment for IT band syndrome. The study consisted of 18 runners with acute onset of symptoms within the last 14 days. Ice was applied to the injection area every 12 hours to alleviate muscle soreness. The participants were instructed to restrict all running activities for 14 days after injection. These 18 runners were then randomly divided into two groups, each group consisted of 9 runners. The first group received a corticosteroid injection that contained 40 mg of methylprednisolone acetate, while the second group received a placebo injection. The first group experienced a decrease in Visual analogue scale (VAS) for pain perception in 53.9% of all participants. The second group did not experience a change in VAS.⁴

Surgical Treatment

When steroid injections failed as a conservative measure and the patient continued to experience pain for more than six months, Strauss proposed surgical interventions through either percutaneous or open iliotibial band release.² Strauss summarized another study by Holmes et al. in which four patients underwent percutaneous procedure under local anesthesia. However, three patients eventually had to be converted to an open procedure due to recurrent IT band syndrome.5 Strauss continued by summarizing a separate case series by Holmes et al. in which 21 cyclists underwent open IT band release procedure through a direct release over the lateral epicondyle. A total of 17 patients were able to return to their normal cycling activity by six to eight weeks.⁵ Similarly, Strauss et al summarized a different study by Martens et al on 19 patients who underwent open IT band release. The technique for this procedure is slightly different than Holmes et al. in which the knee is held in a flexed position at 30 degrees, and a 2 cm incision made over the posterior IT band to release. All 19 patients reported good outcomes and were able to return to normal activities by an average of 7 weeks post-operatively.⁶ Lastly, Holmes described an alternative technique by Richard et al. in which a Z-plasty is made to release the IT band through a 5 cm oblique incision over the IT band. The procedure was performed on 8 patients with an average of 76-month follow-up. Data reported 97% of good outcomes with no complications at follow-up appointments.⁷

Beals and Flanigan analyzed another study in which 45 athletes failed a six-month trial of corticosteroid treatment and sought open IT band release through a transection of the posterior half of the IT band fibers. Postoperatively, 38 patients reported excellent results, 6 with fair results, and 1 had poor results. Ultimately, 75.6% of all the athletes required additional surgery due to recurrent IT band syndrome.³

Walbron et al. proposed an alternative technique to release the IT band from the Gerdy's tubercle. The approach required a 2 cm dissection above the Gerdy's tubercle with the IT band partially released through a longitudinal incision. A total of 14 patients participated in the study with a mean of 27 months follow-up and a standard deviation of 20.6 months. All patients were instructed to resume cycling and swimming at 2 weeks and running at 6 weeks postoperatively. The average time to return to preoperative conditions was 4 months with a standard deviation of 2.8 months. From the total of 14 patients, 8 were very satisfied, 3 were satisfied, and 2 were not. The average Tegner score for activity rating system was 6 with a standard deviation of 2 and the average Lysholm score to measure symptoms and function was 93 with a standard deviation of 7. Deep vein thrombosis (DVT) was observed in 2 patients.8

A 2021 study performed by Villanueva et al. examined the possibility of minimizing risks involved in IT band release by using ultrasound-guided modality. A prospective study was performed on 32 athletes, two of which required bilateral treatment, and 27 of which were males. All patients were refractory to conservative treatment protocol which includes physical therapy and local corticosteroid injections. Patients had confirmed diagnoses of IT band syndrome via MRI and/or CT scan. Patients received either a two-portal Z-plasty or a one-portal transverse cut. Recession was performed between 1-2 cm from the lateral epicondyle and distal to the proximal pole of the patella, along the posterior surface of the IT band. Post-operation, subjects were instructed to take painkillers for 1-2 days and minor hematoma was the main complication in less than half of the subjects. Patients were allowed active flexion and extension immediately post-surgery. Walking on one or two elbow crutches was allowed as well but was typically not needed after 2-3 days post-surgery. Patients were allowed to participate in physical therapy for 1-2

months, in which running was allowed after 4-6 weeks. Complete recovery took approximately 8-12 weeks. All patients reported back as satisfied after three months and were able to return to their sports (soccer, basketball, military, running) without restriction. The average Lysholm score before surgery was 68 and after surgery improved to 97. Similarly, the VAS average scores for sports activity improved from 7 before surgery down to 0 after surgery.⁹

Discussion

IT band syndrome is a common cause for knee pain within the athletic population, especially runners and cyclists. As a result, several techniques have been proposed over the years ranging from conservative to surgical. Although there has been no research that effectively compares corticosteroid injection to IT band release procedures, there were studies that indicate a high recurrent rate with corticosteroid injections. Furthermore, research has shown that multiple corticosteroid injections to the IT band could lead to the tendon to become less pliable and cause restricted movement. As a result, corticosteroid injections are often reserved for chronic IT band syndrome.¹⁰

Additionally, the study Strauss et al. summarized, patients report to symptom relief after the corticosteroid injection. Although, there is a lack of sensitivity to the study due to the fact that neither group reported any pain after 14 days. As a result, there is an insufficient measurement for the long-term efficacy of corticosteroid injections. On top of that, the controlled group also experienced a decrease in SEM score in between visits at day 7, and 14 indicate that icing and rest do play an important role in pain relief.²

Beals and Flanigan's study shows corticosteroid injection does in fact increase pain relief by lowering VAS in more than half of the experimental group.⁴ Unfortunately, corticosteroid injections only provide temporary relief and most patients do experience recurrent IT band syndrome that lead them to seek the surgical route as the ultimate option for pain relief.^{2,10}

IT band release can either be done through the open or percutaneous approach and there are advantages and disadvantages to each technique. The open procedure is slightly more complicated than the percutaneous procedure due to higher risk of common peroneal nerve damage and scarring.² On the other hand, the percutaneous method reduces the risk for both nerve damage, scarring, operating time, and postoperative infection. However, Strauss et al. summarized the study by Holmes et al. found that 75% of percutaneous procedures experienced recurrent IT band syndrome. Ultimately, those patients opted in for the open procedure for a higher success rate.

There are several approaches for the IT band release procedure in this paper and although no research has been conducted to determine if one technique is indeed more effective than the other, all surgical interventions have shown to have positive outcomes. The exception is the open IT band release through transection of the posterior half of the IT band, which shows recurrent IT band syndrome in 3/4 of patients.⁴ Additionally, 2 patients have DVT in Walbron et al. study with partial release through longitudinal transection. However, these cases are mild and clots eventually dissolve with thrombolytics. One of the disadvantages of these studies are the small sample size and short follow-up time. As a result, future studies should include more patient recruitment and a longer follow-up to fully appreciate the potential outcomes of IT band release procedures in the long run.⁸

In the efforts to improve patient outcomes and reduce post-surgical complications, the study performed by Villanueva et al., examined minimally invasive ultrasound-guided IT band release which significantly decreased VAS scores among 32 patients from 7 down to 0. The procedure performed reduced complications by bypassing the need for lowmolecular-weight heparin and large incision. Patients then had greater postoperative cosmetic outcomes and a lower risk of post-surgical pain and thrombosis. The ultrasound-guided function of visibility also reduces the risk of damaging unintended structures such as the lateral genicular arteries and veins during resection. One downside of the effectiveness of this procedure is the limited scope of athletes involved in this study. The study includes only 5 women out of the 32 subjects. 23 of the 32 patients were primarily runners and the other 9 ranged from basketball players, boxers, cyclists, military personnel, and firemen. The need for lateral movements within these physical activities vary and therefore, Z-plasty versus complete resection may be patient-specific.9

By continuing to reduce the risks associated with surgical release of the iliotibial band while producing greater postoperative patient outcomes, surgical treatment could potentially draw near as an efficient and effective protocol for treatment of iliotibial band syndrome, as the use of corticosteroid injections may not be the most stable form of longterm treatment due to the risk of eventual motion restriction leading to the need for surgery. However, some IT band release studies include data on postoperative outcomes as either "excellent," "good," or "fair" without any indication as to how or what these conditions are based upon. Without clarity on these outcomes, it is hard to truly appreciate the full potential of the procedure.

Conclusion

The purpose of this review is to outline the pros and the cons of each technique so that patients can make an informed decision when deciding which route to take for treatment of iliotibial band syndrome. Over the years, there have been discussions as to whether or not one technique is superior to another. Although some studies leaned toward the surgical route due to high recurrent rate from conservative treatments, flaws such as small sample size and immediate positive effects do not necessarily draw a definitive conclusion as to whether one technique is truly superior to another. Therefore, treatment should continue to be tailored to patient-specific lifestyle and activity.

References

1. M. Fredericson and A. Weir, "Practical management of iliotibial band friction syndrome in runners," *Clinical Journal of Sport Medicine*, vol. 16, no. 3, pp. 261–268, 2006.

2. Strass EJ, Kim S, Calcei J, Park D. Iliotibial band syndrome: evaluation and management. *American Academy of Orthopaedic Surgeon*. 2011;19(12):728-36.

3. Gunter P, Schwellnus MP. Local corticosteroid injection in iliotibial band friction syndrome in runners: A randomized controlled trial. *Br J Sports Med.* 2004;38(3):269-72.

4. Beals C & Flanigan D. A Review of Treatments for Iliotibial Band Syndrome in the Athletic Population. *Journal of Sports Medicine (Hindawi Publishing Corporation).* 2013, 367169.

5. Holmes JC, Pruitt AL, Whalen NJ. Iliotibial band syndrome in cyclists. *Am J Sports Med.* 1993;21(3):419-24.

6. Martens M, Libbrecht P, Burssens A: Surgical treatment of the iliotibial band friction syndrome. *Am J Sports Med.*

1989;17(5):651-54.

7. Richards DP, Alan Barber F, Troop RL: Iliotibial band Z-lengthening. *Arthroscopy*. 2003;19(3):326-29.

8. Walbron P, Jacquot A, Geoffroy JM, Sirveaux F, Molé D, Iliotibial band friction syndrome: An original technique of digastric release of the iliotibial band from Gerdy's tubercle. 2018; 104(8): 1208-13.

9. Villanueva, M., Iborra, Á., Sanz-Ruiz, P., & Noriega, C.. Ultrasound-guided release for iliotibial band syndrome: A novel ultraminimally invasive surgical procedure. *The Knee*; 2021; *30*, 9–17.

10. Anderson GS. Iliotibial Band Friction Syndrome. *The Australian Journal of Science and Medicine in Sport* 1991; 81-83.

Efficacy of Stem Cell Therapy on Achilles Tendon Rupture Repair

Alex Dang, B.S., Harsh Varshney, B.S., Douglas Weng, B.S.

ABSTRACT

Objective: The purpose of this literature review was to assess the efficacy of the studies encompassing the following question of if there is a positive correlation between the use of stem cells and Achilles tendon rupture recovery.

Methods: Studies included in this review were held to criteria matching the study of mesenchymal stem cells (MSC) relating to tendon repair. The study focused on the development of MSC as a viable treatment modality to injury. As a literature review correlating data from multiple studies on potential indications and contraindications of use, only peer-reviewed studies were used. Studies collected were then cross-referenced to find support from other peer reviewed sources. To focus the review on the topic of efficacy and not detractors such as questions of morality and legality, studies on the latter topics are referenced but excluded in this discussion.

Results: The use of MSC in the progression of tendon rupture recovery is shown in a multitude of studies. However, opposing research also exists that shows a lack of definitive means to direct the development of stem cells into the specific tissues needed.

Conclusion: The general consensus seems to show a lack of definitive correlation between stem cell use and improvement in Achilles tendon recovery leading to limitations in the implementation of its use.

Introduction

Functional restoration of diseased or damaged tissues utilizing pluripotent cells is a polarizing topic in medicine. From nervous tissue to cartilage to even the notions of limb salvage, a treatment where any type of cell could potentially be grown seems like an ideal treatment modality. The applications of human stem cells as a treatment choice has long been considered a viable while controversial area of focus. The range of possibilities includes treating rare diseases where genetic mutations prevent the development of specific proteins to efforts in reversing normal senescence in cells. From a physiological perspective, these cells have a seemingly limitless potential in scope, and are controversial in the means of cell procurement.

Background:

Tendon tissues have limited healing capacity and the limited functional outcomes of current tendon repair are factors driving for the development of alternative approaches for tendon regeneration. The Achilles tendon is one of the most commonly affected tendons among individuals. The current treatment modalities include exercise therapy, shockwave therapy, NSAIDs, injection therapy, and open surgical repair. Although there is an abundance of viable treatment options, there have been non-satisfactory outcomes associated in each modality.

Mesenchymal stem cells are rich in progenitor capabilities and the multiple-lineage differentiation potential these cells hold alongside the seemingly limitless mitotic potential has a plethora of clinical applications.¹ Stem cells are categorized into four basic types based on transdifferentiation potential: unipotent, multipotent, pluripotent and totipotent, with the human zygote being the only totipotent precursor and the latter having smaller scopes of differentiation.¹ Mesenchymal stem cells are further categorized based on regenerative capabilities from the following derivative tissues: embryonic stem cells, tissue specific progenitor stem cells, bone marrow stem cells, umbilical cord stem cells and adipose stem cells.²

One major factor that contributes to MSC differentiation potential are the microRNA secretions that lead to a paracrine signaling cascade of cell proliferation and development where the gene regulatory factors of non-coding MicroRNAs directly affect gene translation and have subsequent application to musculoskeletal injuries.³ These genetic modifiers are utilized in the critical step of cell seeding, which is a method of cellular attachment to physiological scaffolding proteins that are imperative in the process of tissue regeneration and tissue engineering methods during tendon repair modalities. ^{4,5}

In addition to their proliferative potential, the physiological aspect of increased transplantation acceptance makes stem cells an afficable treatment option. Petersdorf et. al discusses the low expression of major histocompatibility complexes of stem cells, the secretion of specific chemokines that aid in graft tolerance and decreases risk of tissue rejection during transplantation which increases the viability of such treatment options.⁶

Another aspect of consideration in stem cell treatment is stem cell survival rate. Cells must not only survive, but proliferate, differentiate and integrate into the host circulatory system, all of which ultimately depend on the physical number of cells being transplanted into the host. ^{6,7}

These factors all led to the purpose of this literature review. This study is primarily focused on the efficacy of such treatment, specifically in the repair of Achilles tendon rupture. To avoid discussion on implications of morality and legality, this study will mention but not discuss cell culture methods or sources and focus specifically on its use as an adjunct treatment in the healing process of Achilles tendon rupture.

Methods

Studies included in this review were held to criteria matching the study of MSC relating to tendon rupture and repair. Peer reviewed studies were searched for on PubMed, EMBASE, SPORTDiscuss with specific inclusion factors that included randomized controlled trials, cohort studies with eligibility factors including outcome measures or assessment of tendon healing. Keywords and phrases used included "stem cell therapy," "Achilles tendon repair," "tendon rupture," pluripotent stem cells," "mesenchymal stem cell therapy," "cell-mediated repair," "tendon healing," "stem cell for tendon healing," and "stem cell clinical applications." Studies found were also cross referenced with other peer reviewed investigations to account for similarities and contradictions.

The focus was specified to stem cell therapies and associated mechanisms of stem cell physiology, therefore studies including other treatment modalities such as surgical repair, pharmacologic, non medicinal or use of combination therapies were subsequently excluded.

Results

Studies examined the hypothesis that delivering MSC-seeded implants to a tendon gap would significantly improve repair biomechanics.

Young et al.⁸ conducted a study involving autologous mesenchymal stem cell-mediated repair on defective gastrocnemius tendons in rabbits, where a control group was treated with normal suture material and compared to an experimental group treated with MSC-collagen matrix. Mesenchymal stem cells were collected from bone marrow aspirate and cultureexpanded with isolation of pre-differentiation cells. These primary cultures were seeded and the mesenchymal stem cell-matrix implant consisted of a pre-tensioned, polyglyconate suture to which the cultured MSCs were affixed as they contracted a collagen gel. These cells were incubated in physically constrained collagen gels and demonstrated the ability to organize their extracellular matrices along lines of

tension created by cell-mediated contraction of the gels. When prepared with fibroblastic ligament equivalents. results also showed improved biomechanical properties compared with nonorganized matrices. When these MSC-matrix constructs were observed in vitro, histological examination of the construct demonstrated an organized structure of elongated cells aligned with the matrix in the direction of tensile load along the longitudinal axis. Tendon thickness was measured post treatment with the experimental group averaging a cross sectional area of 7.4mm compared to the 5.4mm control group, with average variation of 2.8mm and 2.6mm respectively.

In addition to cross section mass, load-related structural properties were also measured with the experimental group averaging double load values compared to the control at all measured intervals. Young et al. theorized this was due to type-1 collagen gel contraction by mesenchymal stem cells onto pretension suture to double the load-related structural biomechanics of the gap repair. The result was an improvement in material properties of the repair compared with the use of sutures alone.

The data collected by Young was supported by other studies. Yin et al⁴ found similar results in mice showing MSC experiment groups having an average of 19% larger cross sectional area than control groups in tendon repair. Feng et al⁹ found stress capabilities increased by almost six times with material modulus increases of almost 16 times alongside highly aligned fibrils when viewing along a single axis by constraining cell-collagen gel contraction. Additionally, Webb et al¹⁰ showed strain induction can lead to increased collagen matrix deposition and mechanical strengthening of cell constructs and increased cytokine production in mice.

Yu et al.¹¹ hypothesized that tissue proliferation through MSC was due to paracrine signaling on exosomes. In this experimental study, bone marrow mesenchymal stem cells (BMSC) were infused inside exosomes and embedded within fibrin. The solution produced was subsequently injected into damaged/ruptured tendons in an experimental group of rats. Similarly, a control mixture without BMSC was injected in a separate control group of rats. Histological scores were then observed with enhanced expression of transcription factor mohawk (Mkx) that indicated tenogenic differentiation. Additionally, tenomodulin, a family member of the type two transmembrane glycoprotein generally expressed in tendon proliferation, also showed a marked increase in expression. Further analysis also showed an increase in type one collagen, as well as increased neo-tendon mechanical properties when compared to the control group.

Almeida et al.¹² conducted a study on MSC harvested from two sources: bone marrow and adipose tissue to evaluate tendon healing. In this study, bone marrow mesenchymal stem cells (BM-MSC) were harvested from the iliac crest through a minimally invasive aspiration procedure. BM-MSC were known to contain tendon proliferation genes such as extracellular matrix markers, collagen type 1, decorin, and tenascin. In addition to bone marrow extracts, Almeida sampled adipose tissue stem cells (allo-ASC) via extraction liposuction procedures of subcutaneous tissues. While Almeida recognized the limitations in definitive understanding of tendon regeneration mechanisms, it was discovered that the culturing of adipose tissue MSC and tendon explants together presented evidence of up-regulation in tendon related genes. Additionally, Almeida found that adipose tissue MSC led to an increased expression of collagenolytic activity of matrix metalloproteinases, enzymes that seemingly play an important role in the regulation of extracellular matrix degradation and is present in the process of acute and chronic wound re epithelialization.13

The findings by Almeida et al. were supported by a separate study conducted by Usuelli et al.¹⁴ examining the use of allo-ASCs and BMSC in the treatment of Achilles tendon rupture. Following the use of stem cells, efficacy of such treatment was measured utilizing Magnetic Resonance Imaging (MRI) and ultrasonography (US). The allo-ASC injection results were compared to plasma-rich plasma (PRP) treatment and it was found that the American Orthopedic Foot and Ankle Society (AOFAS) score, a uniform rating system combining provider and patient reports to assess function and pain post treatment for ankle/hindfoot fractures (with a max score of 100 for non symptomatic individuals) was significantly higher in the allo-ASC group than in the PRP group after 15 days (80 vs 67, respectively). Usuelli et al. reported after 60 days of follow-up, there was no longer a difference between AOFAS scores between patients treated with the allo-ASC or PRP injection.14

Additional support for the therapeutic benefits of MSC treatment of Achilles tendon repair was provided by Stein et al.¹⁵ Stein followed 27 patients over a two year span of treatment between 2009 and 2011 collecting data on BMSC injection treatment of sport related acute Achilles tendon ruptures following open tendon repair. Stein evaluated the potential of BMSC's effect on the following: operative complications, strength, range of motion, rerupture and functional improvement. The data showed that all patients in the study regained the ability to walk without a boot at 1.8 + -0.7 months with no recurrence of rupture of Achilles tendons reported after a mean follow-up of 29.7 +/- 6.1 months. In addition to the

tendon recovery, it was also noted that no adverse outcomes of soft tissue masses, bone formation or tumors from treatment were observed.

Discussion

The results from the studies analyzed in this paper support the use of stem cells in the treatment of Achilles tendon pathology. Various treatment modalities are currently present for tendon disorders, specifically tendon ruptures. Despite the abundance of options available, no single treatment modality has been completely satisfactory. Within the past decade stem cell therapy has shown promising results in treating tendon ruptures.

MSCs have the potential to be sourced from several different tissues and applied as a therapeutic source in the treatment of Achilles tendon rupture repair. Evidence from in-vitro, in-vivo studies have indicated the ability of MSCs to accelerate and improve tendon healing. MSC has the therapeutic ability to bind to the target site and repopulate the injured tissue. The current research on stem cell therapy for tendon disorders revolve around the theories that tendon healing is due to the paracrine effects of injected stem cells or the stem cell differentiation into tenocytes.

Additionally, MSCs contain tendon related genes tenomodulin, type one collagen, Mkx, decorin and tenascin that all have the ability to potentiate tendon growth and regeneration, as well as speed up the recovery process of a damaged tendon when compared to the controlled studies.^{11,12,13} Another type of MSCs discussed was the allo-ASC and although the direct mechanism is not fully understood, its combination with tendon explants in culture has a positive inductive effect in tendon growth and regeneration.¹² Furthermore, the significant increase in the AOFAS score after 15 days compared to traditional PRP signifies the positive effects of allo-ASC in the potentiation of tendon growth. However, more research is needed to fully appreciate the long term effects of allo-ASC since 60-day follow up shows no statistical difference between allo-ASC or PRP injection.14

There are limitations noted which further complicate the current use of MSC in the treatment of Achilles tendon rupture repair. There is currently not a standardized isolation protocol in place as well as a lack of tendon-specific molecular markers.¹² The collection methods as mentioned above are difficult and quantitative measurements have shown culturing methods to be inefficient for long term use.^{8,10} Methods for long term cell preservation are still undiscovered and as such, more research is needed to not only increase the viability of its use but also to appreciate the long-term effects of allo-ASC since studies show a marked decreased nuclear TF presence after 21 days.^{10,12}

Conclusion

The current literature on the use of stem cell therapy to treat Achilles tendon pathology is promising in a short term setting but does not indicate its use in a clinical setting at the present stage. Further research is still needed on the potentially serious adverse effects of stem cell therapy in the treatment of tendon rupture.¹⁶ Future studies should consider comparing stem cell therapy to current evidence based therapies including those such as extracorporeal shock wave therapy and physical exercise.

References

1. Fortier L. A. Stem cells: classifications, controversies, and clinical applications. *Veterinary Surgery*. 2005;34(5):415–423

 Thomson M., Liu S. J., Zou L.-N., Smith Z., Meissner A., Ramanathan S. Pluripotency factors in embryonic stem cells regulate differentiation into germ layers. *Cell*. 2011;145(6):875–89
 Chung MJ, Son JY, Park S, Park SS, Hur K, Lee SH, Lee EJ, Park JK, Hong IH, Kim TH, Jeong KS. Mesenchymal Stem Cell and MicroRNA Therapy of Musculoskeletal Diseases. Int J Stem Cells. 2021 May 30;14(2):150-67

4. Yin Z, Chen X, Chen JL, Ouyang HW. Stem cells for tendon tissue engineering and regeneration. Expert Opin Biol Ther. 2010 May;10(5):689-700.

5. Lui PP, Rui YF, Ni M, Chan KM. Tenogenic differentiation of stem cells for tendon repair-what is the current evidence? J Tissue Eng Regen Med. 2011 Aug;5(8):144-63.

6. Petersdorf E, Malkki M, Gooley T, Martin P, Guo Z. MHC haplotype matching for unrelated hematopoietic cell transplantation. PLoS Medicine. 2007;4(8):59-68.

7. Thompson P. A., Perera T., Marin D., et al. Double umbilical cord blood transplant is effective therapy for relapsed or refractory Hodgkin lymphoma. *Leukemia & Lymphoma*. 2016;57(7):1607–15 8. Young R.G.,Butller, D.L., Weber, W., Calplan, A.I., Gordon, S.L., Fink, D.J. Use of Mesenchymal Stem Cells in a Collagen Matrix for Achilles Tendon Repair. *Journal of Orthopaedic*

Research. (2005); 16(4):406-13.
Feng Z, Ishibashi M, Nomura Y. Constraint stress,

microstructural characteristics, and enhanced mechanical properties of a special fibroblast-embedded collagen construct. Artificial Organs. 2006; 30:870-877

10. Webb K, Hitchcock RW, Smeal RM. Cyclic strain increased fibroblast proliferation, matrix accumulation, and elastic modulus of fibroblast-seeded polyurethane construct. Journal of Biomechanics. 2006; 39:1136-44

 Yu H, Cheng J, Shi W, Ren B, Zhao F, Shi Y, Yang P, Duan X, Zhang J, Fu X, Hu X, Ao Y. Acta Biomater. 2020;1(106):328-341.
 Costa-Almeida R, Calejo I, Gomes M. Mesenchymal Stem Cells Empowering Tendon Regenerative Therapies. Int J Mol Sci. 2019;20(12):1-17.

13. Caley MP, Martins VL, O'Toole EA. Metalloproteinases and Wound Healing. *Adv Wound Care (New Rochelle)*. 2015;4(4):225-34.

14. Usuelli FG, Grassi M, Maccario C, et al. Intratendinous adiposederived stromal vascular fraction (SVF) injection provides a safe, efficacious treatment for Achilles tendinopathy: results of a randomized controlled clinical trial at a 6-month follow-up. Knee Surg Sports Traumatol Arthrosc. 2018;26(7):2000-2010.

15. Stein BE, Stroh DA, Schon LC. Outcomes of acute Achilles tendon rupture repair with bone marrow aspirate concentrate augmentation. Int Orthop. 2015;39(5):901-05.

16.van den Boom N, Winters M, Haisma H, Moen M. Efficacy of Stem Cell Therapy for Tendon Disorders: A Systematic Review. Orthop J Sports Med. 2020;8(4):1-10.

A Review of the Use of Platelet Rich Plasma in Treatment of Diabetic Foot Ulcers

Gordon Yee, B.S. and Devin Phaguda, B.S., M.P.H.

ABSTRACT

Objective: The purpose of this paper is to review the current literature to assess the efficacy of Platelet Rich Plasma (PRP) in the use of lower extremity wounds, such as diabetic foot ulcers and chronic venous wounds. This paper will also explore its mechanism of action and its cost-effectiveness as a treatment.

Methods: A literature search was performed on the Wiley Library, PubMed, and Google Scholar to identify recent articles that discussed Platelet Rich Plasma and its utility in treating diabetic foot ulcers. The terms used in this search were "Platelet Rich plasma and lower extremity wounds," "Platelet rich plasma and diabetic foot ulcers" "Platelet rich plasma cost" "Diabetic foot ulcer economics."

Results: Platelet rich plasma use on wounds is shown in many studies to be more effective than the standard of care for diabetic foot ulcers, though there is currently no standard method of preparation or concentration of blood components in any of these studies. In vitro studies of platelet rich plasma suggest that it may have antibacterial properties based off a property of platelets, which may show benefit considering the increased risk of complications and morbidity from infection of diabetic foot wounds. Economic models based on currently published data show that platelet rich plasma therapy is also a more cost-effective therapy, especially as affordable methods of preparation become widespread in the future.

Conclusion: The potential for the use of Platelet Rich Plasma as a treatment for diabetic foot ulcers shows promise in terms of increased healing as compared to standard of care and some alternative treatments, as well as in terms of potential cost-effectiveness.

Introduction

Diabetic Foot Ulcers

Diabetes is a chronic metabolic condition that carries significant morbidity and mortality, with diabetic foot ulcers (DFUs) being one of the most devastating and economically costly complications. DFUs occur in about 15-25% of the diabetic population and is most prevalent in diabetic individuals aged 45 years and older.¹

The current standard of care approach to DFUs include surgical debridement of devitalized or necrotic tissue, use of dressings to maintain a moist environment and to prevent infection, off-loading of the wound, and optimization of the patients' vascular status and glycemic control.^{1,2}

Diabetes and Wound healing

The process of healing involves the stages of inflammation, proliferation, and remodeling. Platelets and the growth factors contained within are involved predominantly with the inflammatory stage and are critical in achieving hemostasis and signaling to other cells in the healing cascade.^{3,4}

There are several mechanisms by which diabetes negatively impacts wound healing. Macrophages in diabetics are unable to phagocytose and remove dead tissue or debris as effectively, which interferes with the viability of remaining tissue. Elevated blood glucose leads to increased cross-linking and formation of Advanced Glycation End-products (AGEs) which can negatively impact mechanical integrity of soft tissues such as tendons and skin.^{5,6}

Platelet Rich Plasma (PRP)

PRP is a form of regenerative therapy that uses a preparation of plasma with a supraphysiological concentration of platelets and other components of blood, such as leukocytes and red blood cells (RBCs), along with increased levels of growth factors and cytokines which are known to be stored and released from alpha granules in platelets.^{1,3} These growth factors include platelet-derived growth factor (PDGF), transforming growth factor (TGF-b), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), basic fibroblast growth factor (bFGF), and insulin-like growth factor (IGF-1).³

Leukocytes are a component of PRP that, while involved in certain aspects of the healing process and infection prevention, may counter some of the proposed healing benefits. Leukocytes carry proinflammatory activity that induces local tissue and cellular damage, which is detrimental to healing tissue.³

Red blood cells are normally involved in carrying oxygen, nutrients, waste, nitric oxide production. However, due to a possible reaction of oxygen to the iron in heme, they may release cytotoxic oxygen free radicals that can induce apoptosis of host cells. As such, many PRP solutions choose to reduce its concentration.³ PRP also may contain other proteins involved in wound healing, such as fibrin, which helps form a scaffold for other components to build on.⁷

Preparation of PRP

The general process for preparing PRP involves extracting a sample of blood, separating out the components, and then concentrating or reducing specific substances within the blood, notably increasing the concentration of platelets.^{4,8}

Autologous PRP refers to a method of preparation wherein the plasma is obtained from a sample of the patient's own blood. Meanwhile, homologous PRP refers to the method where the plasma is obtained from another human patient's blood, such as from a blood bank. Autologous blood is more readily available and less costly. Homologous blood can be useful if the patient has severe anemia or thrombocytopenia.⁹

The process of concentrating the platelets by centrifugation increases the concentration of growth factors but does not activate them to release growth factors or cytokines.⁴ Platelets can be activated by a number of methods, such as by the addition of calcium or by freezing the solution.^{1,3,9}

Methods

Data extraction was performed using online resources such as PubMed, GoogleScholar, and Wiley Online Library to identify research articles with information related to the use of PRP in the treatment of DFUs. Articles and papers were identified using search terms such as "platelet rich plasma", "diabetic wound care", "diabetic foot ulcers", "non-healing diabetic foot ulcers", and "financial burden diabetic foot ulcers." From there, articles were chosen as they pertained to the purpose of this review with emphasis placed on time for wound closure, time to maximum rate of healing, and economic viability of treatment. For the purposes of this review, we focused mainly on the use of autologous PRP.

Results

Pietramaggiori et al. performed a study using both an in vitro and mouse model with the goal to determine the mechanism through which PRP exerts its positive effects on wound healing. They prepared PRP by different techniques, storing a sample at room temperature, at -80° Celsius, and one at -80° Celsius with 6% dimethyl sulfoxide (DMSO). They also used plasma as a control. The platelets were assessed for survival and viability. Each preparation was also assessed for hemostatic function and applied to standardized 1 cm² full-thickness wounds on a diabetic mouse model to evaluate healing capability.¹⁰

It was found that freezing the platelets was sufficient to activate them, although the frozen platelets prepared with DMSO showed both activated and non-activated quiescent platelets. Although all preparations showed hemostatic ability, only those with non-activated, quiescent platelets (room temperature and DMSO) were able to induce angiogenesis in the mouse model wounds. Activated platelets were shown to increase wound granulation. In this study's mouse model, the 6% DMSO -80° Celsius preparation showed the greatest healing potential.

Driver et al. conducted a prospective randomized controlled trial. 72 patients were enrolled into either a PRP gel group or a control (saline gel) group. In this study, the researchers found a greater amount of full wound closures in the PRP group (81.3%) than in the control group (42.1%) after removing wounds whose sizes and volumes were calculated to be outliers (p = 0.036). When using a Kaplan-Meier time-to-healing measurement, there was no statistical difference. The rate of healing between the two groups as calculated as change in size per day was not statistically significant.¹¹ In a study by Karimi et al, patients were assigned to either a control group with saline irrigation and sterile gauze or an intervention group in which patients were treated with a sterile gauze impregnated with PRP once at the beginning of the study. For both groups, the dressings were changed every other day with saline and sterile gauze. While the control group did not show any significant change in depth or area of the wound, the intervention group showed a statistically significant decrease in both the ulcer surface area and depth at 3 weeks.⁷

A prospective study by Singh et al. compared PRP with standard therapy involving aseptic wound dressing, with both groups additionally receiving debridement and antibiotics. The PRP group achieved full wound closure faster than the control group, at 36.7 ± 3 days and 60.6 ± 3.7 days respectively (p<0.0001), with all patients treated with PRP fully closing wounds versus the control group, in which two wounds did not close due to infection.¹²

A study was performed by Ahmed et al. comparing the use of antiseptic ointment to PRP gel applied twice a week for wound dressing of clean DFUs. The researchers found a significantly higher healing rate until 8 weeks (0.5 versus 0.7 cm²/week respectively) and percentage of full wound closure in the PRP group compared to the control group at 12 weeks (86% vs 68% respectively). The PRP group was observed to have a lower rate of wound infections, at 4% in the PRP group and 21% in the control group, which they speculated may indicate some immune or antimicrobial effect.⁶

Nolan et al. performed a randomized controlled trial to assess the viability of the use of PRP as an adjunct for fat grafting for DFUs, which aims to use adipose-derived stem cells to treat soft tissue injuries. They found that the treatment with fat grafting and PRP increased angiogenesis and microvessel density. By examining biopsies histologically throughout the study course, there was evidence that the addition of PRP helped improve survival of the fat graft. However, this did not correlate to a clinically significant difference in outcomes.¹³

Antimicrobial Activity

Çetinkaya et al. studied the antibacterial properties of PRP against resistant organisms as assessed in vitro based on bacterial growth on agar plates and on antibacterial susceptibility tests. In addition to their role in hemostasis, platelets also exert effects in host defense. Platelets have demonstrated bacterostatic/bacterocidal effects, with activity shown against methicillin-resistant Staphylococcus aureus (MRSA), extended spectrum beta lactamase (ESBL)positive *K. pneumoniae*, and carbapenem-resistant *P. aeruginosa* in this study. Of the bacteria investigated in this particular study, Vancomycin Resistant Enterococcus (VRE) was the only one that PRP did not show antimicrobial activity against. They found that the antimicrobial activity of PRP was independent of the leukocyte concentrations and instead was based on a property of platelets themselves.¹⁴

Costs

Dougherty created an economic model to analyze the cost-effectiveness and potential quality-oflife benefit of PRP gel for non-healing, full thickness DFUs compared to saline gel wound dressing, an FDA approved therapy used in addition to standard of care. Based off of data from currently published literature, it was found that PRP gel resulted in better outcomes, better quality-of-life as measured in Quality-Adjusted Life-Years (QALYs), and lower cost over a 5 year period due to faster healing rates and fewer incidences of lower extremity infections, osteomyelitis, and amputations.¹⁵

Dougherty also compared PRP gel with other advanced therapies such as ultrasound therapy, human fibroblast derived dermal substitute, allogeneic bilayered culture skin substitute, bilayered cellular matrix, negative pressure wound therapy (NPWT), and recombinant human platelet–derived growth factor BB (rhPDGF) and found that PRP was also less costly and more effective than them.¹⁵

Machado et al. performed a study using readily available supplies and equipment that allowed for multiple spin cycles of centrifugation within a single tube which also yielded concentrations of platelets up to 4.17-fold greater than baseline levels.¹⁶

Hamid et al. also performed a similar study comparing a method for preparing PRP using readily available supplies and single centrifuge spin cycle compared to PRP from commercially available kit system and to levels from blood at a baseline. Based on their study, a single centrifugation preparation for PRP yielded platelet and WBC levels that were within therapeutic range and comparable to those of commercially available methods. This process was more affordable, using readily available equipment than other preparation methods such as apheresis or commercial kits, and also leading to lower chance of contamination due to only requiring one centrifugation round.

Discussion

In general, there are common trends of PRP being more efficacious compared to standard of care and saline gel dressing, with many studies showing increased greater rates of healing, greater percentages of patients with fully closed wounds, and shorter times needed to fully close wounds.

However, the main limitation of all studies observed were small sample sizes and lack of standardization. Although there was a wide range of efficacy displayed in the use of PRP, it is not entirely unexpected given the wide variation in methods of preparation and application. Although there are many studies, the results cannot be directly compared to one another. Number of applications varied, from once at the beginning of the study to twice a week.

An example to illustrate how different preparation methods interfere with the ability to compare studies is in platelet activation. Different methods mentioned for activation of platelets include freezing the platelets, preparing them with DMS, and through combination of freezing and DMSO. Nonactivated and activated platelets exert different properties which can each contribute to the healing process and the method of activation can allow for the presence of both types of platelets in the PRP.¹⁰ This demonstrates that different methods of activation can impact the efficacy of a PRP preparation and may play a role in variances seen in rates of healing and time needed to close wounds.

As previously stated, non-activated and activated platelets have different properties. It has been shown that non-activated platelets stimulate angiogenesis in wound beds.¹⁰ It has also been demonstrated that PRP could be used to induce microvascularization formation, but this has only been shown when PRP is used in conjunction with fat grafting rather than as a standalone treatment.¹³ Given the role that vasculature plays in wound healing and the known association between diabetes and PAD, it may be of benefit in the treatment of DFUs to investigate more into the ability of PRP to affect vasculature.^{5, 10}

Given the significant burden that polymicrobial infections and drug-resistant bacteria play in healing rates of DFUs and the resulting morbidity/complications, the finding that PRP may exert an antimicrobial effect that is useful against these is important. It is important to note that this antimicrobial effect is independent of leukocyte concentrations, as high levels of leukocytes may be detrimental to healing. At this point, the presence of infection in DFUs is generally a characteristic used in patient criteria. All studies in this review were done in clean DFUs. Although PRP has shown antibacterial activity in vitro, this has not been shown in vivo studies. Although clinically, use of PRP in treatment of DFUs is correlated with lower rates of infection, a causal effect cannot be claimed due to the current lack of RCTs.6,9

In order for PRP to be feasible for widespread use in a clinical setting, there needs to be a process that produces a standardized, reproducible product that is still affordable.¹⁷ It is possible to produce a PRP product with therapeutic levels of platelets and WBCs with readily available equipment within many clinical settings, hospitals, and pharmacies. The main limitation for PRP is the need for larger scale studies that use with a standardized preparation protocol in order to better compare and look for results and to allow for reproducibility.^{8,16}

All of the studies examined in this review used either standard of care with saline irrigation and sterile gauze or with a saline gel and sterile gauze. There are other alternative treatments used for DFUs, such as Vacuum Assisted Closure (VAC), hyperbaric oxygen therapy (HBOT), and acellular dermal matrix.⁹ It would be beneficial to compare PRP with these more established, well studied alternative therapies.

Conclusion

Overall, PRP treatment shows promise in the treatment of diabetic foot ulcers due to the hemostatic properties and high concentration of growth factors. However, there is a lack of randomized control trials and longer-term follow-up is needed. Future studies should focus on developing a more standardized preparation and application method, as the variation makes it difficult to reproduce results or draw comparisons between studies.

The financial burden of DFUs is immense. PRP may show long-term benefit in alleviating this burden, especially as the process of preparation becomes more standardized and affordable.

References

- Vicenti G, Bizzoca D, Caruso I, Nappi VS, Giancaspro G, Carrozzo M, Moretti B. New insights into the treatment of non-healing diabetic foot ulcers. J Biol Regul Homeost Agents. 2018 Nov-Dec;32(6 Suppl. 1):15-21.
- Everett E, Mathioudakis N. Update on management of diabetic foot ulcers. Ann N Y Acad Sci. 2018 Jan;1411(1):153-165. doi: 10.1111/nyas.13569.
- Wu PI, Diaz R, Borg-Stein J. Platelet-Rich Plasma. Phys Med Rehabil Clin N Am 27 (2016) 825–853. http://dx.doi.org/10.1016/j.pmr.2016.06.002
- Lubkowska A, Dolegowska B, Banfi G. Growth factor content in PRP and their applicability in medicine. J Biol Regul Homeost Agents. 2012 Apr-Jun;26(2 Suppl 1):3S-22S.
- Andrews KL, Houdek MT, Kiemele LJ. Wound management of chronic diabetic foot ulcers: from the basics to regenerative medicine. Prosthet Orthot Int. 2015 Feb;39(1):29-39. doi: 10.1177/0309364614534296.
- Ahmed M, Reffat S, Hassan A, Eskander F, Platelet Rich Plasma for the Treatment of Clean Diabetic Foot Ulcers, Annals of Vascular Surgery (2016), doi: 10.1016/j.avsg.2016.04.023.
- Karimi R, Afshar M, Salimian M, Sharif A, Hidariyan M. The Effect of Platelet Rich Plasma Dressing on Healing Diabetic Foot Ulcers. Nurs Midwifery Stud. 2016 September; 5(3):e30314. doi: 10.17795/nmsjournal30314.
- Hamid MSA. Cost Effectiveness of a Platelet-rich Plasma Preparation Technique for Clinical Use. Wounds May 2018;30(7):186–190.
- Babaei V, Afradi H, Gohardani HZ, Nasseri F, Azarafza M, Teimourian S. Management of chronic diabetic foot ulcers using platelet-rich plasma. J Wound Care. 2017 Dec 2;26(12):784-787. doi: 10.12968/jowc.2017.26.12.784.
- Pietramaggiori G, Scherer SS, Mathews JC, Gennaoui T, Lancerotto L, Ragno G, Valeri CR, Orgill DP. Quiescent Platelets Stimulate Angiogenesis and Diabetic Wound Repair. Journal of Surgical Research 160, 169–177 (2010). doi:10.1016/j.jss.2008.09.010
- Driver V, Hanft J, Fylling CP, Beriou JM. A Prospective Randomized, Controlled Trial of Autologous Platelet Rich Plasma Gel for the Treatment of Diabetic Foot Ulcers. Ostomy Wound Manage. 2006 Jun;52(6):68-70, 72, 74 passim.
- Singh SP, Kumar V, Pandey A, Pandey P, Gupta V, Verma R. Role of platelet-rich plasma in healing diabetic foot ulcers: a prospective study. J Wound Care. 2018 Sep 2;27(9):550-556. doi: 10.12968/jowc.2018.27.9.550.
- Nolan GS, Smith OJ, Heavey S, Jell G, Mosahebi A. Histological analysis of fat grafting with platelet-rich plasma for diabetic foot ulcers—A randomised controlled trial. Int Wound J. 2021;1–10. https://doi.org/10.1111/iwj.13640
- Çetinkaya RA, Yenilmez E, Petrone P, Yılmaz S, Bektöre B, Şimsek B, Atik TK, Özyurt M, Ünlü A. Platelet-rich plasma as an additional therapeutic option for infected wounds with multi-drug resistant bacteria: in vitro antibacterial activity study. Eur J Trauma Emerg Surg. 2019 Jun;45(3):555-565. doi: 10.1007/s00068-018-0957-0.

- Dougherty EJ. An Evidence-Based Model Comparing the Cost-effectiveness of Platelet-Rich Plasma Gel to Alternative Therapies for Patients with Nonhealing Diabetic Foot Ulcers. Advances in Skin & Wound Care Dec 2008;21(12). DOI: 10.1097/01.ASW.0000323589.27605.71.
- Machado ES, Leite R, dos Santos CC, Artuso GL, Gluszczak F, de Jesus LG, Caldas JMP, Bredemeier M. Turn down - turn up: a simple and low-cost protocol for preparing platelet-rich plasma. Clinics (Sao Paulo). 2019;74:e1132. doi: 10.6061/clinics/2019/e1132.
- DeLong JM, Russell RP, Mazzocca AD. Platelet-rich plasma: the PAW classification system. Arthroscopy. 2012 Jul;28(7):998-1009. doi: 10.1016/j.arthro.2012.04.148. PMID: 22738751.

The Effectiveness of Nerve Growth Factor (NGF) Monoclonal Antibody for the Treatment of Knee Osteoarthritis

Thu Phu, B.S.

ABSTRACT

Objective: To evaluate the efficacy of nerve growth factor (NGF) monoclonal antibody (mAb) for the pain management of knee osteoarthritis (OA).

Methods: Various studies concerning the management of knee OA by NGF mAb were systematically searched in databases including PubMed, Wiley, and Google Scholar. Randomized controlled trials (RCTs) on anti-NGF mAb therapy for knee OA in both mice and human models were included and any articles published prior to the year 2010 were excluded.

Results: Anti-NGF mAb showed significant pain relief in both mice and human models. In human models, tanezumab and fasinumab provided significant improvements in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain, WOMAC physical function, and Patient's Global Assessment (PGA) scores. When compared to traditional monotherapy of naproxen and celecoxib, tanezumab monotherapy showed significant greater reductions in WOMAC Pain.

Conclusion: Anti-NGF mAb is an effective treatment for knee and hip OA patients, but it carries the risk of aggravating progressive OA (PROA), rapidly progressive OA (RPOA), and osteonecrosis. Therefore, the therapeutic dose and the suitable patient population need to be identified to mitigate the risk of these joint-related conditions.

Introduction

Osteoarthritis (OA) is characterized by the gradual wearing down of cartilage mostly affecting the joints in hands, knees, hip, and spine leading to impairment in articular function and ultimately leading to disability. These changes typically develop and worsen gradually, causing pain, swelling, stiffness, and are most prevalent in the elderly populations.1 Additionally, OA is the most common form of arthritis, accounting for 46% of hospitalization among all arthritis diagnoses.² According to the self-reported osteoarthritis survey in the United States from 2008 to 2014 reported by the CDC, 1 in 7 US adults, roughly 32.5 million people, suffer from OA annually.² Among those that are diagnosed with OA, the knee is the most commonly affected area, which accounts for about one-third (31%) of all OA healthcare visits.² Despite these high numbers, OA treatment options remain limited.

OA management has been traditionally focused on relieving symptoms via the use of non-steroidal anti-inflammatory drugs (NSAIDs) or analgesics. However, these medications are unsuitable for long-term use due to their adverse renal effects and their limited efficacy.1 In recent years, there has been substantial progress on the investigation of different OA medications to prevent and treat OA, including nerve growth factor (NGF) monoclonal antibody (mAb), a highly selective humanized immunoglobulin monoclonal antibody that can directly bind to NGF and neutralize its action.³NGF is a type of neurotrophic factors that

functions in nociceptor sensitization following tissue injury.^{3,4} Its interaction with tropomyosin receptor kinase A (trkA) induces acute and chronic pain in adults.⁵ Significant upregulations of NGF and bradykinin receptors were found in the joints of mice with OA that express pain behavior.⁶ Additionally, almost all structures in the joints are innervated with nociceptive nerve fibers which have receptors associated with NGF, thus increased NGF levels may be the source of unmanageable pain in knee OA.⁷

There are several investigational anti-NGF mAb currently in the clinical trial phase of FDA approval for the treatment of knee and hip OA pain, including tanezumab and fasinumab. If approved, NGF mAb would be the first medication in a new class of non-opioid medication for pain relief in OA. Its relevance in treating knee OA and its emergence as another option besides NSAIDs, which have many side-effects often restricting their use in elders, support the reasons why anti-NGF mAb represents an attractive option. Within this context, it is necessary to investigate the effectiveness of NGF mAb in the treatment of OA pain with an emphasis on knee OA.

Methods

PubMed, Wiley, and Google Scholar were used to identify publications. Publications including randomized clinical trials (RCTs), systemic reviews, as well as meta-analyses to provide insights on the effectiveness of NGF mAb on the treatment of knee and hip OA were included. Keywords used to identify relevant publications were "Nerve growth factor," "Knee osteoarthritis," "Anti-nerve growth factor antibodies," "Tanezumab," and "Fasinumab". Publication language was restricted to English and publication date was restricted to be 2010 or more recent to ensure the most up-to-date clinical trials on the novel therapy.

Results

A study conducted by Miyagi et al. on the efficacy of NGF antibody in knee OA in mice using the monoiodoacetate (MIA) model has found that anti NGF therapy suppressed the abnormal gait that is associated with knee OA pain. MIA injection in the knee induces gait disturbances, including small cycle, small swing speed, upregulation dutv of neuropeptides innervating the knee joints, and rapid pain-like responses which resemble some of the symptoms reported by the OA patient population, thus serving as a useful and relevant preclinical model of knee OA pain. The study consisted of a total of 30 six week-old male mice, of which 10 of them received a saline injection into the right knee joints and served as the control group while the 20 other mice received MIA injections into the right knee joints and served as the experimental group. Three weeks after MIA injection, the 20 experimental mice were randomly divided into non-treatment groups which received sterile saline or treatment groups which received systemic anti-NGF antibodies. When comparing the ratio of ipsi and contralateral hind paw values in terms of stand time, swing time, and speed, the ratio values in the anti-NGF group was significantly improved after only one week of treatment compared to that in the non-treatment group (p<0.05). 8

In a double-blind, placebo-controlled phase IIb/III clinical trial, Dakin et al. assessed the efficacy of fasinumab, an anti-nerve growth factor monoclonal antibody introduced by Regeneron-Teva, in OA hip and knee pain. The study selected 421 patients based on having moderate-to-severe OA pain in the knee or hip and having had a history of inadequate or intolerant response to other standard analgesics. Out of 421 patients, 338 were randomized to receive fasinumab (at 1 mg, 3 mg, or 9 mg) and 83 to receive placebo every four weeks for a total of four doses (16 weeks total) and then were evaluated at week 36. Out of the 421 patients, 342 completed the 36-week study (fasinumab group with 294 patients and placebo group with 67 patients). It was found that fasinumab group had significantly greater reductions in WOMAC Pain subscale scores, a widely used measurement in assessing pain, stiffness, and function in patients with OA of the hip or knee, from baseline to week 16 in all doses of fasinumab compared to placebo (p<0.05 for fasinumab doses of 1 mg, 3 mg,

6 mg, and 9 mg). PGA score, a 5-point scoring system to assess disease severity, was reduced in fasinumab from baseline to week 16 as compared to placebo, with reductions that were statically significant with doses of 1 mg and 9 mg (p=0.0132 and p=0.008, respectively).⁹

Besides fasinumab, tanezumab is another humanized NGF mAb. It was introduced by Pfizer-Eli Lilly and has completed phase III clinical trials conducted by Schnitzer et al. in 2008.7 Among the 698 patients who have moderate-to-severe knee or hip OA randomized, 582 completed the trial where they were divided into three dosing regimens: (1) 231 patients received 2.5 mg at day 1 and at week 8; (2) 233 patients received 2.5 mg at day 1 and 5.0 mg at week 8; and (3) 232 patients received placebo at day 1 and week 8. Patients in both tanezumab dosing regimens (groups 1 and 2) reported a statistically significant difference in $\geq 30\%$, $\geq 50\%$, and $\geq 70\%$ reductions in WOMAC Pain (compared to baseline) versus placebo group at week 16 (p<0.05 for all three types of reductions). However, patients who reported \geq 90% reduction did not show a statistically significant difference compared to placebo for both regimens (p=0.11 and p=0.1, respectively). Nevertheless, both tanezumab 2.5 mg and 2.5/5.0 mg dosing regimens showed statistically significant improvement in WOMAC Pain, WOMAC physical function, and PGA at week 16 compared to that of the placebo group (p<0.05); thus underscoring the effectiveness of NGF mAb in knee OA pain relief. 10

A meta-analysis of nine randomized controlled trials conducted by Chen et al. with 7,665 individuals revealed that tanezumab significantly reduced WOMAC Pain compared to placebo in 5,879 patients (p<0.01). Included randomized controlled trials (RCTs) were specific to knee and hip OA. The WOMAC physical function scores were significantly different between the tanezumab group versus placebo group in 6,078 patients (p < 0.01). One included trial comparing tanezumab monotherapy with combined tanezumab and NSAIDs in the treatment of knee or hip osteoarthritis pain with 2,700 patients revealed that patients receiving tanezumab 5.0 and 10.0 mg had significantly greater improvement in WOMAC Pain and Physical Function compared to that of naproxen or celecoxib $(p \le 0.015 \text{ and } p \le 0.007, \text{ respectively})$. Additionally, patients with $\geq 30\%$, $\geq 50\%$, $\geq 70\%$, and $\geq 90\%$ reductions in WOMAC Pain from baseline to week 16 (end of treatment) were significantly greater with tanezumab monotherapy for both 5.0 mg and 10.0 mg than with naproxen or celecoxib alone ($p \le p$ 0.044) except tanezumab 10.0 mg versus celecoxib at the 90% reduction.^{11,12}

Discussion

Miyagi et al.'s study on the efficacy of anti NGF antibody in knee OA pain model in mice revealed that NGF mAb was effective in treating knee OA pain. The study involved OA induction by MIA, which is the standard model to explore pain mechanisms for OA-related pain studies.¹⁶ The ratio of ipsi and contralateral hind paw improvement in the mice that received anti-NGF therapy demonstrated that systemic injection of anti NGF mAb improved gait disturbances, suggesting the potential of anti NGF mAb in ameliorating walking deviations that may be developed from knee OA. It is important to note, however, that the study did not include which specific anti-NGF mAb was used. Furthermore, the efficacy of anti-NGF mAb was based on only one injection and thus, multiple doses effect of anti-NGF therapy was not determined.8 Despite these limitations, this MIA model of osteoarthritis pain in mice improved our understanding of OA-related pain mechanisms and showed that anti-NGF therapy might be valuable in improving gait disturbances in OA patients.

The results from the prospective study conducted by Dakin et al. further confirmed that anti NGF mAb was effective in relieving pain in patients with moderate-to-severe OA pain in the knee or hip. The study focused on fasinumab and found that it was superior to placebo for improving pain and physical function in knee OA. This finding was confirmed by another double-blind, placebocontrolled study conducted by Tiseo et al. on the efficacy, safety, and tolerability of fasinumab for the treatment of pain in patients with knee OA.13 Both of these studies highlighted that fasinumab was associated with a significant reduction in knee pain and an improvement in knee function. However, it should be noted that fasinumab treatment in Tiseo et al.'s study was given intravenously while fasinumab treatment in Dakin et al.'s study was given orally. Though the two routes of administration provided similar efficacy results for fasinumab, it is important to compare which route of administration provided higher efficacy outcome with lower safety risk in future studies. Furthermore, Dakin et al.'s study did not provide clear evidence on the effects of dosing on the differences of WOMAC Pain scores between treatment and placebo groups. Therefore, the therapeutic dose level of fasinumab as an analgesic treatment for knee OA should be placed in the context of future studies.

Similarly, a randomized, doubleblind, multicenter phase III clinical trial evaluating the effectiveness of tanezumab, another humanized NGF mAb introduced by Pfizer- Eli Lilly, on joint pain, physical function, and PGA of OA patients with

hip or knee pain also showed that NGF mAb significantly improves pain and physical function in patients with moderate-to-severe knee or hip OA. Similar to a previous study on fasinumab, Schnitzer et al.'s study also selected patients with hip or knee OA who had not responded to standard analgesics. The results showed that tanezumab was superior to placebo in relieving pain, improving physical function, and PGA in patients with knee or hip OA, thus further underscoring the effectiveness of NGF mAb in knee OA as a pain analgesic.¹⁰ This 2018's finding was similar to another recent phase III clinical trial on tanezumab conducted by Berenbaum et al. in 2020 with 849 patients who also had unmet therapeutic outcomes with standard analgesics.¹⁴ It is important to note that the treatment period in Schnitzer et al.'s study was only 16 weeks, which might be too short to fully access the efficacy of tanezumab in prolonged use. Therefore, longer study durations are required in future studies to estimate the adverse effects of tanezumab.

The ten studies meta-analysis on the efficacy and safety of tanezumab on knee and hip OA confirmed that NGF mAb, specifically tanezumab, significantly provides superior pain relief and improvement in physical function and PGA in knee and hip OA patients with well-tolerated side Thus, anti-NGF monoclonal antibody effects. represents a promising new innovative approach for individuals with OA pain without the gastrointestinal or cardiovascular side effects associated with longterm usage of NSAIDs.11 It should be noted, however, that anti-NGF therapy may lead to progressive (PROA) and osteonecrosis.4,15 OA Furthermore, combination therapy of tanezumab and NSAIDs also increased the risk of rapidly progressive OA (RPOA).¹⁴ Due to these serious joint-related adverse events, FDA has voted against the approval of tanezumab, although clinical trials showed that it was better than placebo for the treatment of pain associated with OA of the knee and hip. Meanwhile, fasinumab is still currently waiting for FDA approval.³ The included studies in the meta-analysis were all double blind and high quality. However, all included trials were published by pharmaceutical companies, making the potential for bias another limitation of this analysis.

Conclusion

Standard therapy of OA with NSAIDs and opiates provided inadequate pain relief and concerns about adverse effects with prolonged use, thus resulting in unmet needs in the therapeutic outcomes in OA patients. Included findings have shed light on the growing body of evidence demonstrating the potential of anti-NGF mAb as an innovative treatment option for knee and hip OA patients over standard-of care NSAIDs and opiates. Nevertheless, the treatment carries the risk of aggravating PROA and RPOA. Therefore, future research on whether the benefits outweigh the risks for anti-NGF mAb is needed to bring this novel therapy to OA patients.

References

- McAlindon TE, Bannuru RR. OARSI recommendations for the management of hip and knee osteoarthritis: the semantics of differences and changes. *Osteoarthritis and Cartilage*. 2010;18(4):473-475. doi:10.1016/j.joca.2010.02.011
- 2. Osteoarthritis | BMUS: The Burden of Musculoskeletal Diseases in the United States.
- Chang DS, Hsu E, Hottinger DG, Cohen SP. Antinerve growth factor in pain management: Current evidence. *Journal of Pain Research*. 2016;9:373-383. doi:10.2147/JPR.S89061
- Miller RE, Block JA, Malfait AM. Nerve growth factor blockade for the management of osteoarthritis pain: What can we learn from clinical trials and preclinical models? *Current Opinion in Rheumatology*. 2017;29(1):110-118. doi:10.1097/BOR.00000000000354
- Mantyh PW, Koltzenburg M, Mendell LM, Tive L, Shelton DL. Antagonism of nerve growth factor-TrkA signaling and the relief of pain. *Anesthesiology*. 2011;115(1):189-204. doi:10.1097/ALN.0b013e31821b1ac5
- Shang X, Wang Z, Tao H. Mechanism and therapeutic effectiveness of nerve growth factor in osteoarthritis pain. *Therapeutics and Clinical Risk Management*. 2017;13:951-956. doi:10.2147/TCRM.S139814
- Cai X, Yuan S, Zeng Y, Wang C, Yu N, Ding C. New Trends in Pharmacological Treatments for Osteoarthritis. *Frontiers in Pharmacology*. 2021;12. doi:10.3389/fphar.2021.645842
- Miyagi M, Ishikawa T, Kamoda H, et al. Efficacy of nerve growth factor antibody in a knee osteoarthritis pain model in mice. *BMC Musculoskeletal Disorders*. 2017;18(1). doi:10.1186/s12891-017-1792-x

- Dakin P, DiMartino SJ, Gao H, et al. The Efficacy, Tolerability, and Joint Safety of Fasinumab in anti NGF mAb is needed to bring this new therapy to the market. Osteoarthritis Pain: A Phase IIb/III Double Blind, Placebo-Controlled, Randomized Clinical Trial. *Arthritis and Rheumatology*. 2019;71(11):1824-1834. doi:10.1002/art.4101
- Schnitzer TJ, Easton R, Pang S, et al. Effect of Tanezumab on Joint Pain, Physical Function, and Patient Global Assessment of Osteoarthritis among Patients with Osteoarthritis of the Hip or Knee: A Randomized Clinical Trial. JAMA - Journal of the American Medical Association. 2019;322(1):37-48. doi:10.1001/jama.2019.8044
- Schnitzer TJ, Ekman EF, Spierings ELH, et al. Efficacy and safety of tanezumab monotherapy or combined with non-steroidal anti-inflammatory drugs in the treatment of knee or hip osteoarthritis pain. *Annals of the Rheumatic Diseases*. 2015;74(6):1202-1211. doi:10.1136/annrheumdis-2013-204905
- Chen J, Li J, Li R, et al. Efficacy and safety of tanezumab on osteoarthritis knee and hip pains: A meta-analysis of randomized controlled trials. *Pain Medicine (United States)*. 2017;18(2):374-385. doi:10.1093/pm/pnw262
- Tiseo PJ, Kivitz AJ, Ervin JE, Ren H, Mellis SJ. Fasinumab (REGN475), an antibody against nerve growth factor for the treatment of pain: Results from a double-blind, placebo-controlled exploratory study in osteoarthritis of the knee. *Pain*. 2014;155(7):1245-1252. doi:10.1016/j.pain.2014.03.018
- Berenbaum F, Blanco FJ, Guermazi A, et al. Subcutaneous tanezumab for osteoarthritis of the hip or knee: Efficacy and safety results from a 24week randomised phase III study with a 24-week follow-up period. *Annals of the Rheumatic Diseases*. 2020;79(6):800-810. doi:10.1136/annrheumdis-2019- 216296
- Lane NE, Schnitzer TJ, Birbara CA, et al. Tanezumab for the Treatment of Pain from Osteoarthritis of the Knee. *New England Journal of Medicine*. 2010;363(16):1521-1531. doi:10.1056/nejmoa0901510
- Gerwin N, Bendele AM, Glasson S, Carlson CS. The OARSI histopathology initiative recommendations for histological assessments of osteoarthritis in the rat. Osteoarthritis Cartilage. 2010;18 Suppl 3:S24-S34. doi:10.1016/j.joca.2010.05.030

A Comparison between Platelet-Rich Plasma and Corticosteroid Injections in the Long-Term Treatment of Plantar Fasciitis

Gillian Mathews, B.S.

Abstract:

Objective: Plantar fasciitis is a common foot pathology managed with a variety of treatment modalities with inconsistent effectiveness and success. This review aims to examine the clinical application and efficacy of plateletrich plasma (PRP) as a treatment for plantar fasciitis when compared to corticosteroids.

Methods: Relevant research articles relating to the use of platelet-rich plasma and corticosteroid treatment of plantar fasciitis were found via PubMed, National Institute of Health databases, and the International Journal of Foot and Ankle.

Results: Preliminary studies show platelet-rich plasma to be a safe modality with the potential to improve functional and pain outcomes over time. Compared to corticosteroid treatment, PRP treatment groups had improved functionality and pain at later time points. Corticosteroid treatment showed to be effective earlier but for shorter intervals.

Conclusion: This review concludes that functional and pain outcomes improved with the use of PRP. Compared to corticosteroids, PRP has greater potential for improvement of plantar fasciitis symptoms over time. The use of PRP for plantar fasciitis is a relatively new intervention, in which the full scope of its benefits remains to be seen and requires continued research.

Introduction

Plantar fasciitis is a deteriorative condition of the plantar fascia that can limit mobility and cause severe pain.1 The etiology of the disease is unknown but is hypothesized to be due to microtrauma of the fascia from repetitive activities.² Plantar fasciitis mostly affects 40 to 60-year-olds and is more common in women, athletes, and people whose careers require standing or walking.¹ Clinical symptoms include heel discomfort with ambulation, tissue stiffness, and tenderness.² Treatment modalities currently used to treat plantar fasciitis include shoe inserts, antiinflammatory drugs, stretching protocols, extracorporeal shock wave therapy, surgery, and corticosteroids. Unfortunately, treatments have resulted in inconsistent responses with non-surgical methods failing in 10-15 percent of patients.^{2,3}

Corticosteroids have an anti-inflammatory effect that can provide accelerated pain relief. In patients with plantar fasciitis, corticosteroids inhibit fibroblast proliferation and ground substance protein expression, which are pathological features of the condition.⁴ However, several studies have linked repeated corticosteroid injections to plantar fascia rupture leading to concern over the use of this modality.³ Additionally, corticosteroid injection's pain-relieving effects are relatively short-term.

In contrast to corticosteroids which manage plantar fasciitis symptoms, platelet-rich plasma (PRP) injection aims to stimulate healing in addition to providing pain relief.⁵ PRP is a newer treatment in which plasma enriched with growth factors is injected into the body to stimulate tissue healing.⁴ In clinical settings the use of PRP in the treatment of muscle injuries has been effective in reducing pain and swelling.⁷ PRP increases collagen gene expression, production of vascular endothelial growth factor, and recruitment of fibroblasts, helping to stimulate the healing process.⁸⁹

This review aims to analyze the efficacy and safety of PRP injection in the treatment of plantar fasciitis when compared to corticosteroid treatment.

Methods

A literature search was conducted on PubMed, National Institute of Health databases, and the International Journal of Foot and Ankle to retrieve articles, from 2012 to present, relating to the use of platelet-rich plasma and corticosteroids for symptomatic relief of plantar fasciitis. When searching the databases, keywords used were platelet-rich plasma, plantar fasciitis, corticosteroids, heel pain, and podiatry. Ten articles were found to be appropriate for the study.

Results

In Ragab et al. 2012, 25 patients with plantar fasciitis were treated with PRP injections. Patient pain was accessed before and after treatment using the Visual Analogue Scale (VAS), a subjective measure used to measure pain. The average pre-injection pain was 9.1 and the average post-injection pain at followup was 1.6. Twenty-two patients (88 percent) were completely satisfied, and 15 patients (60 percent) had no functional limitations.⁶ The mean follow-up was 10.3 months post-injection.⁶ No patients reported complications from PRP injection.

Martinelli et al. 2012, assessed the safety of platelet-rich plasma treatment for plantar fasciitis and the preliminary clinical results of the treatment. The modified Roles and Maudsley score (RMS) and the VAS were used to assess the efficacy of treatment. According to the RMS, one year after the procedure, an excellent or good score was considered a successful treatment.¹⁰ At the end of the one-year period, 92.9 percent of patients reported excellent, good, or acceptable functionality.¹⁰ Four of five athletic patients were able to return to their sports at the same level as before the onset of their plantar fasciitis.¹⁰ Pain scores measured by the VAS decreased significantly from 7.1±1.1 before

treatment to 1.9 ± 1.5 at the one-year follow-up. None of the patients in this study reported adverse reactions to treatment.¹⁰

A prospective study by Sengodan et al. 2020, treated 100 patients with a PRP injection for their chronic plantar fascitis.⁸ Patient pain was assessed before and after injection using the VAS and the American Orthopedic Foot and Ankle Score (AOFAS). The AOFAS evaluates the foot and ankle for pain, function, and alignment. A score of 100 indicated a healthy ankle. The average participant's pain according to the VAS was 9.1 before injection and 1.6 after treatment.⁸ At the end of eight weeks, patient AOFAS improved significantly from 52 to 90.⁸

In the American Journal of Sports Medicine, Peerbooms et al. 2019, assessed the effectiveness of platelet-rich plasma compared to corticosteroids (40 mg/mL)triamcinolone of acetonide) in the treatment of plantar fasciitis.5 The primary measure used was the Foot Function Index (FFI) pain score. The FFI is a questionnaire that measures patients' pain, disability, and activity limitations. High scores correlate to increased pain, disability, and patient limitation. Secondary measures were function and quality of life. Function was assessed per FFI Activity, FFI Disability, and American Orthopaedic Foot and Ankle Society measures. Ouality of life was scored using the short version of the World Health Organization Quality of Life (WHOQOL-BREF). In this randomized controlled trial, patients were divided into a PRP group and a corticosteroid group (control). All outcomes were measured at baseline, four weeks, 12 weeks, 26 weeks, and one year after injection.⁴ The corticosteroid group pain scores decreased more rapidly than the PRP group and remained stable.5 The PRP group pain reduction occurred less rapidly but showed significantly lower FFI pain scores at the oneyear follow-up compared to the corticosteroid group (mean difference, 14.4; 95% CI, 3.2- 25.6).⁴ Additionally, 84.4 percent of the PRP group showed at least 25 percent improvement from 0 to 12-months compared to the corticosteroid group's 55.6 percent.⁵ However, according to the WHOQOL-BREF, the difference in the quality of life between the two groups failed to be significant at the 12- month followup.⁴

In a similar study, Vahdatpour et al. 2016, a single-blind randomized controlled trial was conducted with 32 patients with plantar fasciitis. Patients were randomly assigned into a PRP group and a corticosteroid group (methylprednisolone 1 ml plus lidocaine 1 ml).³ The VAS and the RMS were measured at baseline, one month, three months, and six months. The VAS and RMS access for pain severity, and pain and limitation of activity respectively. The PRP group experienced a higher mean pain severity before injection and at the onemonth and three-month follow-up compared to the corticosteroid group.3 However, according to the RMS, 81.2 percent of the PRP group reported excellent physical ability compared to 6.2 percent of the corticosteroid group at six months.3

Singh et al. 2017, conducted a systematic review comparing pain and functional scores after treatment of plantar fasciitis with PRP or corticosteroid injection at three and six-month followup. The studies included in this review reported outcomes using the visual analogue score (VAS) and American Orthopaedic Foot and Ankle Score (AOFAS). A metanalysis of the included studies was conducted. There was no significant difference in VAS or AOFAS scores between the corticosteroid and PRP groups at the one-month and six-month followups. However, PRP injections were associated with improved VAS and AOFAS scores at the 3-month follow-up when compared to the corticosteroid group.⁹

Discussion

The use of PRP injections for musculoskeletal conditions has become increasingly more common. Injection of PRP stimulates the healing process and reverses the degenerative process by introducing platelets, growth factors, and cytokines that support the healing of the fascia.^s A benefit of using PRP injection is that it is an autologous injection.^s Using the patient's blood decreases the risk of adverse reaction to treatment.

Though PRP's autologous nature has eliminated most risk factors resulting in adverse effects, the increase in growth factors and cytokines introduced by PRP could hypothetically initiate malignancy. For this reason, PRP is contraindicated in patients with active infections. neoplasm. coagulopathies, and pregnancy.8 The application of platelet-rich plasma in the treatment of plantar fasciitis is encouraging considering its decreased risk of having adverse effects in patients compared to corticosteroids alternatives. Corticosteroid injection treatment has shown a high frequency of injury recurrence.4 This is believed to be due to changes in fascia structure from overuse. The quick pain relief provided by these treatments can be counterintuitive to healing because they can promote a pre-mature return to activity.5 Limitations of this review include a low quantity of articles comparing PRP and corticosteroid as PRP is a newer treatment. Additionally, the studies rarely extend past one year, and the preparation and dosage of both types of injections varied between research studies.

The short duration of many of these studies may not have allowed research to show the true longterm efficacy of PRP. Many of these studies showed that PRP required a longer period to achieve clinical efficacy compared to corticosteroids, thus promoting healing, and preventing re-injury from premature return to activity.¹⁰ This longer period required to reach clinical efficacy poses the question of whether there are additional benefits of PRP as compared to corticosteroids than those seen in current studies. All of the included studies in this review assessed treatment efficacy for up to one year or less. Future studies analyzing PRP treatments may benefit from having a longer follow-up period after treatment. Additionally, the preparation of PRP and corticosteroids varied between studies in this review and could account for variation in efficacy in patients.9 The measures of pain and function also differed between studies. Lastly, many of the studies analyzing PRP treatment for plantar fasciitis have had smaller sample sizes and have mostly consisted of pilot studies.9 A standardized measure for the analysis, larger sample sizes, and consistent preparation of PRP would be beneficial in future evaluation to compile data for a more robust analysis.9

Conclusion

PRP is a safe and effective treatment modality. Functional and pain outcomes in patients were shown to improve with the use of PRP. Compared to corticosteroids, PRP has greater potential for improvement of plantar fasciitis symptoms over a longer period of time but corticosteroids were shown to be more effective for short-term pain relief. The use of PRP for plantar fasciitis is a relatively new intervention, in which the full scope of its benefits remains to be seen and requires continued research.

References

1. Rouzier, Pierre, Ehrlich, Ian, Dorshimer, Gary W. Plantar Fasciitis. DynaMed. 2020.

2. Rocco, R., 2014. Platelet-Rich Plasma Efficacy Versus Corticosteroid Injection Treatment for Chronic Severe Plantar Fasciitis. *Foot & Ankle International.* 2014;35(4):,313-318.

3. Vahdatpour B, Kianimehr L, Moradi A, Haghighat S. Beneficial effects of platelet-rich plasma on improvement of pain severity and physical disability in patients with plantar fasciitis: A randomized trial. Adv Biomed Res. 2016;5(179)

4. Chen, CM., Lee, M., Lin, CH. et al. Comparative efficacy of corticosteroid injection and non-invasive treatments for plantar fasciitis: a systematic review and meta-analysis. Sci Rep 8, 4033 (2018).

5. Peerbooms JC, Lodder P, den Oudsten BL, Doorgeest K, Schuller HM, Gosens T. Positive Effect of Platelet-Rich Plasma on Pain in Plantar Fasciitis: A Double-Blind Multicenter Randomized Controlled Trial. Am J Sports Med. 2019;47(13):3238-3246.

6. Ragab EMS, Othman AMA. Platelets rich plasma for treatment of chronic plantar fasciitis. Archives of Orthopaedic and Trauma Surgery. 2012;132(8):1065-1070.

7. Borrione P, Fagnani F, Di Gianfrancesco A, Mancini A, Pigozzi F, Pitsiladis Y. The Role of Platelet-Rich Plasma in Muscle Healing. *Current Sports Medicine Reports*. 2017;16(6):459-463.

8. Sengodan V, Thiagarajan N, Raajendiren I. Evaluating the efficacy of platelet rich plasma injection for the treatment of chronic plantar fasciitis. *Journal of Natural Science, Biology & Medicine*. 2020;11(2):135-139.

9. Singh P, Madanipour S, Bhamra JS, Gill I. A systematic review and meta-analysis of platelet-rich plasma versus corticosteroid injections for plantar fasciopathy. Int Orthop. 2017;41(6):1169-1181.

10. Martinelli N, Marinozzi A, Carnì S, Trovato U, Bianchi A, Denaro V. Platelet-rich plasma injections for chronic plantar fasciitis. Int Orthop. 2013;37(5):839-842.

The Role of Hormesis in Polyphenol Dietary Treatments for Diabetic Neuropathy

Madeleine M. Mendoza, M.A. and Elaine Y. Chu, B.S.

ABSTRACT

Objectives: This literature review aims to examine whether hormesis, in which mild systemic stressors can activate endogenous antioxidant and anti-inflammatory pathways, should be considered when establishing prophylactic dietary treatments with polyphenols for diabetic neuropathy.

Methods: A Google Scholar and PubMed search was conducted on empirical studies investigating the hormetic effect of polyphenols as a dietary treatment for diabetic neuropathy.

Results: Mild consumption of polyphenols has antioxidant and anti-inflammatory effects that are efficacious in preventing diabetic neuropathy. However, the role of hormesis is inconclusive.

Conclusion: Future research should examine the role of hormesis to improve the current use of polyphenol-rich

dietary treatments for diabetic neuropathy. A wider range of dosages should be examined and more standardization on the dosages, frequency, and onset of administration should be considered.

Introduction

Diabetic neuropathy is the most common diabetic complication, affecting around 50 percent of patients with the disease.¹ Diabetic neuropathy is the most common cause of non-traumatic amputations and foot ulcers.¹ Patients with diabetic neuropathy commonly report neuropathic pain disabilities, recurrent hospitalizations, and poor quality of life. Although it is commonly seen in clinical practice, effective preventative treatments are still lacking.¹

Oxidative Stress

Previous studies have demonstrated that oxidative stress plays a key role in diabetic neuropathy. There are many forms of oxidative stressors including reactive oxygen species (ROS), reactive nitrogen species (RNS), and free radicals that are of most concern in biological systems that are derived from oxygen. Oxidative stress is caused by an imbalance between the production of free radicals, and the inability of the body to counteract their harmful effects with antioxidants. This imbalance of excess free radicals can lead to damage of cellular molecules associated with increased oxidative stress-related diseases, such as diabetic neuropathy.²

and/or irritant properties that assists in their natural defense mechanisms against metabolic byproducts (e.g., ROS and RNS) and environmental threats.⁵ Over 8,000 polyphenols have been identified across various fruits, vegetables, spices, oils, nuts, and cocoa and among the best studied are curcumin, quercetin, and resveratrol. They have demonstrated to be efficacious preventative treatments of several chronic diseases based on their antioxidant and antiinflammatory effects, including:

- cardiovascular disease⁶
- cancer⁷
- obesity⁸

Inflammation

In addition to oxidative stress, inflammation has been considered as one of the hallmarks of diabetic neuropathy. The inflammatory reaction begins once the body recognizes the threat. An inflammatory reaction is initiated that consists of nitric oxide and proinflammatory cytokines (e.g. IL-1, IL6, and TNF- α).³ These molecules initiate the inflammatory process by causing dilation of blood vessels and increased permeability of endothelial cells. This increases the amount of red and white blood cells in the damaged area. One of the most important inflammatory mediators mentioned above is the production of proinflammatory cytokines. The release of these cytokines is generally helpful because it is the body's way of healing and repairing itself against damaged tissue; however, when it is released in excessive quantities, it can become toxic to the body.⁴

Polyphenols as Prophylactic Dietary Treatment

A large body of research has demonstrated that polyphenols, a type of phytochemical, may serve as a preventative strategy for diabetic neuropathy. Phytochemicals are broadly defined as plant-derived compounds that play a role in the pigment, odor,

- pancreatitis⁹
- gastrointestinal problems¹⁰
- osteoporosis¹¹
- lung damage¹²
- neurodegenerative diseases¹³
- gut microbiota issues¹⁴

Although some may expect larger amounts of polyphenols to elicit greater benefits, previous research has demonstrated that this is not the case. There have been studies and control trials in animals and humans that have demonstrated that high levels of antioxidants could not prevent or ameliorate oxidative-stress and inflammation related diseases.¹⁵ This may be due to evolutionary-based adaptive responses. When we eat polyphenols in plant-based foods, we consume low levels of these toxic chemicals which mildly stress cells in the body. At these low levels, the body's cells adapt to this mild stress and become stronger. This process of bolstering cellular resilience is an example of hormesis, or the process in which low doses cause stimulation and high doses cause inhibition in a dose-response fashion.¹⁶ Evidence for hormesis does not undermine the effects of antioxidants and anti-inflammatories. Rather, the biochemical processes set in motion by hormetic stress seem to control when these molecules are available to be used by the body.

The purpose of this literature review is to examine whether hormesis, in which mild systemic stressors can activate endogenous antioxidant and anti-inflammatory pathways, should be considered when establishing prophylactic dietary treatments for diabetic neuropathy.

Methods

A Google Scholar and Pubmed search was conducted with the keywords "diabetic neuropathy", "diabetes", "polyphenols", "hormesis", "oxidative stress", and "inflammation" for papers published within the last few decades. A literature review was conducted to determine the efficacy of polyphenols as an effective preventative treatment for diabetic neuropathy and examine the effects of hormesis on outcomes. The excluded criteria restricted non-English publications.

Results

Curcumin

Curcumin, a polyphenol mostly found in turmeric, has been shown to exhibit anti-oxidative and anti-inflammatory properties. Zhao et al. (2014) focused on the efficacy of curcumin in reducing oxidative stress underlying diabetic neuropathy.¹ Curcumin (200mg/kg) was administered over two weeks to streptozotocin (STZ) induced rats (which modeled diabetic neuropathy) and reduced markers of diabetic neuropathy in the spinal cord through reduction of oxidative stress triggered by nicotinamide adenine dinucleotide phosphate (NADPH) oxidase. Not only have the anti-oxidative properties of curcumin been examined, but the anti-inflammatory potential for diabetic neuropathy has also been explored. Research conducted by Sharma et al. (2007) focused on these anti-inflammatory effects of curcumin. Curcumin (60 mg/kg) was administered to mice models of diabetic neuropathy STZ-induced mice over four weeks.¹⁸ They exhibited antiinflammatory effects through reducing levels of nitric oxide and TNF- α , thus reducing symptoms associated with diabetic neuropathy such as neuropathic pain (i.e., allogynia and hyperalgesia).

Quercetin

Additionally quercetin, another polyphenol commonly found in plant-based foods (e.g., onions, grapes, berries, cherries, broccoli, and citrus fruits) was also examined. Anjaneyulu & Chopra (2004) demonstrated the effect of quercetin on oxidative stress.¹⁹ Quercetin (10 mg/kg per day) was orally administered for 4 weeks in both control and STZinduced rats. Results showed that treating with quercetin significantly decreased renal dysfunction and oxidative stress in diabetic rats. Furthermore, Ji et al., (2017) examined guercetin on inflammation and pain associated with diabetic neuropathy.²⁰ A spinal nerve ligation (SNL) model was used to mimic symptoms of neuropathic pain in diabetic rats. The treatment group was orally administered 100mg/kg over 14 days and experienced significantly less inflammation and pain associated with diabetic neuropathy through suppressing the toll-like receptor (TLR) signaling pathway.

Resveratrol

Similarly, resveratrol, а polyphenol commonly found in grapes, peanuts, and a variety of berries has also been explored. To examine the antioxidative properties of resveratrol, Kumar et al. (2007) found dose-dependent improvement in STZ-induced mice given resveratrol (10mg/kg or 20mg/kg) for 14 days.²¹ Treatment with resveratrol at 10 and 20 mg/kg produced significant improvement in the nerve conduction deficits (82 percent and 90 percent, respectively) and nerve blood flow deficits (71 percent and 92 percent, respectively) in the diabetic rats. Both demonstrated significantly improved sensorv alterations in mechanical and thermal hyperalgesia in dinitrophenol rats. This activity may be ascribed to its actions on the pathways related to oxidative stress. Additionally, Tao et al. in 2016 revealed that dosedependent treatment with resveratrol relieved neuropathic pain (i.e., hyperalgesia and allodynia), inhibited the pro-inflammatory cytokine expression (e.g., IL-1 β , and TNF- α), and enhanced the antiinflammatory cytokine expression (e.g., IL-10) most significantly at 40 mg/kg compared to 10 or 20 mg/kg. However, these effects were not significant at 5 mg/kg.²²

Discussion

Limitations of this study were the sparse amount of experiments and literature done on hormesis in relation to diabetic neuropathy. There were multiple studies involving anti-oxidative and anti-inflammatory effects of polyphenols, but very few examined a wide range of dosages or directly examined hormesis. Additionally, all studies included animal models which may limit the overall generalizability to humans. Therefore, results relating to hormesis came out to be largely inconclusive, and more work and experimental design revolving hormesis needs to be done.

First, Zhao et al. (2014) and Sharma (2007) found that curcumin reduced oxidative stress and inflammation associated with diabetic neuropathy, respectively. These studies use different animal species (i.e., rats and mice) which strengthens the generalizability of these findings to humans. However, it does make it more difficult to draw conclusions regarding the effects of dosage because different species have varying metabolisms which could influence the bioavailability of the polyphenol treatment. Additionally, both of these papers only explored the effects elicited from one treatment dosage. Therefore, while the benefits of curcumin have been established, examining a wider-range of doses would be necessary to examine the possibility of a dose-response relationship that is one of the hallmarks of hormesis. It is also difficult to draw conclusions because both studies were administered over different time spans (two and four weeks).

Furthermore, the studies involving quercetin examined its effects on inflammation and oxidation in different models of diabetic neuropathic mice, with the study by Anjaneyulu & Chopra (2004) using the more common method (STZ) and Ji et al. (2017) using a less common method (SNL) to induce diabetic neuropathy in these mice. While both showed a decrease in oxidation, inflammation, pain, and even renal dysfunction, it also introduced the possibility of having different diabetic mouse models eliciting different symptoms.

Lastly, Kumar et al. (2017) and Tao et al. (2016) found that resveratrol decreased oxidative stress and inflammation associated with diabetic neuropathy. Kumar et al. (2017) found that the larger dose of resveratrol (20mg/kg) was more beneficial compared to the lower dose (10mg/kg), which can be interpreted as evidence against the theory of hormesis. However, this study had a limited dose range which may have contributed to a limited dose-response curve to demonstrate hormesis. The same conclusion can be said for the Tao et al. (2016) study. While a larger dosage of polyphenols are demonstrated to be more beneficial, which is consistent with the literature, there is not a wide range of doses being examined.

Therefore, the results of this literature review are inconclusive and more research surrounding the hormetic effect of polyphenols on diabetic neuropathy should be conducted. More standardization on the dosages, frequency, and onset of administration should be implemented to better compare and draw conclusions. Additionally, when comparing the efficacy of polyphenol treatments in different species, the bioavailability of these polyphenols should be examined to better understand the dosages at which these polyphenols may be beneficial or detrimental to humans. Additionally, a much wider range of polyphenol dosages must be examined to determine if there is a dose-response relationship between these dietary treatments and outcomes for individuals with diabetic neuropathy.

Since there are numerous different types of polyphenols, a dose-response curve for each may also differ depending on sex, species, age, etc. Taken together, a review of the literature demonstrated that mild consumption of polyphenols is efficacious in preventing diabetic neuropathy. However, the possible detrimental effects at larger doses have yet to be considered.

Conclusion

Diabetic neuropathy is a salient issue in the podiatric community with the primary underlying mechanisms being oxidative stress and inflammation. While some may expect larger amounts of polyphenols to elicit increased benefits, some research demonstrates that it is not the case due to hormesis. This has been demonstrated to be true for diseases and disorders involved in inflammation and oxidative stress, that are similar to diabetic neuropathy. This review of the literature has demonstrated that mild dietary consumption of polyphenols may serve as a preventative strategy that is convenient to incorporate into a daily routine. However, the role hormesis plays in polyphenols treatments for diabetic neuropathy should be further evaluated.

References

- 1. Vinik AI, Nevoret ML, Casellini C, Parson H. Diabetic neuropathy. *Endocrinology and Metabolism Clinics*. 2013;42(4):747-787.
- 2. Hussain T, Tan B, Yin Y, Blachier F, Tossou MC, Rahu N.Oxidative stress and inflammation: what polyphenols can do for us?. Oxidative medicine and cellular longevity, 2016.1-9 https://doi.org/10.1155/2016/7432797
- 3. Pennisi M, Crupi R, Di PR, Ontario ML, Bella R, Calabrese EJ et al. Inflammasomes, hormesis, and antioxidants in neuroinflammation: Role of NRLP3 in Alzheimer disease. *Journal of neuroscience research.* 2017;95(7),1360-1372.
- 4. Rahman I, Biswas SK, Kirkham PA. Regulation of inflammation and redox signaling by dietary polyphenols. *Biochemical Pharmacology*. 2006;72(11): 1439–1452.
- 5. Rahman I, Biswas SK, Kirkham PA. Regulation of inflammation and redox signaling by dietary polyphenols. *Biochemical Pharmacology*, 2006;72(11),1439–1452.
- 6. Michalska M, Gluba A, Mikhailidis DP, et al. The role of polyphenols in cardiovascular
disease. *Medical Science Monitor*. 2010;16(5).

- Yang CS, Chung JY, Yang G, Chhabra SK, & Lee MJ. Tea and tea polyphenols in cancer prevention. *The Journal of nutrition*. 2000;130(2):472S-478S.
- 8. Wang S, Moustaid-Moussa N, Chen L, et al. Novel insights of dietary polyphenols and obesity. *The Journal of nutritional biochemistry*. 2014;25(1):1-18.
- 9. Shapiro H, Singer P, Halpern Z, Bruck R. Polyphenols in the treatment of inflammatory bowel disease and acute pancreatitis. *Gut.* 2007;56(3):426-436.
- 10. Dryden GW, Song M, McClain C. Polyphenols and gastrointestinal diseases. *Current opinion in gastroenterology*. 2006;22(2):165.
- Đudarić L, Fužinac-Smojver A, Muhvić D, Giacometti J. The role of polyphenols on bone metabolism in osteoporosis. *Food Research International*. 2015;77:290-298.
- 12. Wood LG, Wark PA, Garg ML. Antioxidant and anti-inflammatory effects of resveratrol in airway disease. *Antioxidants & redox signaling*. 2010;*13*(10):1535-1548.
- 13. Hartman RE, Ross DM. Effects and mechanisms of actions of phytochemicals on Alzheimer's disease neuropathology. *Front Bioscience (Elite Edition)*. 2018;1(10):300-333. doi:10.2741/e824
- 14. Singh A, Yau YF, Leung KS, El-Nezami H, Lee JCY. Interaction of polyphenols as antioxidant and anti-inflammatory compounds in the brain-liver-gut axis. *Antioxidants*. 2020;9(8):669.
- Pandey KB, Rizvi SI. Plant polyphenols as dietary antioxidants in human health and disease. Oxid Med Cell Longev. 2009;2(5):270-278. doi:10.4161/oxim.2.5.9498
- 16. Son TG, Camandola S, Mattson MP. Hormetic dietary phytochemicals. *Neuromolecular medicine*. 2008;10(4):236.
- Martel J, Ojcius DM, Ko Y, Ke PY, Wu CY, Peng HH, et al. Hormetic effects of phytochemicals on health and longevity. *Trends in Endocrinology & Metabolism*. 2019;30(6):335-346.
- Zhao X, Xu Y, Zhao Q, Chen CR, Liu AM, Huang ZL. Curcumin exerts antinociceptive effects in a mouse model of neuropathic pain: descending monoamine system and opioid receptors are differentially involved. *Neuropharmacology*. 2012;62(2):843-54. doi: 10.1016/j.neuropharm.2011.08.050.

- 19. Sharma S, Chopra K, Kulkarni SK. Effect of insulin and its combination with resveratrol or curcumin in attenuation of diabetic neuropathic pain: participation of nitric oxide and TNF-alpha. *Phytother Res.* 2007;21(3):278-283. doi:10.1002/ptr.2070
- 20. Anjaneyulu M, Chopra K. Quercetin, an antioxidant, bioflavonoid, attenuates diabetic neuropathy in rats. *Clinical and Experimental Pharmacology and Physiology*. 2004;31(4):244–248. doi:10.1111/j.1440-1681.2004.03982.x
- 21. Ji C, Xu Y, Han F, Sun D, Zhang H, Li X, et al. Quercetin alleviates thermal and cold hyperalgesia in a rat neuropathic pain model by inhibiting Toll-like receptor signaling. *Biomed Pharmacother*. 2017;94:652-658. doi: 0.1016/j.biopha.2017.07.145.
- 22. Kumar A, Kaundal RK, Iyer S, Sharma SS. Effects of resveratrol on nerve functions, oxidative stress and DNA fragmentation in experimental diabetic neuropathy. *Life Science*. 2007;80(13):1236-1244. doi:10.1016/j.lfs.2006.12.036.
- 23. Tao L, Ding Q, Gao C, et al. Resveratrol attenuates neuropathic pain through balancing pro-inflammatory and antiinflammatory cytokines release in mice. *International Immunopharmacology*. 2016;34,165–172. doi:10.1016/j.intimp.2016.02.033.

A Comparison of the Efficacy of Pharmacological, Physical, and Compression Therapy in the Treatment of Stasis Dermatitis: A Literature Review

Marian Banh, B.A., Quang Pham, B.S.

ABSTRACT

Objective: To summarize and compare the current literature on the effectiveness of various pharmacological, physical, and compression therapy in the treatment of stasis dermatitis.

Methods: A literature search was conducted on PubMed and Google Scholar in order to retrieve articles discussing the various available treatments options for stasis dermatitis. Twenty-nine articles were cross-analyzed and included in this review.

Results: Stasis dermatitis can be characterized as skin inflammation in the lower extremities due to poor venous drainage and chronic edema. Untreated chronic edema is progressive and the prognosis for a patient can be drastically improved if identified and treated earlier. Examples of treatment modalities that can be used to manage stasis dermatitis include pharmacological, physical, and compression therapy. Of these treatment options, compression therapy has been shown to be most effective when used alone.

Conclusion: Although compression therapy has the highest efficacy in increasing chronic venous drainage in the lower extremity, studies have shown the efficacy of compression therapy improves when it is used in combination with pharmacological or physical therapies.

Introduction

Stasis dermatitis is a severe form of inflammatory dermatosis resulting from poor chronic venous drainage and chronic edema in the lower extremities.^{1,2} Poor chronic venous drainage scales steeply with age and presents more commonly in men than women.³ Patients with stasis dermatitis clinically present with scaliness and erythema on their legs along the medial malleolus with other common dermatoses such as varicose veins, edema, ulcers, and cellulitis.^{1,2} The risk of chronic venous insufficiency and stasis dermatitis is greatly increased by environmental factors such as obesity, lack of physical exercise, and previous injuries to the lower extremities, due to potential damage and obstruction of venous valves.^{2,4,5} Associated clinical manifestations of chronic venous insufficiency and stasis dermatitis include peripheral artery disease and heart failure.⁶ In a 2021 crosssectional study of 12,423 participants over a 5 year period, chronic venous insufficiency was found to be a strong predictor of cardiovascular disease (P =0.0003), independent of age, sex, and other risk factors.6

Stasis dermatitis is present in an average of 6% of individuals over the age of 50 years old.² Along with the aesthetic, superficial implications of stasis

dermatitis, those suffering from the disease tend to develop cutaneous and musculoskeletal issues in their lower extremities such as itching, tingling, aching, restlessness, and cramping.³ Stasis dermatitis patients have been shown to perceive a reduced quality of life due to their venous ulceration and varicose veins. 7,8 Patients suffering from stasis dermatitis and its comorbidities report feelings of depression and anxiety as well as distress due to the inability to find fitting clothes or perform daily activities.⁹ Stasis dermatitis tends to be undertreated due to a lack of awareness about effective treatment methods, such as pharmacological, physical, and compression therapies, so patients continue to suffer from its effects.10

Methods

PubMed and Google Scholar search engines were used to find a total of 29 published articles relevant to the treatment of stasis dermatitis using pharmacological, physical, and compression therapy. Articles unrelated to the objective of this paper or that discussed treatment options that were beyond the scope of this paper were excluded.

Results

Current pharmacotherapy options have shown to be effective in managing multiple symptoms of stasis dermatitis, ¹¹⁻¹⁵ but there has yet to be a single proven standard for its treatment. This may be due to the vast amount of associated symptoms that can either directly or indirectly be caused by the inflammatory aspect of the vascular disorder. Although there is currently no consensus on the most effective treatment for stasis dermatitis, the amount of progress in development of pharmaceutical drugs alone and in combination is proving to be promising. Doxycycline hyclate, a tetracycline antibiotic with anticollagenolytic and anti-inflammatory properties has demonstrated a favorable response in the reduction of tissue destruction during rheumatoid arthritis treatment.¹² The use of Tacrolimus 0.1% ointment alone in treating stasis dermatitis was found to be more effective than treatment using low-potency corticosteroids across physician and participant assessment.¹³ In a study of 506 participants, it was found that compared to Pimecrolimus 1%, participants treated with Tacrolimus 0.1% were twice as likely to improve by a physician's assessment (RR 1.80, 95% CI 1.34 to 2.42).¹³ A similar study comparing Tacrolimus 0.03% and mild topical corticosteroids among 790 participants found that Tacrolimus 0.03% was superior for a physician's assessment (RR 1.21, 95% CI 1.96 to 3.38).13 Tacrolimus, a class of topical calcineurin inhibitors, may offer a safer alternative to steroidal treatment approach to а various inflammatory skin conditions including eczema, rosacea, and vitiligo.¹⁴ Combination therapy of oral doxycycline and topical tacrolimus has also been effective in reducing pain, erythema, edema, itching, and exudation in dermatitis affected areas among male and female subjects over 18 years of age (p < 0.01, n =15). 11

Calcium dobesilate, a capillotropic agent, has often been used in the treatment of chronic venous diseases.¹⁹ This synthetic drug regulates capillary hyperpermeability by inhibiting platelet aggregation and activating lymphatic drainage.¹⁷ Low daily doses of 500-1500 mg demonstrated relief of symptoms associated with venous-lymphatic insufficiency in the lower extremities.¹⁶ A 2003 study found that treatment using 1000 mg calcium dobesilate over the course of 8 weeks resulted in a significant reduction of ulcer size, leg swelling, reported itch and pain among 25 total

patients, of whom 15 had venous ulcers with/without stasis dermatitis and 10 with stasis dermatitis only.¹⁸ Furthermore, a more extensive double-blind, placebocontrolled study of 256 patients reported improvement in similar symptoms including pain, discomfort, itching, cramps, and leg edema reduction after treatment using 500 mg of calcium dobesilate after 8 weeks.¹⁹ Of these studies, little to no adverse effects were found. However, according to a postmarketing surveillance (PMS) report from OM Pharma covering the period 1995-2003, there was a 26% frequency of fever and 12.5% frequency of gastrointestinal disorders reported with the use of calcium dobesilate, although no deaths were reported.²⁰ Although more evidence is required to analyze the adverse effects of calcium dobesilate, the effectiveness and safety of the oral alternative proves to be promising.

Poor venous drainage caused mainly by lower extremity immobility can induce local tissue to swell with protein-rich fluid.²¹ A method of increasing venous drainage in the lower extremities is muscle pump action which involves using the muscles in the lower extremities, such as the soleus and gastrocnemius, to assist in mobilizing the fluid buildup. Physical therapy interventions have proven to be effective in addressing venous stasis in lower extremities.^{22,23} In a study of 155 venous stasis patients, physical therapy provided significant improvement of leg edema (p < 0.0001).²² Physical therapy mobilized an average of 303.13 ± 69.72 ml (p = 0.00002) and 334.38 ± 62.50 ml (p = 0.000003) of static fluid in patients' lower extremities.²³ However, the physical therapy options are more effective when the lower extremities are elevated above the body to allow the lymphatic drainage to occur with gravity.²⁴ If the edema and venous damage in the lower extremities limit the efficacy of physical therapy, an aquatic exercise regimen where there is less body weight pressure on the lower limbs has proven to be effective in mobilizing the static fluid in the lower extremities.23

Despite the potential benefits of physical therapy on the treatment and management of stasis dermatitis, there are those who are unable to undergo physical therapy due to prior injury or lack of muscle strength.^{2,4,5} Another potential management option is compression therapy where a compression sock or bandage is administered to the lower extremities to passively mimic muscle pump action.^{10,25}

Compression therapy assists the lower extremity musculature to increase venous flow velocity, reduces reflux, and decreases the amount of interstitial fluid trapped in lower extremity tissues.^{10,26} Although compression therapy has been shown to decrease the frequency of stasis dermatitis flare-ups (p = 0.02), its major obstacles are poor compliance and the lack of awareness towards compression therapy as a potential treatment.^{10, 27-28} For some patients, poor compliance with compression therapy is due to the sensation of the compression garment itself and the inability to receive education about compression therapy application from their physicians.^{25,27}

Discussion

In summary, the use of oral antibiotics alone and in combination with topical non-steroidal creams in the treatment of stasis dermatitis has been extremely effective in managing the various symptoms associated with a vascular inflammatory disorder. In particular, the use of low daily doses of 500-1500 mg oral calcium dobesilate has been shown to help in the reduction of ulcer size, leg swelling, pain, itch, and leg edema among patients when taken over the course of 8 weeks.^{16,18,19} Although the reported improvements in symptoms demonstrated no adverse side-effects among the open pilot study of 25 patients, 5 of the 12 patients who were surveyed post-therapy reported recurrence of venous ulcers. More double-blind studies are required in the future to analyze and detect adverse side effects, with a special focus on evaluating the effects of calcium dobesilate post-therapy. In regards to calcineurin inhibitors, such as Tacrolimus 0.1% and Pimecrolimus 0.1%, several studies demonstrated marked improvement in physician's and participants' self-assessment. However, a burning sensation was reported more frequently with the use of calcineurin inhibitors compared to corticosteroids. Although serious adverse events were rare, the reliability and strength of these studies warrant more data. Furthermore, an evaluation of costs, as well as the increased risk of skin atrophy, should be evaluated in future studies. In addition, doxycycline hyclate, when used in combination with topical Tacrolimus 0.1% ointment demonstrated a possible additive effect for addressing the symptoms associated with stasis dermatitis.¹¹⁻¹⁴ In the study of 19 participants, 86% demonstrated improvement in overall dermatitis area but 6.7% failed to show any improvement. The lack of a control arm and financial constraints may have skewed the findings of this study. More extensive studies are warranted in determining the efficacy of combination therapy treatments for stasis dermatitis.

In addition to pharmacological treatments, physical and compression therapy have been effective in managing the associated leg edema of stasis dermatitis. Specifically, physical exercise therapies that minimized the gravitational force on interstitial fluid in the legs have consistently shown to significantly improve fluid mobilization and reduce leg edema.^{15,21,23,24} The physical therapy studies were conducted on a total of 171 participants and concluded physical therapy's effect on stasis dermatitis was statistically significant (p < 0.0001). On the other hand, compression therapy has shown to greatly improve stasis dermatitis symptoms when the pressure exerted by the compression garment is at least 20-30 mmHg.^{2,26,27} The 2012 study reported that compression therapy immediately improved the ejection fraction of extracellular fluid from lower extremities and continued to show statistically significant improvement after seven days (p < 0.001, n = 18). However, in the 2021 study, only 26% of patients (p = 0.02, n = 100) reported wearing their compression stockings daily. Therefore, the greatest barrier to the efficacy of compression therapy may be patient compliance.

Individually, pharmaceutical, physical, and compression therapies have proven to be successful in treating stasis dermatitis. Tandem use of physical and compression therapy has shown to be highly effective in healing venous ulcers and reducing the recurrence of edema.^{2,5} In some patients, stasis dermatitis was successfully managed with only compression and physical therapy.²¹ In addition, combining compression therapy and pharmaceutical treatments has proven to be effective at shortening venous ulcer healing time.⁵ The causes for stasis dermatitis vary greatly leading to difficulty deciding treatment options, but it is proven that compression therapy is crucial to the management of stasis dermatitis because it has been used congruently with pharmaceutical and physical therapies. Past studies have only evaluated the efficacy of using two out of the three treatment options in tandem. The efficacy of the intersection of pharmaceutical, physical, and compression treatment options has yet to be studied and may prove to be the most effective treatment method for stasis dermatitis.

Conclusion

Managing and treating stasis dermatitis has proven to be difficult because the management method depends greatly on factors such as the location, severity, and complexity of the edema as well as the patient's psychological state.¹⁵ Management options for stasis dermatitis and chronic edema include pharmacological intervention through oral drugs, physical therapy, and compression therapy. Although compression therapy is considered to be the most critical to successful treatment, the efficacies of these various management methods have yet to be compared to determine a general consensus on the most effective treatment option.¹⁰

References

- 1. Fransway AF, Fowler J, Corona R. Stasis Dermatitis. In: UpToDate. Wellesley, MA: s.n.
- Sundaresan S, Migden MR, Silapunt S. Stasis Dermatitis: Pathophysiology, Evaluation, and Management. Am J Clin Dermatol. 2017;18(3):383-390. doi:10.1007/s40257-016-0250-0
- Ruckley CV, Evans CJ, Allan PL, Lee AJ, Fowkes FGR. Chronic venous insufficiency: Clinical and duplex correlations. The Edinburgh Vein Study of venous disorders in the general population. J Vasc Surg. 2002;36(3):520-525. doi:10.1067/mva.2002.126547
- Jawien A. The Influence of Environmental Factors in Chronic Venous Insufficiency. Angiology. 2003;54(1_suppl):S19-S31. doi:10.1177/0003319703054001S04
- Werchek S. Diagnosis and treatment of venous leg ulcers. Nurse Pract. 2010;35(12):46-53. doi:10.1097/01.NPR.0000390438.98004.be
- Prochaska JH, Arnold N, Falcke A, et al. Chronic venous insufficiency, cardiovascular disease, and mortality: a population study. Eur Heart J. 2021;42(40):4157-4165. doi:10.1093/eurheartj/ehab495
- Kurz X, Lamping DL, Kahn SR, et al. Do varicose veins affect quality of life? Results of an international population-based study. J Vasc Surg. 2001;34(4):641-648. doi:10.1067/mva.2001.117333
- Palfreyman S. Assessing the impact of venous ulceration on quality of life. Nurs Times. 2008;104(41):34-37.
- Greene A, Meskell P. The impact of lower limb chronic oedema on patients' quality of life. Int Wound J. 2017;14(3):561-568. doi:10.1111/iwj.12648
- Keast DH, Despatis M, Allen JO, Brassard A. Chronic oedema/lymphoedema: Under-recognised and undertreated. Int Wound J. 2015;12(3):328-333. doi:10.1111/iwj.12224
- Maroo N, Choudhury S, Sen S, Chatterjee S. Oral doxycycline with topical tacrolimus for treatment of stasis dermatitis due to chronic venous insufficiency: A

pilot study. Indian J Pharmacol. 2012;44(1):111-113. doi:10.4103/0253-7613.91878

- Nordström D, Lindy O, Lauhio A, Sorsa T, Santavirta S, Konttinen YT. Anti-collagenolytic mechanism of action of doxycycline treatment in rheumatoid arthritis. Rheumatol Int. 1998;17(5):175-180. doi:10.1007/s002960050030
- Cury Martins J, Martins C, Aoki V, Gois AFT, Ishii HA, da Silva EMK. Topical tacrolimus for atopic dermatitis. Cochrane Databas131e Syst Rev. 2015;2015(7). doi:10.1002/14651858.CD009864.pub2
- Woo DK, James WD. Topical tacrolimus: a review of its uses in dermatology. Dermatitis. 2005;16(1):6-21.
- 15. Framework L. Best Practice for Fhe Management of Lymphoedema.; 2006.
- Allain H, Ramelet AA, Polard E, Bentué-Ferrer D. Safety of calcium dobesilate in chronic venous disease, diabetic retinopathy and haemorrhoids. Drug Saf. 2004;27(9):649-660. doi:10.2165/00002018-200427090-00003
- Ciapponi A, Laffaire E, Roqué M. Calcium Dobesilate for Chronic Venous Insufficiency: A Systematic Review. Angiology. 2004;55(2):147-154. doi:10.1177/000331970405500206
- Kaur, C., Sarkar, R., Kanwar, A.J., Attri, A.K., Dabra, A.K. and Kochhar, S., An open trial of calcium dobesilate in patients with venous ulcers and stasis dermatitis. International Journal of Dermatology. 2003;42: 147-152. https://doi.org/10.1046/j.1365-4362.2003.01709.x
- Rabe E, Jaeger KA, Bulitta M, Pannier F. Calcium dobesilate in patients suffering from chronic venous insufficiency: a double-blind, placebo-controlled, clinical trial. Phlebology. 2011;26(4):162-168. doi:10.1258/phleb.2010.010051
- Allain H, Ramelet AA, Polard E, Bentué-Ferrer D. Safety of calcium dobesilate in chronic venous disease, diabetic retinopathy and haemorrhoids. Drug Saf. 2004;27(9):649-660. doi:10.2165/00002018-200427090-00003
- Suehiro K, Morikage N, Murakami M, et al. A study of leg edema in immobile patients. Circ J. 2014;78(7):1733-1739. doi:10.1253/circj.CJ-13-1599
- Ciocon JO, Galindo-Ciocon D, Galindo DJ. Raised Leg Exercises for Leg Edema in the Elderly. Angiology. 1995;46(1):19-25. doi:10.1177/000331979504600103
- Gianesini S, Tessari M, Bacciglieri P, et al. A specifically designed aquatic exercise protocol to reduce chronic lower limb edema. Phlebology. 2017;32(9):594-600. doi:10.1177/0268355516673539
- Sims D. Effects of positioning on ankle edema. J Orthop Sports Phys Ther. 1986;8(1):30-33. doi:10.2519/jospt.1986.8.1.30
- Ramelet, A.-A., Compression Therapy. Dermatologic Surgery, 2002; 28: 6-10. https://doi.org/10.1046/j.1524-4725.2002.01181.x
- Partsch H. Compression Therapy: Clinical and Experimental Evidence. Ann Vasc Dis. 2012;5(4):416-422. doi:10.3400/avd.ra.12.00068
- 27. Shaikh S, Patel PM, Armbrecht ES, Hurley MY. Patient survey reports association between compression

stocking use adherence and stasis dermatitis flare frequency. J Am Acad Dermatol. 2021;84(5):1485-1487. doi:10.1016/j.jaad.2020.06.1030

 Nicole L. Stout, Pierre Brantus & Christine Moffatt. Lymphoedema management: An international intersect between developed and developing countries. Similarities, differences and challenges, Global Public Health, 2012; 7:2, 107-123, DOI: 10.1080/17441692.2010.549140

Intravenous vs. Oral Antibiotics for Nonhematogenous Osteomyelitis: A Review

Tal Boussi B.S. and Aleksa Martin B.S.

ABSTRACT

Objective: The objective of this review is to assess studies which compare the efficacy of oral antibiotics to intravenous antibiotics for the treatment of nonhematogenous osteomyelitis.

Methods: A search on PubMed was conducted to isolate studies from the past twenty years, 2001–21, which focused on oral and intravenous antibiotic therapy in cases of nonhematogenous osteomyelitis.

Results: Three studies were selected for review. A randomized open-label trial by Lipsky et al. compared oral linezolid with intravenous aminopenicillin/beta-lactamase-inhibitors for treatment in patients with various severities of diabetic foot infections. A retrospective study by Embil et al. evaluated cases of nonhematogenous osteomyelitis of the foot treated with oral antibiotics plus or minus debridement. Li et al. conducted a noninferiority trial which evaluated the one-year post-therapy outcomes of intravenous antibiotic therapy versus oral antibiotic therapy for osteomyelitis when given in the first six weeks of treatment.

Conclusion: There is a noninferiority to the use of oral antibiotics when compared to intravenous therapy for treating nonhematogenous osteomyelitis.

Introduction

The spectrum of osteomyelitis is commonly differentiated by its mechanism of infection: hematogenous or nonhematogenous. Hematogenous osteomyelitis is more likely to occur in children than adults and is associated with bacteremia. Nonhematogenous osteomyelitis is caused by direct inoculation to the bone by trauma, injury, or surrounding soft tissue infection, especially with the presence of а wound.¹ Nonhematogenous osteomyelitis is of particular interest to foot and ankle providers because of its common presentation in diabetic foot infection and because of its economic burden.2,3,4

Historically, intravenous (IV) antibiotics reigned as the standard of care for the treatment of osteomyelitis. This standard was set in a review by Waldvogel et al. in 1970, which claimed IV antibiotics, instead of oral, were necessary for adequate pharmacokinetic penetration into bone.⁵ The claim that adequate bone penetration could only be accomplished by IV therapy was later disproved.⁶ In the early 2010s, studies began emerging on the successes of oral antibiotic therapy for treating osteomyelitis. This began with the revelation of oral linezolid's equivalency to IV antibiotic therapy in osteomyelitis treatment. The literature then evolved to supporting other oral antibiotic therapies for osteomyelitis, including trimethoprimsulfamethoxazole, fluoroquinolones, metronidazole, clindamycin, and amoxicillin-clavulanate.⁷ These foundational studies were summarized in a review by Spellberg and Lipsky in 2012.^{7,8}

When evaluating risk and benefit, allowing patients with nonhematogenous osteomyelitis to be discharged with oral antibiotics would be more cost-

effective for the patient and decrease risks associated with inpatient IV antibiotic therapy and peripherally inserted central catheters.⁹ However, to confidently send the patient home with oral antibiotics, the provider must be certain that oral antibiotics are a comparable and noninferior management for the pathology when compared to their IV counterparts. The objective of this review is to assess studies published in the past twenty years, 2001–21, to evaluate the recently evolving literature on oral antibiotics as a noninferior treatment for nonhematogenous osteomyelitis when compared to IV antibiotic therapy.

Methods

Studies were identified via a search on PubMed, using the following key words and phrases: "oral vs IV," "antibiotic trial," "complications of antibiotics," "osteomyelitis treatment," "foot osteomyelitis," "antibiotic treatment," "osteomyelitis oral and intravenous antibiotic treatment." Studies were limited to articles published from 2001–21, to evaluate the more current literature on the topic. Articles were not included nor excluded solely based on their associated journal or publication. The review excluded articles which focused on a trial of one antibiotic and articles not published in English.

Results

Three articles were selected for review based on the search criteria. The first study is a randomized open-label trial which compared IV and oral formulations of antibiotics for treatment in patients suffering from nonhematogenous spread of osteomyelitis of varying severity. The second article is a retrospective study of cases of nonhematogenous osteomyelitis of the foot treated with oral antibiotics with or without a prior IV antibiotic course plus or minus debridement. The last article is a noninferiority trial which evaluated the one-year post-therapy outcomes of IV antibiotic therapy versus oral therapy given in the first six weeks of treatment, including cases of nonhematogenous osteomyelitis.

In 2004, Lipsky et al. published a randomized, open-label trial that compared IV and oral formulations of linezolid, IV aminopenicillinsulbactam, and oral amoxicillin-clavulanate for treatment in patients with nonhematogenous osteomyelitis. Of the osteomyelitis cases, fifty-seven patients received oral linezolid therapy and twenty patients received IV aminopenicillin/beta-lactamaseinhibitors. Cure rates for both the linezolid arm and the aminopenicillin/beta-lactamase-inhibitors arm were found to be statistically similar. Both arms included similar cure rates for IV vs oral therapy in osteomyelitis treatment, for linezolid 77% vs 83% respectively and for aminopenicillin/b-lactamase inhibitors, 68% vs. 72% respectively. The authors concluded that there were no significant difference in clinical cure rates when comparing patients treated in an inpatient or outpatient setting, neither was there when comparing patients treated with oral or intravenous antibiotics.10

In 2006, Embil et al. published a retrospective study of cases of nonhematogenous foot osteomyelitis treated with oral antibiotics with or without previous course of IV antimicrobial agents to evaluate for differences in outcome. A second arm of the study included grouping of patients to therapy with or without office debridement for diabetic foot osteomyelitis. The authors hypothesized that prolonged oral antibiotic therapy, without an initial short course of intravenous antimicrobial agents, with or without debridement, would be sufficient for successful remission.¹¹

This retrospective study reviewed cases that presented in a period of two years, evaluating 325 patients. Antibiotics were chosen based on culture and susceptibility results, with amoxicillin/clavulanic acid being the most commonly used. Of the 325 patients treated at the clinic, 117 were diagnosed with osteomyelitis, and 93 were included in the results. Of the 93 episodes of osteomyelitis treated with oral antimicrobial therapy, 75 of them resulted in remission (80.5%). The results showed that osteomyelitis of the foot was successfully treated in 80% of the cases studied with oral antibiotic therapy of a mean duration of 40 weeks plus-or-minus 30 weeks, with or without in-office debridement, was not significant (p > 0.05).¹¹ Further, results showed associated ulcer healed in all but six (8%) of 75 episodes and radiographic evidence of osteomyelitis healing in 55 (73%) of 75 episodes.¹¹

In 2019, Li et al. conducted a noninferiority trial which evaluated the post-therapy outcomes of IV antibiotic therapy compared with oral antibiotic therapy given in the first six weeks of treatment. The failure of these therapeutic managements was assessed within one year of time. A total of 1,054 patients, of which 205 included patients with diabetes and within those 175 of those cases included foot osteomyelitis cases. The physician managing each patient assigned the most appropriate antibiotic for the case. The most commonly prescribed intravenous antibiotics were glycopeptides and cephalosporins, and the most commonly prescribed oral antibiotics were quinolones and combination therapy. Within inclusion criteria for osteomyelitis was both nonhematogenous and hematogenous osteomyelitis. Between 2010 and 2015, patients participated in the study and were randomly assigned to the following treatment groups: IV group and oral antibiotic groups. Failure was broken down into four categories: uninfected, possible treatment failure, probable treatment failure, or definite treatment failure. The findings of Li et al. showed results of "no advantage of IV therapy over oral therapy." The risk of treatment failure between the groups—oral antibiotics versus IV antibiotics—in the intention to treat the population was -1.4% points (90% confidence interval [CI], -4.9 to 2.2; 95% CI, -5.6 to 2.9). This meets noninferiority threshold based on the margins set (7.5% or 5% point margins). Further, this trial found no evidence for heterogeneity or a low p value: p = 0.51 and concluded there is no outcome advantage between IV or oral antibiotic therapy with p > 0.05 for all analyses conducted across the various hospitals. They further stated there was no found difference in rates of Clostridium difficile colitis between IV and oral antibiotics.¹²

Discussion

In his landmark review published in 1970, Waldvogel concluded that treatment failure of osteomyelitis was due to treatment that was too casual, with too low of doses of antibiotics and too short a duration of treatment. Further, Waldvogel stated that to control cases of recurrent osteomyelitis, treatment needed to include a combination of surgical debridement and the use of high-dose, long-term parenteral antibiotic therapy.⁵ The definitions of the Waldvogel study created structural bias by defining intensive antimicrobial treatment as "parenteral administration of the appropriate antibiotic at high dosage." Despite Waldvogel's previously seeded caution, many antibiotics available today have proven to have good bone penetration without necessarily parenteral administration.¹³

Lipsky et al. determined equivalency of oral and IV antibiotics, concluding patients with nonhematogenous osteomyelitis who present as clinically stable could be sent home with oral antibiotics.10 Further analysis showed that these findings can provide the option for a prompter switch from IV therapy to oral antibiotics for patients who are responding well to the medication. Embil et al. findings concurred, showing successful treatment of osteomyelitis related to nonhematogenous spread from a wound with oral antibiotics, with or without wound debridement. Embil et al. elaborated that the oral antibiotic agents are appropriate treatment because the oral antimicrobial therapy regimens have adequate bioavailability to achieve proper soft tissue and bone antimicrobial penetration level to that of IV agents. They supported their analysis by the fluoroquinolones and clindamycin concentrations within macrophages and neutrophils at the same site of osteomyelitis and inflammation. More recently, in agreement to Embil et al.,¹¹ Li et al. analyzed their findings through the pharmacokinetic principle. Li and colleagues interpreted the noninferiority of oral to IV antibiotics due to pharmacokinetic principle that proper oral agents can reach sufficient threshold of antibiotic concentrations at the location of osteomyelitis or infection. Additionally, Li and colleagues went further than noninferiority, finding that oral therapy was associated with shorter hospital stay and fewer complications than that of its IV counterpart.¹²

There were certainly limitations for each study. Interestingly, Lipsky et al. failed to mention any limitations of their study in their article. Even though this was a large study, only a portion of the total participants had diagnosed osteomyelitis instead of simply a soft tissue infection.¹⁰ This may make the results of this paper difficult to interpret when only evaluating for osteomyelitis. Another notable weakness to consider is the article's choice to exclude more severe cases of infection. The results of this paper should be interpreted with caution when considering its application to more acute cases of osteomyelitis.¹⁰ Regarding the article by Embil et al, the most commonly isolated pathogenic microbe was Staphylococcus aureus, but only one isolate was resistant to methicillin. The authors theorized that populations with higher incidences of methicillinresistant Staphylococcus aureus may require different antibiotic regimens, operative management, and increased duration of therapy. The practicality of the study by Li et al. may be questioned given its tightly regimented care planning for each patient, which may

not be commonly reproduced in a true clinical setting.¹²

Future research on nonhematogenous osteomyelitis treatment may discuss oral versus IV antibiotic use in chronic versus acute cases of osteomyelitis, given that acute cases would likely require inpatient management, and therefore IV access, more often than chronic cases. Another area of research may evaluate the role of debridement and surgical measures for osteomyelitis source control. Lastly, future studies may seek to compare specific antibiotic agents to stipulate which agents to use, may explore the risk of later treatment failure with a more prolonged prospective study, or consider the chronicity of osteomyelitis cases when comparing treatment groups.

Conclusion

There is a noninferiority to the use of oral antibiotics when compared to IV therapy in nonhematogenous osteomyelitis. With review of these three articles, one may consider utilizing oral antibiotics instead of strictly IV for treatment of nonhematogenous osteomyelitis. This counters the previously established standard set by Waldvogel et al.⁵ Given this review of the most current literature, patients with a chronic case of lower extremity osteomyelitis may undergo oral antibiotic treatment, especially if IV antibiotic treatment is the only cause for inpatient management. For patients with a more severe presentation, which would require regular monitoring and medical management, admission with possible IV antibiotic therapy is recommended. The morbidity of foot and ankle osteomyelitis complications is high. The foot and ankle practitioner should be encouraged to review the pharmaceutical interventions most supported in the literature.

References

- Lalani T, Schmitt SK. Nonvertebral osteomyelitis in adults: Clinical manifestations and diagnosis. In: Post TW, ed. *UpToDate*. Waltham, MA: UpToDate; Updated February 26, 2021. Accessed February 12, 2022.
- Lindbloom BJ, James ER, McGarvey WC. Osteomyelitis of the foot and ankle: diagnosis, epidemiology, and treatment. *Foot Ankle Clin.* 2014;19(3):569-588. doi:10.1016/j.fcl.2014.06.012
- King CM, Castellucci-Garza FM, Lyon L, Doyle MD, Nimick C, Williams ML. Microorganisms Associated With Osteomyelitis of the Foot and Ankle. J Foot Ankle Surg. 2020;59(3):491-494. doi:10.1053/j.jfas.2019.08.032
- Geraghty, T., & LaPorta, G. (2019). Current health and economic burden of chronic diabetic osteomyelitis. *Expert review of pharmacoeconomics & outcomes research*, 19(3), 279–286. <u>https://doi.org/10.1080/14737167.2019.1567337</u>
- 5. Waldvogel FA, Medoff G, Swartz MN. Osteomyelitis: a review of clinical features, therapeutic considerations

- 6. and unusual aspects. *N Engl J Med.* 1970;282(4):198-206. doi:10.1056/NEJM197001222820406
- Landersdorfer CB, Bulitta JB, Kinzig M, Holzgrabe U, Sörgel F. Penetration of antibacterials into bone: pharmacokinetic, pharmacodynamic and bioanalytical considerations. *Clin Pharmacokinet*. 2009;48(2):89-124. doi:10.2165/00003088-200948020-00002
- Cortés-Penfield NW, Kulkarni PA. The History of Antibiotic Treatment of Osteomyelitis. *Open Forum Infect Dis.* 2019;6(5):ofz181. Published 2019 Apr 8. doi:10.1093/ofid/ofz181
- Spellberg B, Lipsky BA. Systemic antibiotic therapy for chronic osteomyelitis in adults. *Clin Infect Dis.* 2012;54(3):393-407. doi:10.1093/cid/cir842
- McMeekin, N., Geue, C., Briggs, A., Rombach, I., Li, H. K., Bejon, P., McNally, M., Atkins, B. L., Ferguson, J., Scarborough, M., & OVIVA collaborators (2019). Costeffectiveness of oral versus intravenous antibiotics (OVIVA) in patients with bone and joint infection: evidence from a non-inferiority trial. *Wellcome open* research, 4, 108.

https://doi.org/10.12688/wellcomeopenres.15314.4

- Lipsky BA, Itani K, Norden C; Linezolid Diabetic Foot Infections Study Group. Treating foot infections in diabetic patients: a randomized, multicenter, open-label trial of linezolid versus ampicillinsulbactam/amoxicillin-clavulanate. *Clin Infect Dis.* 2004;38(1):17-24. doi:10.1086/380449
- 12. Embil JM, Rose G, Trepman E, et al. Oral antimicrobial therapy for diabetic foot osteomyelitis. *Foot Ankle Int.* 2006;27(10):771-779.

doi:10.1177/107110070602701003

- Li HK, Rombach I, Zambellas R, et al. Oral versus Intravenous Antibiotics for Bone and Joint Infection. N Engl J Med. 2019;380(5):425-436. doi:10.1056/NEJMoa1710926
- Thabit AK, Fatani DF, Bamakhrama MS, Barnawi OA, Basudan LO, Alhejaili SF. Antibiotic penetration into bone and joints: An updated review. *Int J Infect Dis.* 2019;81:128-136. doi:10.1016/j.ijid.2019.02.005

The Importance of Foot Hygiene and Proper Footwear for Preventing Disease in Homeless Populations

Mary Trumble, B.S.

ABSTRACT

Objective: The goal of this article is to discuss the prevalence of foot pathology, the contribution of poor foot hygiene, and improper fitting footwear on foot pathology in homeless populations. Additionally, this article makes suggestions to improve the homeless population's foot hygiene and access to resources in local communities.

Methods: A literature search was conducted using online databases to evaluate research that analyzes the importance of foot hygiene and properly fitting footwear for preventing disease in homeless populations.

Results: The homeless community is at higher risk for developing foot pathology with the most prevalent problem being associated with toenail pathology. Homeless individuals have decreased access to nail clippers, nail file, clean socks, shoes, water, and soap, and have increased exposure to harsh environments and crowded living situations, increasing risk of disease.

Conclusion: Foot hygiene and proper fitting footwear have a clear association to improvement of foot conditions and pain. Implementation of programs that provide medical and procedural treatment of foot pathology along with protective footwear, will improve quality of life of homeless individuals.

Introduction

Oregon ranks seventh in the nation with the most homelessness, totaling about 14,655 people as of January 2020.¹ Homelessness is a major health concern as the majority of homeless individuals experience unmet healthcare needs due to lack of access.² A common health concern of homeless individuals is inadequate foot hygiene and inappropriate footwear leading to increased risk for injury and disease. This problem is exacerbated by the reliance on walking as a mode of transportation. Homeless individuals walk a median of five miles a day and stand on their feet for an average of five hours a day.³ Additionally, homeless individuals often have improperly fitting shoes leading to increased foot pain and exacerbation of foot complications.⁴ Therefore, foot hygiene and proper footwear can have major impacts on a homeless individuals' activities of daily living.

The homeless population is a vulnerable, underserved, and understudied patient population. The objective of this review is to analyze the limited research available to determine the prevalence of foot pathology and the contribution of poor foot hygiene and improper fitting footwear on foot pathology in homeless populations. Results of this review will be used to provide suggestions to improve the homeless population's foot hygiene and access to resources in local communities.

Methods

A literature search was conducted using online databases Pubmed and Embase with an additional search of reference lists. The key words searched included "homelessness,"AND "foot conditions," AND "foot hygiene." Most relevant articles were determined by which articles contributed to the research goal of evaluating the importance of foot hygiene and properly fitting footwear for preventing disease in homeless populations. Due to the lack of recent research with this special population, articles from 1996 to present were included.

Results

Chen et al. conducted a 37-question survey regarding foot hygiene practices, associated risk factors, and self-reported lower-extremity pathologic conditions. This study was completed by 299 homeless individuals. Results of this study found foot pain was reported by 56% of participants, with 12% reporting they had pain all the time. Foot hygiene was analyzed, it was determined that 61% of the individuals changed to a clean pair of socks daily and 72% of the participants were able to wash their feet daily. Additionally, 73% of participants trimmed their toenails at least once a month. The most common podiatric medical conditions reported included fungal nail (30%), calluses (26%), and athlete's foot (24%). It was determined that 31% of homeless individuals seek healthcare for foot related complaints.

This study also analyzed types of footwear worn by homeless individuals and found that sneakers were the most common footwear (84%), followed by dress shoes (28%), sandals (22%), heels and boots (3% each), and no shoes and slippers (1% each). It was found that 74% of participants stated they were on their feet five hours or more each day and 73% of the participants indicated that they were able to change shoes at least every six months.

Matteoli et al. studied interventions to treat foot pathology. Participants examined included 930 homeless individuals, for a total of 2,526 interventions. Risk factors were assessed and of the 930 participants, 79% were alcohol consumers. A variety of interventions were employed, 76% of interventions were related to diabetes, 10% related to trauma, 8% related to infections, and 5% to other pathologies. Ulcer and wound care, surgery, revascularization, and protective footwear were used to treat foot complaints and diabetic foot disease. These interventions contributed to an 86% improvement of foot pathology. This study also determined that homeless individuals are more likely to have pain with walking than housed individuals.

Muirhead et al. analyzed the implementation of a foot care clinic at a local soup kitchen. A questionnaire about foot care practices and use of health services was completed by 100 participants. Of the 100 participants, 48% reported visiting the emergency department in the last year with most visiting a frequency of one to three times. Of this 48% of participants, 25% of the emergency department visits were for foot related complaints. Another 26% of the 100 participants had never had their feet evaluated by a healthcare provider.

Foot care practices were evaluated, it was found that only 68% of homeless individuals had access to clean water, 70% to soap, 56% to a towel, 44% to a nail clipper, 31% to a nail file, and 15% to a mirror. When asked what deters participants from using provided foot services, 62% reported embarrassment associated with the smell of feet and the poor condition of their shoes and socks.

Robbins et al. evaluated implementation of "Stand Down for the Homeless" events. It compared the podiatric needs of the veteran homeless population versus the general population. It determined that the most common foot pathology of homeless individuals is associated with toenails. Additional pathologies included (listed in decreasing order of prevalence) fungal disease, corns and calluses, injuries to feet, neurologic feet complaints, hallux abducto valgus, other dermatologic manifestations, fasciitis, circulation complications, and foot deformities.

Moes et al. evaluated 30 recruited homeless individuals with a baseline foot pain rated 7/10. The intervention included providing each individual experiencing 7/10 foot pain a new pair of podiatristrecommended shoes. Overall, it was found that approximately 55% of homeless individuals experience foot pain and 34% of homeless individuals do not have proper fitting shoes. After wearing new, properly fitting, supportive, podiatrist-recommended shoes for six weeks, participants reported decreased pain, decreased pain medication use, improvement in gait speed, and improvement in almost all aspects of foot health. D' Souza et al. performed a study to evaluate foot care in a homeless population using a new foot care assessment tool. The study included 65 recruited homeless individuals. From the completed foot care assessments, it was determined that homeless populations have higher incidence of frostbite, frostnip, immersion foot, hypothermia, sunburn, and heatstroke due to increased exposure to weather. Additionally, homeless individuals often are unable to lay flat while sleeping due to living conditions which leads to increased edema and increased risk of peripheral vascular disease.

This study found that 41% of participants had a history of foot pathology and 38% of participants had a history of emergency department visits for foot complaints. At the time of the study, 76% of participants had current foot pathology. Study participants reported a history of foot problems that included callus and corn formation, foot ulcers, ingrown and infected nails, bunions, hammertoes, plantar warts, frostbite, and street feet. Many (55.38%) participants reported foot pain, with 12.31% reporting constant pain and 44.62% recurrent pain related to these conditions

Discussion

Each study discussed the limitations and complications associated with this sensitive population. Matteoli et al. discussed the language and cultural barrier as well as difficulty following up with the participants due to their unstable living situations. Mental health status of the participants often created a barrier to obtaining reliable information. Chen et al. mentioned the prevalence of substance abuse in the participant population; it was unknown whether participants were under the influence while participating in the study. Moes et al. mentioned difficulty with compliance to the intervention due to varying lifestyle factors. Additionally, studies that rely on self-report like Muirhead et al. and Chen et al. are subject to variation and error within subjective measures. All studies discussed are not generalizable because each state and community differ in respect to healthcare access, community support availability, and the nature of local government.

Homeless individuals are considered a "vulnerable" population which creates a barrier to researching this patient population as special precautions must be taken. Attitudes and lifestyle factors including lack of access to transportation, lack of access to technology like phones and computers, and unstable living situations may also hinder further research. There is a wide knowledge gap due to lack of current information. Very little research has been published within the last five years. The previous research indicates that homeless individuals have increased risk factors for developing foot pathology. These risk factors include smoking, alcohol use, long hours on their feet, poor living conditions, and inability to lie flat.^{6,7} This special population also has an increased risk of developing diabetes due to low-income status and diminished access to proper nutrition.⁸ To treat foot pathology in homeless populations, often these social factors must be addressed.

Foot hygiene and proper fitting footwear have a clear association to improvement of foot conditions and pain as demonstrated throughout the research analyzed. However, the above studies discuss the lack of resources and proper healthcare to address this. Homeless individuals often do not have health insurance, and most seek healthcare from free clinics. It is important that providers at these clinics are educated on the importance of examining the feet and how to treat foot pathology. Addressing foot pathology should start with the core of the problem, foot hygiene.

As healthcare professionals evaluating feet, it is important to clean the homeless individual's feet before examining to enable a thorough evaluation and avoid feelings of embarrassment the individual may be experiencing. Additionally, to adequately address the foot pathology, it is essential that providers ensure access to clean socks and proper fitting shoes to avoid worsening of problems.

To address the prevalent problem of foot disease in homeless populations, it is suggested that communities take action by implementing volunteer health care clinics to bridge the gaps of care. These volunteer health care clinics with a large homeless patient population should make targeted efforts to screen and treat for foot pain and pathology. Implementing programs to create a more inclusive space at local soup kitchens and homeless shelters to provide foot washing stations, clean socks, nail clippers, and supportive and proper fitting shoes may provide homeless individuals easier access to these vital resources.

A common barrier to accessing resources is lack of knowledge of where and how to access them. Increasing the programs and facilities that provide these services may help close this gap. Reducing foot pain and discomfort may provide more freedom for the individual to walk further distances to access resources, decrease medication use, increase physical ability to work, and improve confidence and productivity.

Conclusion

Foot hygiene and proper fitting footwear have a clear association to improvement of foot conditions and pain. Implementation of programs that provide medical and procedural treatment of foot pathology along with protective footwear will improve quality of life of homeless individuals. Homelessness is a prevalent public health crisis and addressing social factors and increasing access to resources should be prioritized.

References

1. Oregon homelessness statistics. Homeless in Oregon Statistics 2019. Homeless Estimation by State | US Interagency Council on Homelessness. https://www.usich.gov/homelessness-statistics/or/. Published January 2020. Accessed November 15, 2021.

2. To MJ, Brothers TD, Van Zoost C. Foot conditions among homeless persons: A systematic review. PLOS ONE. 2016;11(12). doi:10.1371/journal.pone.0167463

3. Muirhead L, Roberson AJ, Secrest J. Utilization of Foot Care Services among homeless adults: Implications for Advanced Practice Nurses. Journal of the American Academy of Nurse Practitioners. 2011;23(4):209-215. doi:10.1111/ j.1745-7599.2011.00598.x

4. Moes J. Proper fitting shoes: Reducing pain, increasing activity, and improving foot health among adults experiencing homelessness. Public Health Nursing. 2019;36(3):321-329. doi:10.1111/phn.12604

5. Robbins JM, Roth LS, Villanueva MC. "stand down for the homeless". podiatric screening of a homeless population in Cleveland. Journal of the American Podiatric Medical Association. 1996;86(6):275-279. doi:10.7547/87507315-86-6-275

6. Sheila D'Souza M, Mirza NA, Nairy Karkada S. Development of a foot care model to determine the risk of foot problems among homeless adults in Canada. Health & Social Care in the Community. 2021;29(5). doi:10.1111/hsc.13271

7. Chen, B., Mitchell, A., & Tran, D. (2014). "Step up for foot care." Journal of the American Podiatric Medical Association, 104(3), 269–276. https://doi.org/10.7547/0003-0538-104.3.269

8. Matteoli, M., Scaringi, C., Carella, P., Fruttaldo, L., Angeloni, U., & Laurenza, M. (2015). A mobile health service to manage diabetic foot in homeless patients. Journal of the American Podiatric Medical Association, 105(5), 424–428. https://doi.org/ 10.7547/13-152

9. Beckles, G., & Chou, C.-F. (2017, August 14). Disparities in the prevalence of diagnosed diabetes - United States, 1999–2002 and 2011–2014. Centers for Disease Control and Prevention. Retrieved December 3, 2021, from https://www.cdc.gov/mmwr/volumes/65/wr/mm6545a4.htm.

Foot Pain and Plantar Pressure in Pregnancy: A Literature Review

Angel Lin, B.S. and Tia Furness, B.S.

ABSTRACT

Objective: Women often encounter foot problems during pregnancy. A literature review will be conducted on the current research of foot pain and plantar pressure during pregnancy. There will be an investigation of the changes in plantar pressures during pregnancy and how it contributes to foot pain among pregnant women.

Methods: A literature review of peer reviewed articles from 1997-2017 were included using the PubMed, Google Scholar, Pumerantz Library, and ScienceDirect databases. Keywords used were plantar pressure, pregnancy, foot pain, and trimester. Data regarding the postpartum pressure point at the foot was excluded from this review. A total of nine articles were analyzed in this literature review.

Results: There were higher peak pressures under the midfoot and increased contact time during the third trimester of pregnancy. The plantar forces shifted posterior to anterior as weight gain increased with gestation progression. **Conclusion**: It was found that pregnant women tend to have increased plantar pressures in the midfoot a majority of the time, however, some studies found that forefoot and hindfoot pressures were also increased. The increase in plantar pressure tended to be associated with a later stage of pregnancy where the women had more weight affecting their overall posture in gait and orthostasis.

Introduction

Numerous physical and hormonal changes occur during pregnancy. These changes include systems such as cardiovascular, respiratory, and endocrine systems. Physiological changes can also lead to changes in the musculoskeletal system such as ligaments and joints. Body shape and weight changes can be seen and the center of gravity of pregnant women will also be displaced anteriorly and superiorly.¹ The alterations of the center of gravity can affect the postural balance and increase the risk of falls.² Pregnant women also often complain about foot pain especially in the third trimester as the center of gravity is altered due to weight gain.³ Such changes may cause an effect on the plantar pressure and foot biomechanics and these alterations will advance during pregnancy. Addressing the balance ability and preventing frequent falling for pregnant women is crucial. An older article, "Plantar foot pressures in pregnant women" by Nyska et al. 1997 suggested that the plantar pressure load increases at the lateral aspect and hindfoot in pregnant women and contributes to limb pain.⁴ However, other studies have proven otherwise and have indicated that the pressure load increases on the forefoot. The goal of this peer review article is to understand the changes in plantar pressure during pregnancy by examining the current literature. Through these findings, physicians can better educate

pregnant women on what to expect on the physical changes throughout the pregnancy phases.

Methods

A literature review of peer-reviewed articles from 1997-2017 were included using the PubMed, Pumerantz Library, Google Scholar. and ScienceDirect databases. The search included the following keywords: foot pain, plantar pressure, pregnancy, and trimester. The articles were analyzed for clinical changes in the plantar pressures and foot related pain found in pregnant women. Articles regarding plantar pressure changes during gait and orthostasis throughout the three trimesters of pregnancy were included, as well as comparisons to non-pregnant women. Articles containing postpartum findings were excluded from the review. To assess the risk of bias during the analysis of the articles, contraindications to some of the studies were also mentioned in the review. A total of nine research studies were analyzed and used in this literature review.

Results

The study done by Braz has concluded that there was a positive correlation between weight gained and anteroposterior displacement during pregnancy as well as increased contact area in the second trimester group.⁵ It was also suggested that the decreased postural equilibrium in the third trimester pregnancy was associated with the greater anteroposterior displacement and concluded that the center of force shifts towards the forefoot throughout the gestational period. The research was done by analyzing the plantar pressure of sixty volunteers with fifteen subjects in the non-pregnant, first, second, and third-trimester groups using a pressure platform.

Gaymar et al. aimed to quantify the plantar pressure of women in late pregnancy by recruiting twenty-two pregnant women who were at thirty-eight weeks gestation and twenty non-pregnant women using an in-shoe measurement system. They concluded that there was no significant effect on the forefoot and hindfoot plantar pressures in comparison with the non-pregnant group.⁶ However, the pregnant group exerted higher mean peak pressure than the control group in all areas of the foot overall. The pregnant women recruited in this study did not complain about foot pain.

Karadag-Saygi et al. concluded that the forefoot pressure was higher on the right side with standing and walking in pregnant women and that there was a significant increase in floor contact times, specifically under the forefoot.³ Thirty-five pregnant women in their third trimester who complained of foot pain and thirty-five non-pregnant women who weighed similar to the pregnant group were recruited. The foot pain and plantar pressure on the forefoot and hindfoot were measured and compared to the control group.

Ribeiro et al. has done a longitudinal study that looks at the plantar pressures in orthostatic posture and gait during the phases of pregnancy. Six healthy pregnant women were followed for eleven months. Their gait was recorded using the pedar-x-system, which measures pressures in gait cadence. They found little alteration in the plantar pressures during orthostatic posture.⁷ However, the plantar load shifted from rearfoot to forefoot in gait. The forefoot pressure and contact time at the midfoot and medial forefoot were also noted to be increased as the pregnancy progressed towards the last trimester.⁷

Varol et al. concluded that forces increased from the posterior to the anterior during pregnancy due to hormonal and body weight changes.⁸ The force was also significantly higher in pregnant women who experienced foot pain. One hundred and thirty-one pregnant women without prior foot or ankle problems were recruited in this study. They were divided into two groups based on the pain scale quantified by the visual analog scale (VAS).⁸ Tekscan HR Mat were used to measure plantar pressure.

Opposing the previous studies, the research done by Mikeska et al. found that plantar pressures were noted in the hindfoot and midfoot during pregnancy, which is consistent with the Nyska et al. article. They analyzed the plantar pressure during gait in pregnant women in their third trimester. In this study, the women were split into two groups, with or without customized orthopedic shoes. Results showed that the plantar pressure peaked in the midfoot area of the left foot and the hindfoot of the right foot for both groups.⁹ However, the increase was more significant in those without customized orthopedic shoes.

Another study done by Ramachandra et al. also stated that the hindfoot pressure values were higher than that of the forefoot pressure as the result of their study.¹⁰ Fifty-six women at twelve weeks, twenty-four weeks, and thirty-two weeks of gestation were recruited and the plantar pressure patterns of the forefoot and hindfoot were recorded as well as navicular height, width of feet, and static plantar pressure.¹⁰ They have noticed that the navicular height was reduced, suggesting an increase in pronation and static plantar pressure as pregnancy advanced. The shift in the center of gravity toward the posterior aspect of the foot in addition to hormonal effects on ligament laxity could indicate a compensatory lengthening of the ligament supporting the arch of the foot.¹⁰ This could lead to the reduced arch height during pregnancy. This study, however, used a subjective annual method to measure the navicular height, it has been proven to be comparable with the radiographic method.¹⁰

There was a recent study done by Gimunova et al. that tested out a special type of footwear that could prevent the associated foot pains during pregnancy.¹² The special footwear in this study was designed to help redistribute the plantar pressures on the foot during pregnancy.¹² There were 50 pregnant women participants who were measured once per trimester using eight cameras from the Simi Motion System and then converted to 3D kinematic data. From this article, it was chosen to only look at the results from the pregnancy group and exclude the postpartum findings. It was concluded that the special footwear given to the pregnant patients helped prevent arch falling and foot pain during their gait cycle.¹²

Another study by Jang et al. tested out a different type of special footwear for pregnant women. The special footwear used in this study was a balanced incline shoe.¹³ Only ten pregnant women participants were followed in this study and their plantar pressures were obtained using the Vicon Motion System while wearing the special type of footwear. The conclusion from this study is that pregnant women wearing a balanced incline shoe had reduced plantar pressure and fatigue from foot pain.¹³

Discussion

The findings from the analysis suggest that three out of the nine articles addressing plantar pressures found that pregnant women in their third trimester have an increase in plantar pressures in the midfoot. One interesting comparison is that Varol et al. concluded the plantar pressure force was higher with pregnant women who experienced foot pain.8 This conclusion was further strengthened by the results from Karadag-Saygi et al. stating higher forefoot pressure on pregnant women experiencing foot pain³ and from Gaymar et al. stating there was no significant increased plantar pressure as they recruited pregnant women who were not experiencing foot pain.6 It was also concluded that there was an increased plantar load of the forefoot in women during their last trimester of pregnancy.^{3,5,7} Pregnant women have significant body weight changes that lead to the posterior to anterior shift in plantar pressures and associated foot pain. There was not much noted about the plantar pressures in the early trimesters which could be due less weight gain compared to the third trimester. Out of the nine studies, Gaymar et al., Ribeiro et al., and Mikeska et al. stated the pressure increases at the midfoot.^{6,7,9} However, the pregnant women from the Gaymar et al. study did not experience foot pain.⁶ Nyska et al., Mikeska et al., and Ramachandra et al. all stated that it is the hindfoot pressure of pregnant women that is increased in the third trimester.^{4,9,10} Further studies should be done to investigate the specifics of the reported foot pain and how consistent the foot pain is among pregnant women.

Understanding what the changes are to the plantar pressures and the associated foot pain during pregnancy is relevant to patient education and guides the podiatric care to alleviate the symptoms for pregnant patients. These articles helped identify some of the changes in plantar pressures during pregnancy. The next step is for researchers to do further studies on how different treatment options can alleviate the foot pains and altered pressures during pregnancy.

From two articles, one by Gimunova et al. and the other by Jang et al., both conclude that using a special type of footwear can alter the plantar pressures in pregnant women to relieve their foot pain.^{12,13} Although the types of footwear used in each study were different, it seems that having some type of shoe modifications can improve the plantar pressure changes and associated pain in pregnant women.

The increase in body weight during pregnancy and the findings that midfoot plantar pressures tend to be increased in pregnant women, indicate that these factors can lead to over pronation in the feet of pregnant women. Assuming that over pronation can be a result of pregnancy, physicians can try to apply the types of orthotics used for flatfoot patients in the treatment of over pronation in pregnant women. There is a lack of studies that specifically test this idea out and more research is needed to be done. Overall, it appears there needs to be more studies on the different types of treatment options such as orthotics, physical therapy, and other types of shoe wear specifically for pregnant women. When further studies that test the different treatment options and their efficacy for the pregnant population, physicians will be able to cater to more satisfying outcomes for relieving the foot pain pregnant women may experience.

Limitations to the literature review is the possibility of selection bias since there is still limited information regarding this topic. More research is needed to be done to further explore this topic thoroughly. Selection of the articles was chosen by what was available to the databases that were used. Some studies compared pregnant women with non pregnant women. Other studies used a longitudinal analysis or compared pregnant women in different gestation stages. There is also the possibility that there is a chance of interpretation bias towards one outcome in the analysis of the results that were read and compared from each of the studies, which could lead to lower efficacy of our review.

Conclusion

Although there are mixed results regarding where the plantar pressure is increased, it was found that there were higher peak pressures under the midfoot a majority of the time and increased contact time during the third trimester of pregnancy as indicated by more recent studies. The plantar forces shifted posterior to anterior as weight gain increased with gestation progression. However, some studies found that forefoot and hindfoot pressures were also increased. The increase in plantar pressure tended to be associated with a later stage of pregnancy where the women had more weight affecting their overall posture in gait and orthostasis. A future literature review to consider is to investigate the lasting effects pregnancy has on the changes in plantar pressure and foot pain postpartum. With the findings collected from the peer reviewed articles, medical practitioners can help educate pregnant women on the podiatric changes that are to be expected throughout the pregnancy phases.

References

- Takeda K, Shimizu K, Imura M. Changes in balance strategy in the third trimester. *Journal of Physical Therapy Science*. 2015;27(6):1813-1817. doi:10.1589/jpts.27.1813
- Cakmak B, Ribeiro AP, Inanir A. Postural balance and the risk of falling during pregnancy. J Matern Fetal Neonatal Med. 2016;29(10):1623-1625. doi:10.3109/14767058.2015.1057490
- Karadag-Saygi, E., Unlu-Ozkan, F., & Basgul, A. (2010). Plantar pressure and foot pain in the last trimester of pregnancy. Foot & Ankle International, 31(2), 153–157. https://doi.org/10.3113/fai.2010.0153
- Nyska M, Sofer D, Porat A, et al. Planter foot pressures in pregnant women. Israel Journal of Medical Sciences. 1997 Feb;33(2):139-146. PMID: 9254877.
- Braz. J. (2007) Analysis of plantar pressure and postural balance during different phases of pregnancy. *Scielo Brazil.* <u>https://doi.org/10.1590/S1413-35552007000500010</u>

- Gaymer, C., Whalley, H., Achten, J., Vatish, M., & Costa, M. L. (2009). Midfoot plantar pressure significantly increases during late gestation. *The Foot*, 19(2), 114–116. https://doi.org/10.1016/j.foot.2009.02.001
- Ribeiro, A. P., Trombini-Souza, F., de Camargo Neves Sacco, I., Ruano, R., Zugaib, M., & João, S. M. (2011). Changes in the plantar pressure distribution during gait throughout gestation. *Journal of the American Podiatric Medical Association*, *101*(5), 415–423. https://doi.org/10.7547/1010415
- VAROL, T., GÖKER, A., CEZAYİRLİ, E., ÖZGÜR, S., & TUÇ YÜCEL, A. (2017). Relation between foot pain and plantar pressure in pregnancy. *TURKISH JOURNAL OF MEDICAL SCIENCES*, 47, 1104–1108. https://doi.org/10.3906/sag-1601-185
- Mikeska O, Gimunová M, Zvonař M. Assessment of distribution of plantar pressures and foot characteristics during walking in pregnant women. Acta Bioeng Biomech. 2019;21(3):49-56. PMID: 31798025
- Ramachandra, P., Kumar, P., Kamath, A., & Maiya, A. G. (2016). Do structural changes of the foot influence plantar pressure patterns during various stages of pregnancy and postpartum? *Foot & Ankle Specialist*, 10(6), 513–519. https://doi.org/10.1177/1938640016685150
- Agyekum EK, Ma K. Heel pain: A systematic review. Chin J Traumatol. 2015;18(3):164-9. doi: 10.1016/j.cjtee.2015.03.002. PMID: 26643244
- Gimunová, M., Zvonař, M., Sebera, M., Turčínek, P., & Kolářová, K. (2020). Special footwear designed for pregnant women and its effect on kinematic gait parameters during pregnancy and postpartum period. *PloS one*, *15*(5), e0232901. <u>https://doi.org/10.1371/journal.pone.0232901</u>
- Jang SI, Lee YR, Kwak HS, Moon KS, Shin J, Kim J. The effect of balanced incline shoes on walking and feet for the pregnant women. *Korean Journal of Obstetrics and Gynecology*, 2010;53:988–997.

Psychological Impact of Lower Limb Amputations on Patients with Diabetes

Bridget L. Humphrey B.S., Aleksa J. Martin B.S.

ABSTRACT

Objective: The purpose of this review is to identify the risks of patients with diabetes developing psychological pathologies after a lower limb amputation.

Methods: A review was conducted using keyword searches on one database, PubMed. Only articles published in the past ten years, 2011-2021, were included for review.

Results: Amputation due to diabetes complications can have negative psychological patient outcomes. Some of the psychological effects that patients may experience are symptoms of depression and anxiety. There are time dependent correlations in the manifestation of psychological symptoms. The magnitude and type of the psychological symptoms that patients experience preoperatively correlates to postoperative psychological symptoms experienced.

Conclusion: Health interventions applied at specific times during diabetic amputation related patient care will improve patients' psychological wellbeing postoperatively.

Introduction

In 2017, the prevalence of diabetic foot ulcerations (DFU) globally was approximately 6.3%, with the United States having the highest prevalence of 13%.¹ Pathophysiologically, diabetic foot ulcers are a result of a combination of several sequelae from diabetes, including peripheral neuropathy, impaired immunological response to infection, foot deformity, peripheral vascular disease, arterial vascular disease, and trauma.² Approximately 20% of diabetic foot ulcerations result in amputation.³ The five-year mortality rate for patients with diabetes who undergo a major or minor amputation is very high, at 52% to 100%. Increased age, renal disease, peripheral vascular disease, and a more proximal amputation can all cause the risk of mortality to increase.⁴

The literature has established that populations with traumatic amputations have a higher prevalence of anxiety and depression than the general population.⁵ Whether a population with lower limb amputations (LLA) secondary to DFU also carry the risk of developing poor psychological symptoms is pertinent information for primary care physicians, podiatrists, vascular surgeons, psychiatrists, and psychology specialists to better understand the patient and provide optimal care.

The purpose of this review is to identify the risks of patients with diabetes developing

psychological sequelae, such as depression or anxiety, after a lower limb amputation.

Methods

This review was conducted using keyword searches to find articles which met certain selection and exclusion criteria. Keywords and phrases used included "amputation, diabetes, psychological," "amputation, mental health," "amputation, quality of life," "diabetes amputation, depression, anxiety" "lower extremity amputation" "lower extremity amputation, diabetes," "lower limb amputation, diabetes, depression," "lower limb amputation, diabetes, depression anxiety," "lower limb diabetes, amputation, psychosocial," and "psychological, amputation." PubMed was used as the database. Articles were included in the review if they were either written in or translated into English. Articles were also included if they involved lower extremity amputations secondary to peripheral arterial disease (PAD) if their subject selection criteria included patients with diabetes, given that PAD is a common comorbidity to diabetes. Articles were excluded from the review if they were published before 2011, required payment for full access, or assessed the psychological impact of only traumarelated lower extremity amputations.

Results

Three studies met the established inclusion criteria for this review: a study by Pedras et al published in 2018, another study by Pedras et al published in 2020, and a final study by Norvell et al published in 2019.

In 2018, Pedras et al published a longitudinal study on patients with Type 2 diabetes mellitus (T2DM) requiring amputation.⁶ Patients were screened for anxiety and depression levels during hospitalization before amputation and one month after the procedure at follow-up. The results from their study showed that levels of anxiety or depression during hospitalization were significant for predicting anxiety and depression symptoms one month postoperatively.⁶

The study sample included 179 patients with T2DM and 113 patients responded to postoperative evaluation.⁶ Amputation cases in this study were secondary to diabetic neuropathy and/or peripheral arterial disease, and the study included patients that had previous amputations, instead of only patients undergoing an amputation for the first time. The study also included only patients without a previously diagnosed psychiatric disorder.⁶

The Hospital Anxiety and Depression Scale was used to determine the presence of a mood disorder, with a score of 11 or higher indicating a probability the patient had acquired one. Additionally, at the one month follow up, a multiple hierarchical regression model was used to find the predictors of anxiety and depression symptoms.⁶

Anxiety symptoms were found in 63.7% of the patients during their hospital stay and 41.6% of patients one month post-operatively.⁶ the Symptoms of depression were found in 42.5% of the patients within their hospital stay and 46.9% of the patients one month postoperatively.⁶ The study concluded that there were significant differences regarding anxiety and depression from pre- and even after controlling post-operation, for previous amputations.⁶ Anxiety symptoms were found to be significantly decreased with duration while depressive postoperatively, of time symptoms were not. Symptoms of anxiety and depression before the procedure were found to be the best predictors of anxiety and depression symptoms at one-month follow up. Initially, age was positively correlated with increased anxiety symptoms postoperatively. After controlling for preoperative anxiety symptoms, there was no significant correlation between age and postoperative anxiety symptoms.6

In 2020, Pedras et al published a longitudinal, multicenter study to evaluate the quality of life in patients with diabetes and lower limb amputations.⁷ The study assessed patients twenty-four hours before surgery, at one-month post-operative follow up, at six

months post-operatively, and at ten-months postoperatively. In total, the study assessed 206 patients and included 86 participants, who completed all four assessments, in their results.⁷ The authors stated that their objective was to analyze the relationship between patients' level of functionality before and after their lower limb amputation and emotional reactions, such as anxiety, depression, and traumatic stress symptoms. Their objective was also to analyze the role of supportive mediation between mental and physical quality of life and emotional responses. The authors hypothesized that patients' emotional status and functionality before surgery would be predictive for health-related quality of life (HRQoL) when evaluated ten months after lower limb amputation.⁷

The study included only patients who were over eighteen years old, had T2DM, and had a diabetic foot ulceration in which an amputation was indicated for treatment. The study utilized the Revised Impact of Events Scale to evaluate traumatic stress symptoms, the Hospital Anxiety and Depression Scale to evaluate for depression and anxiety, and the Barthel Index for measuring functionality. Additionally, the study included Short Form Health Survey for Physical Component Score (PCS) and Mental Component Score (MCS), measurements which are used in total to evaluate for HRQoL.⁷

The results included data from a population that was 73.33% male, with a mean age of 63.7 About half of the participants already had a previous amputation before the study. The study found that symptoms of anxiety at baseline were associated with anxiety symptoms at the one month postoperative follow up. Symptoms of depression and poor functionality before the surgery were associated with symptoms of depression and poor functionality at the one month postoperative follow up as well. Traumatic symptoms had a significantly negative effect on PCS. What the study found to be associated with a higher and therefore better PCS was good social support at six months postoperatively and good functionality at baseline and at one month postoperatively. Symptoms of anxiety at baseline and symptoms of depression one month postoperatively were associated with a poor MCS.7

In 2019, Norvell et al published a retrospective case-control study.⁸ Their aim was to develop a one-year mortality risk prediction model for patients undergoing their first amputation due to complications relating to diabetes. They collected patient data from the Veterans Affairs (VA) hospital system. Their data set consisted of 7,168 patients from VA hospitals across the United States.⁸ Initially, data from 5,028 patients were used to develop a prediction model. Another data set from 2,140 patients was used to validate their prediction model.⁸ Participants were

approved if they were 40 years old or older and their amputation was due to diabetes and/or PAD. Subjects were excluded if they had a previous amputation sooner than five years prior or the current amputation was bilateral. Participants were also excluded if they had other severe risk factors including a coma, certain cancers, or were dependent on a ventilator.⁸

A large list of 33 predictor variables were evaluated using the initial sample size. Selection of these variables was informed by the current literature and the feasibility of measurement using the VA data set. Researchers identified mental health as a significant risk factor to be analyzed. They evaluated this through establishing if there was "any mental health diagnosis" in a participant's data set.⁸ Mental health diagnoses tracked included depression, anxiety, post-traumatic stress disorder, bipolar disorder, and schizophrenia. The developmental sample showed 42.1% of patients with a mental health diagnosis.⁸ The validation sample showed 40.5% of participants with a mental health diagnosis.8 Of the total 7168 patients, 5267 survived one-year postoperatively and 1,901 did not survive one-year postoperatively.8 Of the surviving participants, 42.6% had a mental health diagnosis and 38.8% of deceased participants had a mental health diagnosis.8 There was no data published that stratified the participants by specific mental health diagnosis.

After completing a series of statistical analyses, there were ten statistically significant factors that were linked with one-year mortality predictions. Participants with greater BMI and demographic identification with 'Black' or 'Other' had a decreased risk of death one-year postoperatively. Participant factors that were linked with a greater risk of death one-year postoperatively include: more proximal level of amputation, increased age, partially dependent functional status, totally dependent functional status, previous diagnosis of congestive heart failure, currently receiving dialysis treatment, increasing blood urea nitrogen levels, and white blood cell counts of at least 11,000 units per microliter.⁸

Discussion

The methodology of this review allows the comparison of prospective and retrospective studies. Pedras et al. illustrate an example of how the construction of prospective data collection methodologies can be utilized to gather rich qualitative and quantitative data regarding the psychological impact of a diabetes related LLA.⁶ They used Likert scale questionnaires to investigate the presence of anxiety and depression symptoms among their participants. This type of questionnaire allowed them

to assess the potential effects of the presence of anxious or depressive symptoms and the magnitude of those symptoms. Likert scale patient questionnaires can be easily integrated into an office visit. First, they are very time efficient. They can be completed by a patient within minutes and require little to no staff training concerning how to administer them. Second, they are cost efficient. Medical equipment can be expensive and may deter physicians from implementing care strategies that are novel to them. This is not a factor for a Likert scale questionnaire. Third, a Likert scale is accessible to almost all patients, regardless of their abilities. The questionnaire can be given through a recording for people that cannot read, as is relevant for patients with limited vision from diabetic complications. It can easily be translated in advance for patients with limited English language proficiency. Pedras et al present an easily adoptable methodology that will allow us to better our patients' health outcomes.

The methodology used by Norvell et al shows the difficulty in obtaining psychological information from retrospective data sets.8 It is difficult to implement a consistent methodology for evaluating patient charts, especially with respect to mental health and associated symptoms. They used diagnostic codes when reviewing the mental health of their participants. They did not report data specifying when the participants were diagnosed. Nor did they report with which mental illness the patient was diagnosed. A few topics that future researchers could examine when using retrospective data include: comparing dates of mental health diagnoses and the date of the amputation, comparing trends and changes in mental health medications with the date of the amputation, and stratifying data by type of mental illness to discern if there are any trends between health outcomes and the type of mental illness diagnosis.

One limitation of this review is the exclusion criteria for papers published before 2011. From initial scouring through article databases, it was noted that many applicable articles were published before 2011. If the publication date had been extended, there would have been more articles to consider in our review. Colleagues interested in replicating this review should broaden the publication date inclusion criteria to evaluate more of the literature. Instead of changing the exclusion criteria, this review chose this established methodology to examine the most up to date literature. The small sample size of articles highlights the gap in the literature concerning patient's psychological wellbeing concerning diabetes related LLA.

Overall, this review establishes the importance of recognizing symptoms of depression and anxiety in patients before their amputations, as having these symptoms immediately before the procedure are predictive of poor outcomes postoperatively, especially for continued depression and anxiety one month after the procedure. A complete review of the patient's past medical history, including psychological diagnoses, may be helpful in predicting such sequelae. More research is necessary on identifying how providers may prevent these symptoms from occurring post-operatively and therefore improve patients' quality of life.

Conclusion

Amputations due to diabetes related complications can have a negative psychological impact on patients.⁵⁻⁷ Patient questionnaires given preoperatively help to indicate if patients are at high risk for experiencing postoperative psychological symptoms. Implementing efficient questionnaires allow physicians to provide patients with better health outcomes. Future research in this topic is warranted to evaluate the best methodologies for improving patient care relating to the psychological symptoms that may accompany an amputation.

References

- Zhang P, Lu J, Jing Y, Tang S, Zhu D, Bi Y. Global epidemiology of diabetic foot ulceration: a systematic review and meta-analysis †. *Ann Med.* 2017;49(2):106-116. doi:10.1080/07853890.2016.1231932
- Noor S, Zubair M, Ahmad J. Diabetic foot ulcer--A review on pathophysiology, classification and microbial etiology. *Diabetes Metab Syndr*. 2015;9(3):192-199. doi:10.1016/j.dsx.2015.04.007
- Armstrong DG, Boulton AJM, Bus SA. Diabetic Foot Ulcers and Their Recurrence. N Engl J Med. 2017;376(24):2367-2375. doi:10.1056/NEJMra1615439
- Thorud JC, Plemmons B, Buckley CJ, Shibuya N, Jupiter DC. Mortality After Nontraumatic Major Amputation Among Patients With Diabetes and Peripheral Vascular Disease: A Systematic Review. J Foot Ankle Surg. 2016;55(3):591-599. doi:10.1053/j.jfas.2016.01.012
- Mckechnie PS, John A. Anxiety and depression following traumatic limb amputation: a systematic review. *Injury*. 2014;45(12):1859-1866. doi:10.1016/j.injury.2014.09.015
- 6. Pedras S, Carvalho R, Pereira MG. A predictive model of anxiety and depression symptoms after a lower limb

amputation. *Disabil Health J.* 2018;11(1):79-85. doi:10.1016/j.dhjo.2017.03.013

- Pedras S, Vilhena E, Carvalho R, Pereira MG. Quality of Life Following a Lower Limb Amputation in Diabetic Patients: A Longitudinal and Multicenter Study. *Psychiatry*. 2020;83(1):47-57. doi:10.1080/00332747.2019.1672438
- Norvell DC, Thompson ML, Boyko EJ, Landry G, Littman AJ, Henderson WG, Turner AP, Maynard C, Moore KP, Czerniecki JM. Mortality prediction following non-traumatic amputation of the lower extremity. *Br J Surg.* 2019;106(7) 879-888. doi:10.1002/bjs.11124

Treatment and Impact of Accessory Navicular Syndrome in an Athlete and Non-Athlete Populations

Savannah Santiago, B.S. and Hadia Bharoocha, B.S.

<u>Abstract</u>

Objective: The objective of this review is to assess the difference in treatment for athlete versus non-athlete individuals suffering from symptomatic accessory navicular syndrome (ANS). It will then analyze the potential treatment outcome differences between the two groupings. To then evaluate the potential impact that ANS can have on the training regimen and athletic performance in the athlete population.

Methods: A search was done on PubMed and Google Scholar using the keywords "symptomatic accessory navicular," "young athletes," "accessory navicular syndrome," "athletic performance." The articles were then examined, and retrospective case studies were utilized to analyze data on symptomatic ANS in athletes.

Results: Conservative treatment showed more success in non-athlete ANS patients and more invasive treatment was required for athletic individuals to achieve optimal outcomes.

Conclusion: Symptomatic ANS requires different treatment in athletes vs. non-athlete individuals. It was found that a higher success rate with conservative treatment in non-athlete individuals than in the athlete populations. These findings are contributory to the differences in exercise level and the impact of athletic training on the severity of ANS between the two populations studied.

Introduction

An accessory navicular bone is the presence of an extra bone on the center of the arch of the foot on the medial aspect adjacent to the navicular.¹ There are three types of accessory navicular bones, and their shape and exact location can vary.¹ This article will be focusing on when the presence of the accessory navicular bone becomes pathological. According to the American College of Foot and Ankle Surgeons (ACFAS) website, the prevalence of Accessory Navicular Syndrome (ANS) in the general population is estimated to be between 2-14%.² While having the presence of an accessory navicular bone is already considered uncommon, it is even more uncommon to have symptoms from the accessory navicular bone itself, occurring in only about 10% of those with an accessory navicular bone.⁴ Despite a relatively low incidence in the population, ANS is an important pathology to study because it can cause tension, shearing, and/or compression through the posterior tibial tendon and to the fibrocartilaginous surface of the foot.

Patients with ANS present in adolescence with complaints of medial midfoot pain, vague pain, or swelling that commonly occurs during periods of activity or directly after.¹ In athletes presenting with symptomatic ANS, the pain can become exacerbated during exercise such as walking or running, affecting their ability to train. This not only impacts their dayto-day life but also their future athletic performance. This does not differ from the presentation of a non-athlete with ANS. Both athletes and non-athletes may present with redness and swelling of the bony prominence with vague pain of the mid-arch when walking or completing daily life tasks.⁶ The major difference between the athlete and non-athlete population would be the worsening and severity of the pain and symptoms due to daily physical activity and exertion.

In a study done by Jegal et al, it was determined that the athlete population required more invasive treatment compared to their non-athlete counterparts. This study also showed a much higher prevalence of a history of foot trauma presenting as inflammation, bone marrow edema, stress fractures, and pain associated with ANS in the athlete population compared to the non-athlete population. These findings supported the findings of a study by Dr. Shiochiro Nakayama which studied 29 young athletes with type II ANS.⁵ A type II ANS is an accessory navicular where there is a larger secondary ossification center within the navicular bone, typically where the posterior tibial tendon inserts.⁴ The type II accessory navicular is the most common symptomatic variant commonly due to repetitive tension and shear stress across the syndesmosis due to the action of the posterior tibial tendon.² This can cause posterior tibial dysfunction which can contribute to ANS-associated pain.3 It was concluded that treatment of ANS in young athletes often showed athletic performance was inhibited due to the exaggeration of the symptoms from walking, running, and overall exercise needed for athletic performance and training.

The objective of this review was to analyze the impact on athletic performance that ANS could have and

the difference in treatment methods for athlete and nonathlete patients.

Methods

A review of published literature within the half-century was conducted. Due to the relatively small percentage of the population that suffers from ANS, the date range of the published literature was widened. The search criteria included the need for case studies of ANS shown in athletes. The keywords used in the search engines of PubMed and Google Scholar were "symptomatic accessory navicular", "young athletes", "accessory navicular syndrome", "athletic performance", and "ANS". The parameters for the athletic population (by definition of athlete) were set as individuals with fused growth plates who participate in some form of competitive, scholastic, or organized sport. Articles were then eliminated based on being outside of time range, not including athlete case studies, research on individuals without ANS, and the inclusion of conditions that were not specifically ANS.

Results

In total, five articles were selected that met the outlined criteria, and another article was referenced for surgical outcomes to draw parallels around differences in treatment and healing.

To study the general prevalence of ANS, Knapki et al. conducted a study to evaluate 73 patients with clinical and radiographic evidence of ANS. Patient history related to sex, race, age, date of pain onset, laterality, and treatment were recorded and compared. From the study, it was determined that 71% of the patients were female and presented with ANS symptoms at earlier ages (P=0.06) as compared to their male counterparts. According to Knapki et al., ANS prevalence occurred in 14% of the general population with athletes being more likely to be symptomatic and highly impacted.

To compare the difference in prognosis between conservative care and surgical treatment in athletes, Rietveld et al. conducted a retrospective case study involving athlete dancers with ANS. In the study, a total of six athlete dancers diagnosed with ANS were treated and studied. Of these athletes, five were treated surgically and one conservatively.¹⁰ A splitting posterior tibial transfer (PTT) procedure was chosen to be the surgery performed on selected athletes. The non-surgical treatment used was immobilization using a cast and in-soles. Of the five surgically treated athletes, there were no postoperative complications, and the athletes were able to go back to competitive dancing without restriction.

The rehabilitation period for these athletes to go back to their high-demand exercise regiments was

found to take an average of 3 months. In one of these patients, rehabilitation was prolonged to 12 months due to a painful PTT insertion. The athlete, however, was able to begin competitive dancing within five months. In the one patient that was treated non-operatively, it was found that 6 months after the removal of the cast, the patient was unable to return to competitive dancing without significant pain and was later scheduled for operative treatment.¹⁰

To assess the clinical progression of athletes vs. non-athletes with ANS, Jegal et al. Evaluated 79 patients with ANS for a full year, 50 of the patients were non-athletes while 29 were athletes. The improvements or lack thereof were measured after periodic conservative treatment using clinical features and radiological imaging. It was determined that 34% of the non-athletes improved after conservative treatment compared to a minor 6.9% improvement seen in athletes with a P-value of <0.001. Furthermore, comparisons were made to assess the effectiveness of ANS treatment concerning age in athletes vs non-athletes with ANS. The mean age group at the time of surgery in Jegal et al.'s research was 16.1 years vs the 24.3 years for non-athletes (P<0.001).

To investigate the impact of percutaneous drilling for symptomatic Type II ANS on athletic performance, Nakayama et al. conducted a study reviewing 29 patients with Type II ANS. The patients were all treated with minimally invasive percutaneous drilling of accessory navicular synchondrosis to induce or accelerate bone union between the accessory and primary navicular bones which in turn would lead to ANS symptom relief. Bone union was determined using x-rays taken 4-52 weeks post-operation with a tarsal navicular view. Of the feet studied, 79.3% were assessed as excellent, 17.2% as good, and 3.5% fair with 0% poor and no patients whose symptoms worsened post-operation. Bone union rate between patients with and without mature bone (i.e., older vs younger athlete patients) was statistically significant (P=0.001). In conclusion, it was determined that this procedure allowed all patients (athletes and nonathletes) to resume their daily activities and training without any post-procedure complaints.

To contrast the surgical treatment of percutaneous drilling utilized in athletes described in Nakayama et al.'s research with the surgical treatment of ANS in non-athlete patients, Kopp et al.'s study was analyzed. In the study, 13 patients with a total of 14 feet were followed up pre-operatively and postoperatively for a minimum of 45 months. Patients with ANS were selected and screened based on the American Orthopedic Foot and Ankle Score (AOFAS) system and reassessed using the same scale to assess outcomes. The surgical technique utilized involved shelling the navicular from the posterior tibial tendon at the dorsal aspect of the bone. The severed tendon was reattached to the periosteal or connective tissue flap using sutures. The outcome of the surgery had an average postoperative AOFAS score of 94.5 vs. the pre-operative average of 48.2 (p<0.001). The average recovery time was found to be 103.4 months and no postoperative complications were reported.

Discussion

The results of the studies showed the impact that ANS has on athletes vs non-athletes and how the treatment between both sets of patients varies along with prognosis variance. Having a significant prevalence of 14% in the general population and symptomatic manifestation in most athletes and obese patients,⁴ all literature focused on the most efficient, non-invasive, and quickest route of prognosis. In the study conducted by Jegal et al. in 2016, it was seen that athletes with ANS treated with non-conservative treatment via modified Kidner operation had more symptoms than their non-athlete refractory counterparts.

This recovery difference could be further explained by the ANS in athletes being exacerbated to bone marrow edema observed in 100% of the athlete patients with ANS. According to Macnicol et al, while patients can begin physical rehabilitation and be ambulatory in footwear four weeks post-procedure, it takes around three months for the patient to resume exercise activities. This confirmed the difference in recovery duration for athletes vs. non-athletes. The findings of this minor improvement in athletes with just conservative care show that athletes required more treatment than just conservative care. The lack of success with conservative care is a factor in the significant impact that ANS can have on an athlete's training regimen and schedule. Not only are they experiencing pain associated with exertion, but conservative treatment overwhelmingly failed in the athlete population causing increased time away from training along with prolonged pain.⁹ These symptoms then further impacted their competition performance and ability.

In the research by Kopp et al, general (nonathlete) patients were treated with excisional surgery of the navicular. These patients were found to have excellent recovery based on their post-operative AOFAS score with an average recovery time of 103.4 months. In comparison, in the study by Jegal et al, athlete patients were found to have recovery times of 12 months with percutaneous drilling and three months seen in Rietveld et al. with a PTT transfer. While the findings from all three of these surgical studies showed excellent prognosis, with the demands around athletes returning to their respected sport as soon as possible,² recovery time becomes a crucial factor in determining the surgical course.

From the retrospective case study conducted by Rietveld et al., a stark difference was noted in the recovery time and return to athletic performance between competitive dancers diagnosed with ANS based on treatment. The athletes treated with surgery recovered without complication and were able to return to their full athletic performance within three months of their surgeries. Of those five athletes, one athlete that was surgically treated had an extended rehabilitation due to painful PTT transfer but was able to completely recover and return to full athletic function. On the other hand, the athlete treated with a conservative and more widely used treatment method of immobilization did not have positive outcomes. This athlete was unable to return to his previous athletic performance level and had to be scheduled for surgery. It was concluded that while there was sufficient evidence in the literature that conservative treatment of ANS had favorable outcomes, surgical treatment was demonstrated in this study to be the better option for athletes.¹⁰ The post-operative care for athletes is also starkly different than non-athletes and focuses on intense strength conditioning. proprioception, and cross-training to hasten their return to their sport.¹¹ Two noteworthy shortcomings of this case study were the small sample size researched and the lack of comparison with other treatment options both surgical and non-surgical.

To understand why ANS recovery between athletes and non-athletes varied significantly, Nakayama et al. assessed the impact of athletic activities on ANS II manifestation. These findings suggest that athletic performance was inhibited by ANS symptoms and exacerbated by athletic training. In the review, Nakayama et al. also determined that percutaneous drilling through the fibrocartilaginous layer had the best prognosis with athletes. This procedure was minimally invasive and had an excellent prognostic outcome. This was, however, true for younger athletes with immature basal phalanxes of the big toe. For older athletes with mature basal phalanxes, the bone union and hence, prognosis, was significantly poorer.

During this review. the American Orthopaedic Association and the Japanese Orthopaedic Association scales could not be used to determine the efficacy of the treatment due to the disparity in the calibration not considering minor complaints that for general patients may not be as impactful but for athletes can present major challenges. Nakayama et al. had to calibrate the complaints independently which can present challenges for future comparative studies by other researchers.

Overall, the literature reviewed highlights the importance of early diagnosis of ANS and conservative treatment for efficient and effective prognosis of ANS in athletes. Even with early diagnosis and treatment, the overall impact of ANS irreversibly impairs athletic performance, delays recovery, and thus more research and advanced, minimally invasive treatment options need to be researched. Studies to further advance percutaneous drilling and effectiveness in older patients with matured basal phalanxes of the big toe need to be conducted as the effectiveness of percutaneous drilling was significant only in younger athletes. For nonathletes, the current and previously described procedures boded well for recovery times as well as effectiveness.

Conclusion

In conclusion, the literature supports that ANS in athletes significantly impairs athletic performance both before treatment in the form of symptomatic presentation and exacerbation and postoperatively compared to non-athletes. The impairment is physiological due to the recovery time needed from the procedure itself. While percutaneous drilling was determined to be a desirable treatment option with favorable results for young athletes, extensive research must be conducted to find the best possible treatment option for older athletes with ANS.

References

 1.
 ACFAS. 2021. Accessory Navicular Syndrome - ACFAS.

 [online]
 Available

 Attach
 Attach

http://www.acfas.org/footankleinfo/Accessory_Navicular_Syndro me.htm> [Accessed 21 November 2021].

2. Abe, K., Hashiguchi, H., Sonoki, K., Iwashita, S. and Takai, S., 2019. Tarsal Navicular Stress Fracture in a Young Athlete: A Case Report. *Journal of Nippon Medical School*, 86(2), pp.122-125.

3. Cho YS, Lee KT, Kang HS, Kim EK. MR imaging findings of painful type II accessory navicular bone: correlation with surgical and pathologic studies. *Korean J Radiol.* 2004;5(4):274-279. doi:10.3348/kjr.2004.5.4.274

4. Fraser JJ, Feger MA, Hertel J. Clinical commentary on midfoot and forefoot involvement in lateral ankle sprains and chronic ankle instability part 2: clinical consideration. *Int J Sports Phys Ther.* 2016;11(7):1191-1203.

5. Jegal H, Park YU, Kim JS, Choo HS, Seo YU, Lee KT. Accessory Navicular Syndrome in Athlete vs General Population. *Foot Ankle Int.* 2016;37(8):862-867. doi:10.1177/1071100716644791

6. Kalbouneh, H., Alajoulin, O., Alsalem, M., Humoud, N., Shawaqfeh, J., Alkhoujah, M., Abu-Hassan, H., Mahafza, W. and Badran, D., 2017. Incidence and anatomical variations of the accessory navicular bone in patients with foot pain: A retrospective radiographic analysis. *Clinical Anatomy*, 30(4), pp.436-444.

 Knapik, D., Archibald, H., Xie, K. and Liu, R., 2019. A retrospective study on factors predictive of operative intervention in 8. symptomatic accessory navicular. *Journal of Children's Orthopaedics*, 13(1), pp.107-113.

9. Nakayama, S., Sugimoto, K., Takakura, Y., Tanaka, Y. and Kasanami, R., 2005. Percutaneous Drilling of Symptomatic

Accessory Navicular in Young Athletes. *The American Journal of Sports Medicine*, 33(4), pp.531-535.

10. Macnicol, M. and Voutsinas, S., 1984. Surgical treatment of the symptomatic accessory navicular. *The Journal of Bone and Joint Surgery. British volume*, 66-B (2), pp.218-226.

11. Rietveld A.B.M, Diemer W., 2016. Surgical treatment of the Accessory Navicular (Os Tibiale Externum) in Dancers. *Journal* of Dance Medicine and Science. Volume 20 (3)

11. Smith TR. Management of dancers with symptomatic accessory navicular: 2 case reports. *J Orthop Sports Phys Ther*. 2012 May;42(5):465-7

Outcomes of Operative vs. Nonoperative Management of Displaced, Intra-Articular Calcaneus Fractures: A Current Review

Bezon Rustomi B.S.

ABSTRACT

Objective: To review the current literature on the comparison of outcomes following operative and nonoperative treatments for displaced, intra-articular calcaneus fractures.

Methods: Relevant research articles for the treatment of displaced, intra-articular calcaneus fractures, with results of subsequent outcomes from operative treatment, nonoperative treatment, or both, were found via the PubMed, Google Scholar, and BIOSIS databases. Eleven articles were analyzed and included in this review.

Results: Most studies that were reviewed found similar outcomes following operative and nonoperative treatment of displaced, intra-articular calcaneus fractures. However, studies that measured Böhler's angle and the time taken to return to pre-injury work following treatment for each group found that the results favored operative management., though they were generally associated with higher rates of postoperative complications. Conversely, the nonoperative treatment groups were associated with a higher risk for subtalar arthrodesis.

Conclusion: In managing calcaneus fractures, careful evaluation of a variety of factors prior to selecting treatment, such as severity of injury, Worker's compensation status, and patient occupation, are vital for achieving optimal outcomes. With the main concern for operative treatment being postoperative complications, the emergence of less invasive surgical techniques has made the decision to opt for operative treatment more convincing for surgeons. Assuming adequate postoperative wound care following minimally invasive surgical techniques, operative management of displaced, intra-articular calcaneus fractures should generally be favored in most cases.

Introduction

Fractures of the calcaneus compose about 2% of all fractures and are the most common fracture of the tarsal bones.¹ These fractures are often considered serious injuries and usually occur following a fall from varying heights or a high energy traffic collision. Intraarticular fractures that involve the subtalar joint can often be problematic and can be managed operatively or nonoperatively. Conservative, nonoperative care consists of elevation, early mobilization of the affected joint, and the use of a splint for stabilization. Patients are generally advised to abstain from weight-bearing for six weeks, followed by partial weight-bearing for another six weeks. With such management, although the fragments of bone will ultimately heal together, the shape of the calcaneus becomes deformed and results in incongruent joint surfaces and eventual malalignment of the leg through the heel and ankle. This results in severe and painful osteoarthritis of the subtalar joint, as well as suboptimal mechanics in walking that can negatively alter additional structures upstream through the kinetic chain. The detrimental effects of this are especially cumbersome for patients who rely on physical labor for work, since they are unable to resume their pre-injury work due to the difficulty of finding shoes that fit to the shape of their deformed foot and experience severe discomfort when walking, often requiring the use of an assistive device such as a walking stick. The consequences of suboptimally healed calcaneus fractures on the working class became apparent by the early 1900s, after which point the need to determine more effective strategies of management became necessary.¹

Operative management of intra-articular calcaneus fractures began to gain popularity in the 1950s, at which point a percutaneous "spike" was used for stabilization.¹ This method guickly lost its momentum in the 1960s due to the difficulty of performing the procedure effectively. A multitude of surgical techniques were utilized until the use of plates and screws allowed orthopedic surgeons to better realign the broken bone fragments and subsequently restore the subtalar joint. More recently, minimally invasive techniques have gained some popularity but the potential benefits of endorsing such procedures requires more evidence. The operative management of displaced, intra-articular calcaneus fractures most often consists of open reduction and internal fixation approximately two weeks after the initial injury, to give sufficient time for swelling to reduce and to minimize the potential for soft tissue complications postoperatively.² One operative treatment modality utilizes an extensile lateral approach, which allows the fracture to be directly reduced and the fracture fragments in the posterior facet to be adequately visualized. Once the calcaneus is visualized, interfragmentary screws are used to stabilize a neutralization plate along its lateral wall.1 Postoperatively, a splint is applied, and patients are advised to remain non-weight bearing for six weeks followed by partial weight bearing for another six weeks. This is supplemented with physical therapy

that focuses on early active mobilization of the ankle and subtalar joints. Advocacy for this approach is based primarily on the benefit of restoring the functional and anatomical structure of the calcaneus.³ The main complication associated with operative management for calcaneus fractures is the risk of infection at the incision site. However, it has been historically believed that the advantages of restoring the normal shape of the foot and the subsequently decreased risk of post-traumatic osteoarthritis outweigh such risks. Additionally, the emergence of minimally invasive surgical techniques can further minimize such risks.² However, there remains controversy surrounding whether to treat displaced, intra-articular calcaneus fractures operatively or nonoperatively.⁴

The goal of this study is to compare the outcomes for operative and nonoperative management of displaced, intra-articular calcaneus fractures, and to suggest which treatment is more effective based on the available evidence.

Methods

Eleven relevant research articles to compare the outcomes for operative and nonoperative treatment of displaced, intra-articular calcaneus fractures were identified through the PubMed, Google Scholar, and BIOSIS databases. Key search words included "displaced, intra-articular calcaneus fracture", "operative", "nonoperative", "functional outcomes", and other similar terms. Inclusion criteria included patients who were diagnosed with displaced, intraarticular calcaneus fractures and had received either conservative or surgical treatment, with follow-up to determine functional outcomes following the respective treatment modalities. Exclusion criteria included studies that did not report at least a 1-year post-treatment follow-up and those that reported functional outcomes without a standardized scoring system for objective analysis of results. Articles were excluded if they were published before the year 1999, were not in English, and did not grant free access to the entire article.

Results

A randomized controlled trial conducted by Griffin et al. consisted of 151 patients with closed, displaced, intra-articular calcaneus fractures and investigated whether surgery by open reduction and internal fixation provided better outcomes than nonoperative treatment. 73 patients and 78 patients were randomly allocated to operative and nonoperative treatment groups, respectively. Initial treatment for all participants was composed of bed rest, analgesia, elevation of the injured foot, and application of ice. Operative treatment consisted of

open reduction and internal fixation within the first three weeks post-injury, with an extensile lateral approach and the application of interfragmentary screws and a neutralization plate along the lateral wall of the calcaneus. Postoperative care included the use of a splint, six weeks non-weight bearing followed by six weeks of partial weight bearing, with early active mobilization of the ankle and subtalar joints. Nonoperative treatment consisted of gentle mobilization of the ankle and subtalar joints within the limits of tolerated pain, and the use of a removable splint. Patients within this group were mobilized and non-weight bearing for six weeks, followed by six weeks of partial weight bearing. The same standard physiotherapy rehabilitation regimen was utilized in both the operative and nonoperative treatment groups.¹ The primary outcome measured was the patient reported Kerr-Atkins score, which is a composite score quantifying pain and function after calcaneal fracture. With 100 possible points, a score of 100 represents normal pain and function; a score in the range of 80-100 represents slight pain or minor difficulties in the ability to walk without assistance, such as the use of a walking cane; and a score in the range of 60-80 represents moderate pain, restriction in walking, and consistent use of walking assistance. This primary outcome was measured at two years post-injury. Additional secondary measures reported were the EuroQol EQ-5D, SF-36, and the American Orthopaedic Foot and Ankle Society (AOFAS) scores, which measure quality of life, general health status, and global hindfoot function, respectively. All patient reported outcomes were gathered prior to randomization, and by questionnaires after 6, 12, and 18 months. Additional functional assessments were completed by a single, blinded physiotherapist at the two-year follow-up. Results of the study indicated the Kerr-Atkins scores after two years were similar between the operative and nonoperative treatment groups, with scores of 69.8 and 65.7, respectively.¹ These scores, along with all predetermined secondary outcome measures, were found to be statistically insignificant, which further reinforced the authors conclusion that operative treatment of closed, displaced, intra-articular calcaneus fractures does not improve outcomes when compared with the nonoperative treatment protocol. It was found, however, that significantly more patients in the operative treatment group (17/73; 23%) experienced complications and subsequent reoperations than in the nonoperative group (3/78; 4%).¹ The most reported complication was surgical site infection, all of which occurred in the operative group within six weeks postoperatively. Complications reported that were exclusive to the nonoperative group were subtalar arthrodesis for the treatment of painful arthritis. The

study concluded that outcomes following open reduction and internal fixation of closed, displaced, intra-articular calcaneus fractures were no different than nonoperative management at two years. The higher rate of complications and reoperations following operative treatment make the justification for such an intervention less convincing, unless in the setting of severe displacement.¹

A retrospective cohort study by Zhang et al. included 21 patients with calcaneus fractures that were treated using a minimally invasive approach. The surgical approach consisted of reduction, bone grafting, and plate fixation by a small incision. The primary outcomes that were measured were changes in the Böhler and Gissane angles, as well as the calcaneus width after surgical fixation. Additional clinical outcomes were evaluated by assessment of soft tissue complications and the Maryland foot scoring system, which includes patient-reported pain, functional capacity, and cosmesis.3 The calcaneal width and Böhler and Gissane angles were measured preoperatively and on postoperative day three. Soft tissue complications were also recorded at this time. The clinical functional outcomes, as measured by the Maryland foot scoring system, were recorded during a postoperative examination at least one year postoperatively. Postoperative care consisted of elevation and drainage of the incision with minimal exercise of toes and ankle joints on postoperative day one. The wound was consistently cleaned every two days until eventual suture removal at two weeks postoperatively. At three months after surgery, patients were advised to initiate full weight bearing. The study found that the Böhler angle improved from a preoperative mean of 17.25° to a postoperative mean of 33.18°, while the Gissane angle improved from a preoperative mean of 93.58° to a postoperative mean of 125.32°.3 Both improved outcomes were found to be statistically significant. According to the Maryland foot score, the rate of excellent and good outcomes was 85.7%, and the rate of soft tissue complications was found to be 14.3%.³ Soft tissue complications that were reported included wound inflammation and superficial wound infection without deep infection following the use of antibiotics and alcohol compresses. It was therefore concluded that the treatment of calcaneus fractures with a minimally invasive internal fixation with a thin plate and bone grafting can provide excellent clinical outcomes with a relatively minimized risk of soft tissue complications.³ It should be noted that such a procedure has limitations when applied for the reduction of extensive articular surfaces, which create technical challenges and prolong the overall operative time.

A meta-analysis study by Shi et al. sought to compare 5 main treatment approaches for displaced. intra-articular calcaneus fractures: extensile lateral approach (ELA), minimally invasive longitudinal approach (MILA), sinus tarsi approach (STA), percutaneous reduction and fixation (PRF), and nonoperative treatment. These treatment modalities, four of which are operative in nature, were compared and ranked in terms of Böhler's angle, American Orthopaedic Foot and Ankle Society score, selfreported satisfaction ratings, and incision complications.⁴ The study found that the Böhler's angle after treatment was substantially lower in the nonoperative group than in any other treatment group. with no significant difference in postoperative Böhler's angle measurements among the various operative groups. No significant difference was identified in terms of clinical and functional effectiveness between all operative and nonoperative treatment groups. Higher satisfaction ratings were substantially more prevalent and statistically significant in all operative treatment groups when compared to the nonoperative treatment group. Postoperative incision complications were significant in the extensile lateral approach group when compared to the other three operative treatment modalities, with percutaneous reduction and fixation reporting the fewest number of complications.⁴ The study concluded that operative treatment approaches appear to be favored over nonoperative treatments in the context of displaced, intra-articular calcaneus fractures, although the risk of postoperative incision complications should be acknowledged. For this reason, minimally invasive approaches should be utilized depending on the skill level of the surgeon. unique patient requirements, and the severity of the injury to the bone and surrounding soft tissue.4

Jiang et al. conducted a meta-analysis of six randomized controlled trials and four clinical controlled trials that compared the outcomes of surgical and nonsurgical treatments for displaced, intra-articular calcaneus fractures in a total of 891 patients who met inclusion criteria. Only randomized and clinical controlled trials that compared surgical with nonsurgical methods specifically for displaced, intra-articular calcaneus fractures were taken into consideration. The Böhler angle was compared before and after surgical and nonsurgical treatments. Results of the meta-analysis indicated that patients who had received nonsurgical treatments were found to have significantly smaller mean Böhler angles than their surgically treated counterparts.⁵ In further assessment of the anatomy of the calcaneus following the respective interventions, it was found that the operative treatment group had more stable calcaneal widths and significantly less calcaneal height loss.

Functional measures were also assessed in this study, with the operatively treated patients reporting fewer difficulties in wearing shoes than the nonoperatively treated patients. Additionally, a greater number of patients in the operatively treated group were able to return to their pre-injury work. No significant difference in residual pain was identified, with 75 of 119 (63.0%) patients in the operative group and 85 of 121 (70.2%) patients in the nonoperative group reporting the presence of residual pain during followup. A significant difference was identified regarding the incidence of complications, with 22.8% of operatively treated patients and 16.2% of nonoperatively treated patients experiencing complications.⁵ The study concluded that operative treatment of displaced, intra-articular calcaneus fractures can adequately restore the anatomic structure of the calcaneus and improve overall functional recovery but carries a greater risk of complications.⁵ It should be noted that the operative treatment in the included studies utilized open repairs, as opposed to percutaneous repair, which carries a slightly higher overall risk of postoperative complications.

With the risk of postoperative complications being the primary hurdle facing clinicians who are deciding whether to treat calcaneus fractures surgically or conservatively, the push for less invasive surgical techniques has increased in recent years. Such techniques allow for the same benefits as the extensile lateral approach with open reduction and internal fixation, with the main difference being visibility of the calcaneus, and the added benefit of lower potential risk for postoperative wound complications. A review of four prospective and six retrospective trails by Mehta et al. compared the outcomes for calcaneus fractures that were treated operatively by the extensile lateral approach and the less invasive sinus tarsi approach. The study found that within the context of displaced, intra-articular calcaneus fractures, patients who were treated by the extensile lateral approach were more likely to experience postoperative complications (OR=2.98) when compared to the sinus tarsi approach.⁶ The authors of the review noted that the major limitations of the presented evidence comparing these two methods is the lack of data on functional outcomes and postoperative articular displacement, as well as the inability to assess postoperative function through statistical analysis of a large sample size of patients.

A meta-analysis conducted by Liu et al. sought to determine whether the surgical treatment of displaced, intra-articular calcaneus fractures can offer protection against subsequent early subtalar arthrodesis. The authors found that surgically treated patients had significantly fewer cases of early subalar arthrodesis than the patients who were treated nonoperatively, which had a calculated relative risk of 4.40 and was deemed significant.⁷ The conclusion made from the study was that surgery for displaced, intra-articular calcaneus fractures is necessary, as the risks of subtalar arthrodesis outweigh the risks of postoperative complications and infections.⁷ The limitation of the study is the lack of comparison of additional outcomes, such as Böhler's angle, between the operative and nonoperative treatment groups.

A prospective, randomized, controlled multicenter trial consisting of 424 patients was conducted by Buckley et al. and found that there was no significant difference in outcomes between patients who had been treated operatively and nonoperatively at the two-year follow-up.8 However, upon careful stratification of the patient population, significant evidence in support of operative management was identified. Further analysis found that patients with higher Böhler angles, lighter post-recovery workloads, less severe fractures, or an absence of Workers' compensation were found to have significantly better results from operative treatment than nonoperative treatment.⁸ The study also found that ideal candidates for nonoperative treatment include those who are at least 50 years old, involved in occupations with heavy workloads, or receiving Workers' compensation.8 Limitations of the study include the lack of information regarding potentially confounding demographic information, such as smoking status, personality type, and body-mass index, which could all play a role in recovery.

One prospective, randomized cohort study by Loucks et al. sought to evaluate the correlation between Böhler's angle and subsequent functional outcomes in displaced, intra-articular calcaneus fractures. The study found that regardless of treatment modality, patients who initially presented with severely depressed Böhler angles had poor two-year follow-up outcomes. It has been concluded that Böhler's angle carries significant prognostic value in predicting morbidity. Patients who presented with a markedly diminished Böhler's angle due to a severe fracture consistently demonstrated poorer two-year outcomes irrespective of the selected treatment modality. Additionally, operative treatment of these fractures was found to significantly increase Böhler's angle, especially when compared with patients who were treated conservatively.9 While an increase in Böhler's angle following treatment would be expected to result in better outcomes, the significantly decreased Böhler's angle often found to be persistent in nonoperatively treated patients subsequently led to poorer outcomes.

Discussion

There has been much scrutiny regarding the preferred method of management, either operative or nonoperative, for displaced, intra-articular calcaneus fractures.⁴ The goal of management for displaced, intra-articular calcaneus fractures is to restore the anatomy of the calcaneus and the affected joints to their pre-injury baseline, and in doing so, facilitate proper function while limiting pain and the possibility for additional unnecessary procedures. In the setting of calcaneus fractures, Böhler's angle is consistently assessed to determine the severity of the injury, as well as, whether to treat operatively or nonoperatively. The determined "normal" value for this angle is between 20° and 40°, and a value below this acceptable range is typically associated with calcaneus fractures.¹ Current evidence illustrates that direct impact injuries tend to produce reduced Böhler's angles with a greater degree of bone and soft-tissue injury, which ultimately results in worse long-term outcomes in significantly displaced, intra-articular calcaneus fractures.9 Historically, Böhler's angle has been considered an excellent prognostic factor in determining morbidity in calcaneus fractures.¹

Operative management of displaced, intraarticular calcaneus fractures does not guarantee optimal results in all cases, as there is a risk for postoperative infections, along with residual pain and subsequent arthritis due to the traumatic nature of the injury. Also, due to the nature of the injury and the disproportionately high rate of occurrence among individuals who depend on physical labor for their livelihood, additional factors such as the classification of the injury, along with Worker's compensation status, may affect the perceived outcomes of treatment. In most cases, however, it is often the severity of the injury that is the primary determining factor when opting for surgical treatment. When considering operative management for severely displaced, intra-articular calcaneus fractures, the risks of potentially eliminating the possibility of returning to the functional baseline far outweigh the risk of a post-operative infection. However, it remains imperative to ensure that there is a careful assessment of all factors that may predispose patients to poorer outcomes. Such factors include but are not limited to the nature and severity of the injury, changes in Böhler's angle, patient occupation, and Workers' compensation status.

In managing displaced, intra-articular calcaneus fractures, each intervention, whether operative or nonoperative, has its own individual risks. Despite most of the literature scrutinizing the risk of post-operative infection when surgically treating displaced, intra-articular calcaneus fractures, conservative management carries risks of its own. Most notable of which, is the risk for subtalar arthritis and the necessity for subsequent subtalar arthrodesis, which is an additional surgical procedure that reintroduces the risk of post-operative infection and potentially suboptimal outcomes. In the setting of high injury fractures with significant displacement, the decision to treat surgically is often endorsed by the fact that operative management can help decrease the incidence and severity of posttraumatic arthritis, when compared to nonoperative management.¹⁰ This notion further endorses the use of surgical interventions when treating displaced, intra-articular calcaneus fractures to optimize functional recovery.

The current data measuring outcomes for the operative and nonoperative management of displaced, intra-articular calcaneus fractures is vast. Most studies indicate no significant difference in outcomes between the two treatment modalities. With each having its own unique post-treatment risks and complications, the decision to opt for one or the other is largely dependent on a variety of factors, such as severity of injury, initial Böhler's angle, post-injury Böhler's angle, and Worker's compensation status. In most cases, adequate restoration of the calcaneus' functional anatomy should be prioritized. Since the functional outcomes for both operative and nonoperative treatment are similar, careful attention is required to assess the potential for post-treatment complications.

Conclusion

The severe nature and long-term complications associated with displaced, intraarticular calcaneus fractures make its management cumbersome. Individuals with more severe fractures who are young, less likely to return to demanding physical labor, and who are not currently receiving workers' compensation make excellent candidates for operative treatment. However, the risk of associated complications such as wound infection and reoperation cannot be ignored. Although this risk is much lesser when treated conservatively, such an approach presents specific concerns. Examples of such are posttraumatic subtalar arthritis and subsequent subtalar arthrodesis. In general, patients with more severe fractures, as indicated by a flatter Böhler's angle, seem to gain more benefit from operative repair due to restoration of the functional anatomical structure of the calcaneus and subtalar joints. Nonoperative repair should be advised in older patients and in those with less severe fractures. Further studies are needed to systematically compare outcomes in patients beyond the one-to-two-year follow-up, to provide more longitudinal data that can be used to create a more convincing argument in support of either operative or nonoperative treatment

and their respective outcomes. Additionally, more studies are needed to compare the various surgical approaches used in the treatment of displaced, intraarticular calcaneus fractures, as newer and less invasive approaches have gained popularity in the recent years. Comparative data between the various procedures, and a subsequent comparison to nonoperative outcomes can provide valuable information regarding the optimal management for displaced, intra-articular calcaneus fractures.

References

- Griffin D, Parsons N, Shaw E, et al. Operative versus non-operative treatment for closed, displaced, intraarticular fractures of the calcaneus: Randomised controlled trial. *BMJ*. 2014;349(jul24 5). doi:10.1136/bmj.g4483
- Yu, X., Pang, Q.-J., Chen, L., Yang, C.-C., & Chen, X.-J. (2013). Postoperative complications after closed calcaneus fracture treated by open reduction and internal fixation: A Review. *Journal of International Medical Research*, 42(1), 17–25. https://doi.org/10.1177/0300060513495626
- Zhang, G., Ding, S., & Ruan, Z. (2019). Minimally invasive treatment of calcaneal fracture. *Journal of International Medical Research*, 47(8), 3946–3954. https://doi.org/10.1177/0300060519853402
- Shi, F. L., Wu, S. Y., Cai, W., & Zhao, Y. M. (2020). Comparison of 5 treatment approaches for displaced intra-articular calcaneal fractures: A systematic review and Bayesian network meta-analysis. *The Journal of Foot and Ankle Surgery*, 59(6), 1254–1264. https://doi.org/10.1053/j.jfas.2020.03.021
- Jiang, N., Lin, Q.-rong, Diao, X.-cai, Wu, L., & Yu, B. (2012). Surgical versus nonsurgical treatment of displaced intra-articular calcaneal fracture: A metaanalysis of current evidence base. *International Orthopaedics*, 36(8), 1615–1622. https://doi.org/10.1007/s00264-012-1563-0
- Mehta, C. R., An, V. V., Phan, K., Sivakumar, B., Kanawati, A. J., & Suthersan, M. (2018). Extensile lateral versus sinus tarsi approach for displaced, intraarticular calcaneal fractures: A meta-analysis. *Journal* of Orthopaedic Surgery and Research, 13(1). https://doi.org/10.1186/s13018-018-0943-6
- Liu, Y., Li, Z., Li, H., Zhang, Y., & Wang, P. (2015). Protective effect of surgery against early subtalar arthrodesis in displaced intra-articular calcaneal fractures. *Medicine*, 94(45). https://doi.org/10.1097/md.00000000001984
- Buckley, R., Tough, S., & McCormack, R. (2010). Operative compared with nonoperative treatment of displaced intra-articular calcaneal fractures. *Orthopedic Trauma Directions*, 8(02), 29–36. https://doi.org/10.1055/s-0028-1100885
- Loucks, C., & Buckley, R. (1999). Böhler's angle: Correlation with outcome in displaced intra-articular calcaneal fractures. *Journal of Orthopaedic Trauma*, *13*(8), 554–558. https://doi.org/10.1097/00005131-199911000-00007
- Bruce, J., & Sutherland, A. (2013). Surgical versus conservative interventions for displaced intra-articular calcaneal fractures. *Cochrane Database of Systematic Reviews*.

Compare and Contrast Keller Arthroplasty versus Arthrodesis for Hallux Rigidus

Alex Dang, B.S., Rahul Natarajan, B.S., Harsh Varshney, B.S.

ABSTRACT

Objective: To compare and contrast pain relief and joint range of motion (ROM) between the two joint destructive procedures, Keller arthroplasty and arthrodesis, for the management of end-stage hallux rigidus. Additionally, complications such as metatarsalgia, nonunion, malalignment, interphalangeal joint pain, and delayed union were compared between the two procedures.

Methods: A PubMed and a ResearchGate search on relevant research pertaining to the interventional treatment options: Keller arthroplasty and arthrodesis of end-stage hallux rigidus were reviewed. This included data from multiple studies detailing and comparing the use of surgical interventions for treatment of hallux rigidus.

Results: In our literature review, we observed that Keller arthroplasty and arthrodesis are successful surgical interventions in treating symptomatic end-stage hallux rigidus. Both treatment interventions provide a similar degree of patient satisfaction and symptom relief. It is noted that arthrodesis alters the biomechanics of gait due to decreased motion at the 1st metatarsophalangeal joint. On the other hand, the Keller arthroplasty improves pain while preserving the biomechanics of the foot. The research indicates that an arthrodesis is the preferred choice of long-term intervention to address hallux rigidus that has failed conservative treatment.

Conclusion: Recent studies indicate that both methods significantly improve pain outcome. However, there are limitations present with both surgical options. Additionally, when considering these surgical treatments, it is important to outline the patient's functional and long-term mobility goals prior to surgery. While clinical outcomes are similar between the two methods, other factors such as athletic capability, age, disease severity, patient satisfaction, and physician preference ultimately determine the optimal treatment method to use.

Introduction

Advanced stage hallux rigidus is described as a painful restriction in dorsiflexion of the great toe due to degenerative arthritis of the metatarsophalangeal joint.¹ Plantarflexion is limited to a lesser degree than that of dorsiflexion.² There are many predisposing conditions that contribute to hallux rigidus. Although the exact cause of hallux rigidus is unknown, trauma or osteochondritis dissecans have been known to damage the articular cartilage of the MTP joint.³ Additionally, biomechanical and structural factors have been known to contribute to the pathogenesis of hallux rigidus. Hallux rigidus is classified using the Regnauld classification system with grades 3 and 4 considered as hallux rigidus. This classification system has a total of 4 classes with Grade 3 described as arthrosis with severe flattening of the first metatarsal head with increased osteophyte formation and the loss of joint space.⁴ Grade 4 is defined as having less than 10 degrees of range of motion and obliteration of the joint space within the first metatarsophalangeal joint. Due to the limited motion at the MPJ joint, patients will compensate through supination of the foot during midstance. Additionally, the patient will have an apropulsive gait to avoid further pain during push-off during the propulsive phase of the gait cycle. The pressure during gait is transferred to the less MPJs and can further contribute to lower extremity pathologies.

Current intervention for the treatment of hallux rigidus primarily involves surgical intervention ranging

from simple procedures such as a cheilectomy to more complex osteotomies and joint arthroplasty. As hallux rigidus advances, conservative treatments become less effective and, thus, surgical intervention must be considered. The treating surgeon must take into consideration the progression of the symptoms as well as the longterm outcomes of each procedure.

Each procedure involved in the treatment of hallux rigidus has inherent advantages and disadvantages. Thus, there is contention in the use of each procedure and not one universally accepted treatment for the treatment of hallux rigidus. It is important to understand the concept of jointpreserving and joint-destructive procedures. The latter pertaining to the arthrodesis and the Keller arthroplasty.

It is important to examine the components and outcomes involved with each of the above mentioned procedures. The arthrodesis procedure fuses the bones of the joint and prevents the movement of that specific joint. This procedure provides effective correction for a wide range of 1st MPJ pathologies.⁵ These pathologies result in extreme pain, and include but are not limited to osteoarthritis, rheumatoid arthritis, traumatic injuries and fractures.⁶ This procedure has been considered a salvage procedure for severe stages of hallux rigidus. The procedure involves a standard dorsomedial incision and a linear capsulotomy. Following this, exostoses are excised, and the opposing joint surfaces are resected by abrasion of the cartilage. The hallux is repositioned and fixation techniques are used to secure the 1st MPJ. In regard to postoperative recovery, patients are in a short leg cast for 3 weeks followed by limited weight-bearing for another 3 weeks.⁷

The Keller arthroplasty in association with hallux rigidus involves the resection of the metatarsal head and the implantation of a soft tissue to essentially create a false joint. This procedure is done under local anesthetic ankle block and following the incision over the first metatarsal shaft and head of the proximal phalanx, the adductor hallucis, abductor hallucis, flexor hallucis brevis, and extensor hallucis brevis muscles are released from their insertions on the proximal phalanx.⁸ The proximal third of the proximal phalanx is removed and the capsule is closed using subcuticular sutures. In a postoperative setting, patients wear rigid post-op shoes for 2 weeks followed by a closed-in lace-up shoe to help compress swelling.⁸

Both the Keller arthroplasty and arthrodesis are considered salvage procedures and carry similar risk factors, however, the arthrodesis has added risks of nonunion, fixation irritation, and the development of hallux IPJ arthrosis.⁸ On the other hand, transfer metatarsalgia was a common risk associated with the Keller arthroplasty due to shortening of the hallux postoperatively.

When considering the treatment of choice, it must be taken into consideration the level of physical activity that the patient engages in on a daily basis. The accumulation of patient factors and specific aspects of the case are determinants of the procedure of choice. The focus of this literature review is to compare and contrast the arthrodesis and Keller arthroplasty procedure in treating and managing the pain associated with advanced stage hallux rigidus.

Methods

Relevant articles were found through PubMed and other educational sources to analyze the benefits and limitations of both the Keller arthroplasty and arthrodesis in treating advanced stage hallux rigidus. Inclusion criteria includes patients who are 18 years of older and patients with hallux rigidus. Exclusions in the study include patients who are younger than 18, patients with hallux limitus, blogs, opinions, or commentary Search terms included "Keller arthroplasty vs. arthrodesis" and "treatment for end stage hallux rigidus."

Results

Silva et al. conducted a retrospective study on 36 patients with hallux rigidus. The study consists of 12 patients who underwent arthrodesis, while 26 underwent arthroplasty with an average of two-year follow-up. The American Orthopedic Foot and Ankle Society Hallux Metatarsophalangeal-Interphalangeal (AOFAS-HMI) scale was used to evaluate the functional status postoperatively and showed that the arthroplasty group a score of 89.7 versus a score of 65.7 for the arthrodesis group. The visual analog scale was used to assess the post-operative pain level and revealed a score of 1.6 for arthroplasty group and 3.9 for arthrodesis group. Additionally, one case of post-op infection was found in the arthroplasty group and two cases of pseudarthrosis in the arthrodesis group.⁹

In a comparative study by Stevens et al., 63 toes on 57 patients were observed. Some patients suffered unilateral hallux rigidus, while others had bilateral hallux rigidus. The study consists of 33 toes that underwent first metatarsophalangeal joint (MTPJ) arthrodesis and 28 toes underwent arthroplasty. Similar to the previous study by Silva, the AOFAS-HMI was used for functional status and VAS score was used for pain. Additionally, the Manchester-Oxford Foot Questionnaire (MOXFQ) was used to evaluate the outcome of foot and ankle surgeries and the Forgotten Joint Score (FJS-12) for the assessment of joint-specific patient reported outcomes. The AOFAS-HMI score for the arthroplasty group went down between follow ups, from 86.1 to 83.9. However, the arthrodesis group went up from 82.2 to 91.0. On the other hand, the VAS score was 0.72 for the arthroplasty group, while 0.66 for the arthrodesis group. The FJS-12 was 82.6% for the arthroplasty group and 83.1% for the arthrodesis group. The MOXFQ index score for the arthroplasty group was 27.9 and 19.6 for the arthrodesis group.¹⁰

In a double cohort study by Ibrahim, surgery was performed on 40 patients, 20 with arthrodesis, and 20 with arthroplasty. The average follow up for all patients was 22.16 months with a range of 12 to 36 months. The minimum qualification for the study is a grade three or a grade four using the Coughlin and Shurnas classification system for hallux rigidus. The study found the AOFAS-HMI score for the arthrodesis group was a 42, while the score for the arthroplasty was a 44. A modified AOFAS score or American College of Foot and Ankle Surgeon (ACFAS) score was utilized and found the arthrodesis group with a score of 90, while the arthroplasty with a score of 92. However, when comparing the risks analysis and negative outcomes between the two groups, the arthrodesis group reported a 15% incidence of metatarsalgia, 10% of nonunion, 10% of malalignment, 5% of interphalangeal joint pain, and 5% of delayed union. In contrast, the arthroplasty reported 30% of floating hallux, 20% of metatarsalgia, 10% of sesamoiditis, and 5% of regrowth and remodeling.¹¹

In a study by O'Doherty et al., a prospective randomized trial was done comparing Keller's arthroplasty and arthrodesis of 1st MTPJ for management of hallux rigidus in older patients. Eighty-one patients over the age of 45 with symptomatic hallux rigidus received surgical intervention and were followed up in at least 2 years. Of the 81 patients, 37 received an arthrodesis while 44 received an arthroplasty. The results showed that patient satisfaction was high with either procedure, with about 75% showing complete satisfaction and 98% admitting to improvement seen. However, nonunion occurred in 44% of patients in the arthrodesis group, requiring certain patients to undergo revision surgery for repeated arthrodesis to achieve solid union and complete relief of pain. It was also noted that postoperative incidence of metatarsalgia was similar between the two groups.¹²

In a retrospective study conducted by Beertema et al., long term clinical outcomes and patient satisfaction were analyzed in patients who had received surgery for symptomatic hallux rigidus. Seventy-seven patients received a Kelly arthroplasty or arthrodesis between 1990 and 2000. Outcomes were assessed after a 2 year follow-up using average visual analogue and American Orthopedic Foot and Ankle Society (AOFAS) scores. For grade III patients according to the Regnauld's classification of hallux rigidus, the Keller arthroplasty group had an average visual analogue score of 2.3 and AOFAS score of 87, while the arthrodesis group had an average visual analogue score of 2.0 and AOFAS score of 73. In the arthrodesis group, 4 patients required surgical revision due to complications.¹³

Discussion

The arthrodesis procedure has been considered as the gold standard for patients with advanced arthritis and grade 3 and 4 Regnauld Classification for end-stage hallux rigidus by decreasing pain and stabilizing the medial foot column. However, its complications include nonunions, foot immobility, and altered gait patterns. On the other hand, the Keller arthroplasty procedure has the potential to maintain a patient's gait and biomechanics to a greater extent. The results from the studies analyzed present data that supports the use of either procedure, but upon closer examination of the AOFAS score and visual analogue there are clear distinctions present between them.

When comparing the two procedures, both show significant improvements in pain level and functional status. However, the arthroplasty group has a more drastic change in comparison to the arthroplasty group. The AOFAS-HMI score for the arthroplasty group indicates that it has a better functional outcome compared to the arthrodesis group. Additionally, the lower VAS score from the arthroplasty group indicates a better pain alleviation than the arthrodesis group. Several disadvantages such as post-operative infection and revision rate, with the arthroplasty group lower in both categories, making it a more superior technique.⁹

In contrast, Steven et al. comparative study supports arthrodesis over arthroplasty as the procedure of choice for long term functional outcomes and pain alleviation.¹⁰ The MOXFQ and FJS-12 scores were inconclusive due to being statistically insignificant. However, both the AOFAS-HMI and the VAS scores leaned toward arthrodesis as the superior of the two procedures. When compared to the study by Silva et al.,⁹ it appears that arthroplasty provides short-term relief and improved functional outcomes. However, Steven et al. data's supports that arthrodesis might be a better option of the two over time.¹⁰

However, Ibrahim's results were inconclusive as to which method is more effective of the two. His data showed no statistical difference in AOFAS-HMI score and First Ray Scoring scale and concluded that either option is viable for the treatment of hallux rigidus.¹¹ Comparing the data from this study to the previous two by Silva et al. and Steven et al. conclude that differences in improvement of functional outcomes and pain relief between the two procedures might not begin until after the 36-month follow up appointment.^{9,10,11}

In the study of a prospective randomized comparing Keller's trial arthroplasty and arthrodesis of 1st MTPJ for management of hallux rigidus by O'Doherty et al., it was found that both procedures had no statistical differences in terms of patient satisfaction, relief of pain, improvement in walking distance, and reduction in footwear complaints (O'Doherty). However, the two procedures can be differentiated by 44% incidence of nonunion in the arthrodesis group postop. This shows that arthrodesis for hallux rigidus has more complications than when performing a Keller arthroplasty. As the Keller arthroplasty has technical incidence simplicity, low of complications, and low revision rates, the study concluded that Keller's arthroplasty is the more suitable procedure to perform for hallux rigidus in older patients. There was also no statistical differences in terms of postoperative incidence of metatarsalgia.¹²

From the retrospective study conducted by Beertema et al., it was concluded that the Keller arthroplasty was favored over arthrodesis of the 1st MTPJ in patients with end-stage hallux rigidus without preexistent metatarsalgia.¹³ This can be seen from the differences in average visual analogue and AOFAS scores in patients with grade III deformities according to the Regnauld's classification of hallux rigidus. The difference of 0.3 in average visual analogue scores between Keller arthroplasty and arthrodesis shows that there is more postoperative pain subjectively in patients who receive the arthroplasty. However, the AOFAS scores themselves, 87 and 73 for Keller arthroplasty and arthrodesis respectively, show that the procedures are ranked in different categories. A score of 87 ranks as "good" while 73 ranks as "fair" in terms of categories assessing pain, function, and alignment.^{14,15} Thus, the Keller arthroplasty may have increased short term postoperative pain, but will have long term increase in function and alignment more so with reduced pain when compared to arthrodesis.

Conclusion

The purpose of this study was to compare and contrast the arthrodesis and Keller arthroplasty procedure in the management of advanced-stage hallux rigidus. The arthrodesis and Keller arthroplasty are successful operative interventions for the treatment of end-stage hallux rigidus.

Overall, no statistically significant differences between the two procedures were found in terms of patient satisfaction and function. However, the analysis of our data presents that the arthrodesis procedure has a greater rate of postoperative complications. Thus, the Keller arthroplasty is preferred due to its technical simplicity, and lower rates of complications and revisions.

When applying these procedures in a practical setting, it is important for the physician to take into consideration the patient's goals from the procedure as well as the severity of the hallux rigidus. Further studies with larger sample sizes and longitudinal follow ups will provide insight into the long-term outcomes of each procedure. Furthermore, taking into consideration the long-term outcomes, advantages, and disadvantages of each procedure allows for determination for the procedure of choice in a specific case. Thus, it is based on surgical preference for which technique to use for the long term management of end-stage hallux rigidus.

References

1. Coughlin MJ, Shurnas PS. Hallux rigidus: demographics, etiology, and radiographic assessment. Foot Ankle Int. 2003;24(10):731–74.

2. McMaster MJ. The pathogenesis of hallux rigidus. The Bone & Joint Journal. 1987;60(1), 82-86.

3. Yee G, Lau J. Current concepts review: hallux rigidus. Foot & Anklelinternational. 2008; 29(6), 637-46.

4. Coughlin MJ, Shurnas PS. Hallux rigidus. Grading and long-term results of operative treatment. Journal Bone Joint Surg Am. 2003; 85 (11), 2072-88.

5. Dillard, S., Schilero, C., Chiang, S., Pharm, P. Intra and Interobserver Reliability of Three Classification System for Hallux Rigidus. *Journal of American Podiatric Medicine Association.* (2010); 110(3):

6. Lombard CM, Silhaneck AD, Connolly FG, Dennis LN, Keslonsky AJ. First metatarsophalangeal arthrodesis for treatment of hallux

rigidus: a retrospective study. Journal of Foot and Ankle Surgery. 2001; 40(3): 137-86.

7. Beauchamp CG, Kirby T, Rudge SR, Worthington BS, Nelson J. Fusion of the first metatarsophalangeal joint in forefoot arthroplasty. Clin. Orthop. 1984; 190: 249- 53.

8. Coutts A, Kilmartin TE, Ellis M. The long-term patient focused on the outcomes of Keller's arthroplasty for the treatment of hallux rigidus. *The International Journal of Clinical Foot Science*. 2012;22(3): 161-171.85.

9. Santos-Silva M, Rodrigues-Pinto R, Barros LH, Sousa A, Muras J. Arthrodesis versus arthroplasty of the first metatarsophalangeal joint in the treatment of hallux ridigus- a comparative study of appropriately selected patients. Rev Bras Ortop. 2020 Feb; 55(1): 40-47.

10. Steven J, De-Bot RTAL, Witlox AM, Borghans R, Smeets T, Beertema W, Hendrickx RP, Schotanus MGM. Long-term effects of cheilectomy, Keller arthroplasty, and arthrodesis for symptomatic hallux rigidus on patients-reported and radiologic outcome. Foot and Ankle Int. 2020; 41(7):775-83.

11. Elsayed M and Elsayed I. Arthrodesis and modified keller interposition arthroplasty in the surgical treatment of end state hallux rigidus. Benha University Department of Orthopedic Surgery. 2019: 1-12.

12. O'Doherty DP, Lowrie IG, Magnussen PA, Gregg PJ. The management of the painful first metatarsophalangeal joint in the older patient. Arthrodesis or Keller's arthroplasty? J Bone Joint Surg Br. 1990; 72(5): 839-42.

13. Beertema W, Draijer WF, van Os JJ, Pilot P. A retrospective analysis of surgical treatment in patients with symptomatic hallux rigidus: long-term follow-up. J Foot Ankle Surg. 2006;45(4):244-51.

14. IIchenko DV, Korolev AV, Kardonov AA. Long-term functional results of first metatarsophalangeal joint arthrodesis for hallux rigidus. Genjii Ortopedii. 2020; 26(1): 30-36.

15. SooHoo, N. F., Vyas, R., & Samini, D. (2006). Responsiveness of the foot function index, AOFAS clinical rating systems, and SF-36 after foot and ankle surgery. Foot & ankle international, 27(11), 930-934.

Retrospective Comparison of Tarsal Coalition Resection versus Arthrodesis

Alex Dang, B.S., Rahul Natarajan, B.S., and Nathan Fischer, B.A.

ABSTRACT

Objective: The purpose of this study is to compare and contrast the efficacy of resection versus arthrodesis for the treatment of tarsal coalitions.

Methods: A search on relevant research pertaining to tarsal coalition resection and arthrodesis was reviewed via the PubMed, National Institute of Health, and ScienceDirect databases. Articles were reviewed for each method of treatment due to a lack of direct comparison in literature.

Results: In studies observed, the surgical resection was recommended over arthrodesis for primary treatment of tarsal coalitions in the pediatric population. Arthrodesis provides higher revision rates and risks of complications that are not viable in pediatric patients. Growth plates are disturbed, and joint fusion would not provide good quality of life for the patient post op. Thus, the research indicates that resection should be used as the primary form of treatment for congenital tarsal coalitions with arthrodesis as a salvage procedure to be performed if resection fails.

Conclusion: The majority of research suggests that surgical resection is a better form of primary treatment when compared to arthrodesis. Multiple surgeries are not ideal for the pediatric population. It is intuitive that arthrodesis has higher rates of complications due to the fusion of joints in a growing adolescent. Based on the patient population and risk of complications with revisional surgery, resection is the ideal form of treatment for tarsal coalitions, with arthrodesis only being viable if needed.

Introduction

Tarsal coalition is a foot condition in which there is connection between two bones, typically between the talus and calcaneus, the calcaneus and navicular, or the talus and navicular. The most common hindfoot tarsal coalitions are the talocalcaneal and the calcaneonavicular coalitions, which consist of the connection between the talus to the calcaneus, and the calcaneus to the navicular bone, respectively. Studies have found associations between pes planus, hindfoot rigidity, and tarsal coalitions. Additionally, peroneal spastic flatfoot can be attributed to talocalcaneal coalitions.¹

Typically, patients present with foot pain between the ages of 8 and 12. Although there have been asymptomatic cases until adulthood, symptoms begin to propagate with trauma and worsen over time. In the case of subtalar or talocalcaneal coalitions, pain is localized to the subtalar joint (STJ). In addition to pain, patients might report difficulty ambulating and decreased range of motion with inversion and eversion of the STJ. On a single heel raise test, the calcaneus often remains in a valgus position to demonstrate the relationship between pes planus and tarsal coalitions. Alternatively, pain is localized to the sinus tarsi for cases of calcaneonavicular coalition.²

Radiographs are often used to make a firststep diagnosis of tarsal coalitions. Most commonly, the weight bearing dorsal-plantar and lateral views will show signs of coalition. Additional radiographic views such as the medial oblique view are sometimes used to confirm the diagnosis. On the lateral view, a "C" sign or an "anteater nose" sign can be seen. The "anteater nose" sign represents the connection between the calcaneus and navicular as the calcaneus protrudes anteriorly, making it diagnostic for calcaneonavicular coalition. For cases of talocalcaneal coalition, a dysmorphic sustentaculum tali, shortened talar neck, and absent facet are all signs on radiographs. In addition, CT and MRI can be used to detect early stages of coalition that are otherwise not detected by radiographs. These advanced imaging modalities both provide a 3-D view of the foot to accurately describe the size and shape of the coalition.³

The first line of treatment for most foot pathologies is through conservative measures. Activity modification, insertion of a medial heel wedge, and custom orthotics have all been shown to be effective for treating asymptomatic coalitions. For symptomatic tarsal coalitions, it is suggested that patients should be immobilized in a cast for 4 to 6 weeks. Operatively, tarsal coalition resection and arthrodesis procedures are available as existing treatment options.⁴

Though surgical resection and arthrodesis are both forms of operative treatment for tarsal coalitions, resection is indicated more for the adolescent population. Surgical resection entails removing the coalition and replacing the defect with fatty tissue as interposition material. Fat is obtained from the proximal medial thigh or buttock as it is structurally more robust in these regions than local fat.⁵ Resection
helps preserve normal foot functionality and relieves pain from symptomatic coalitions. Arthrodesis on the other hand, is fusion of the joint that is used to salvage coalitions that have failed resection or reconstruction.⁵ It is also indicated for patients with advanced arthrosis in tarsal coalitions and more than 50% involvement of joint hindfoot malalignment.⁶

The purpose of this review is to compare and contrast the indications and complications of surgical resection versus arthrodesis for the management of tarsal coalitions. These specific operative procedures were chosen because they are common techniques for the management of tarsal coalitions, with open surgical resection being the gold standard and arthrodesis for end-stage treatment. By understanding the underlying mechanisms and intended patient populations of these procedures, minimal surgery can be done for optimal treatment of tarsal coalitions.

Methods

Relevant research articles for tarsal coalition resection and arthrodesis were identified via the PubMed, National Institute of Health, the Journal of Pediatric Orthopedic, and ScienceDirect database. Inclusion criteria included patients with subtalar or talocalcaneal, talonavicular, and calcaneonavicular coalitions as evidence on radiographs, American Orthopedic Foot and Ankle Society score (AOFAS) for functional outcomes, and University of California at Los Angeles (UCLA) activity score to evaluate the patient's activity level. Exclusion criteria included blogs, author's opinions, and foot pain without evidence of tarsal coalition on radiographs.

Results

Surgical resection

Docquier et al. analyzed a retrospective study on surgical resection of tarsal coalition by Mahan et al. that included 63 patients with a minimum of two-year follow-up. Out of the total of 63 patients, 37 had bilateral coalitions, 20 had talocalcaneal coalition, and 43 with calcaneonavicular coalition. The AOFAS score was used to measure functional outcomes, and UCLA activity score was used to evaluate the patient's activity level. At the average of 4.62 years follow-up, the average AOFAS score was 88.3 and UCLA activity score was 8.33. When breaking the data down further, the talocalcaneal coalition had an average AOFAS score of 88.4 with a standard deviation of 2.44 and UCLA activity score of 8.4 with an standard deviation of 0.50. On the other hand, the calcaneonavicular coalition group had an average score of 88 with a standard deviation of 2.13 for AOFAS and 8.3 with a standard deviation of 0.32 for UCLA activity score (Table 1). There were 46 patients who reported no activity restrictions due to foot pain and 17 patients with activity restriction due to foot pain. Additionally, 40 out of the total of 63 patients had a CT to compare the degree of heel valgus due to tarsal coalition. There were 33 patients who had less than 16 degrees of valgus, while there were 7 with greater than 16 degrees. The group with less than 16 degrees of valgus had an average AOFAS score of 88.3 with a standard deviation of 2.0, and average UCLA activity score of 8.3 with a standard deviation of 0.38. Additionally, there were 21 patients from this group denying any pain associated with the coalition. On the other hand, the group with greater than 16 degrees of valgus had an average AOFAS score of 88.7 with a standard deviation of 5.57, while the average UCLA activity score of 7.7 with an standard deviation of 0.75. There were 5 patients from this group without any pain (Table 2).^{7,8}

	Calcaneonavicular (n = 43)	Talocalcaneal $(n = 20)$
AOFAS	88 ± 2.13	88.4 ± 2.44
UCLA	8.3 ± 0.32	8.4 ± 0.50

Table 1. Comparison of Patient and OutcomecharacteristicsforTalocalcanealandCalcaneonavicular Coalitions (N=63).

Heel Valgus	<16° (n = 33)	> 16° (n = 7)
AOFAS	88.3 ± 2.00	88.7 ± 5.57
UCLA	8.3 ± 0.38	7.7 ± 0.78
Painless coalitions	21	5

Table 2. CT Comparison on 40 of the total 63 Patients with Tarsal Coalition Resection.

Docquier et al. further analyzed tarsal coalitions in research by Gantsoudes et al on functional outcomes over the average follow-up of 42.6 months. The total of 49 feet were evaluated with an average of 90 with a standard deviation of 9.8 for AOFAS Ankle-Hindfoot score. Additionally, 32 feet reported excellent outcomes, 10 with good outcomes, 6 with fair outcomes, and 1 with poor outcomes. When breaking down the AOFAS Hindfoot score, there was a mean of 35.2 with a standard deviation of 6.5 for pain, 46.2 with an standard deviation of 2.3 for function, and 8.4 with an standard deviation of 2.3 for alignment (Table 3). Further analysis showed that 45 feet improved ankle range of motion (ROM), unchanged in 3 feet, and 2 with no ROM due to rigid

hindfoot. Additionally, 2 feet underwent revision surgeries, and 11 had additional surgeries to correct foot alignment. The average AOFAS score for these 12 feet was 87.75 with a standard deviation of 15.5. Revision surgeries found in 2 feet, one was due to tarsal coalition recurrence, the other was due to failure to excision coalition completely. However, postoperative wounds for both feet healed without further complications. All 49 feet were followed-up at 3 different time intervals, at less than 24 months, between 2 and 4 years, and again greater than 4 years. At the less than 24-month follow-up, the AOFAS score was 93.3. At the follow-up between 2 and 4 years postoperatively, the AOFAS score was 86.8, and 89.9 at greater than 4 years.^{7,9}

Subcategories (Maximum)	Mean	Standard Deviation
Pain (40)	35.2	6.5
Function (50)	46.2	4.3
Alignment (10)	8.4	2.3
Total	90	9.8

Table 3. AOFAS Hind-Foot Score Breakdown

Kothari and Masquijo conducted a metaanalysis on postoperative outcomes of tarsal coalitions attempting to answer the question as to whether or not to perform resectional surgery based on heel valgus severity. A total of 25 feet were assessed, 13 of which were the right feet, 12 were the left feet. From the total of 25 feet, 16 had less than 21 degrees of heel valgus, while 8 had more than 21 degrees, and 1 was not classified due to the lack of a CT scan assessment. From the group with less than 21 degrees of heel valgus, 15 reported with excellent outcomes. On the other hand, only 4 of 8 reported good outcomes from the group with greater than 21 degrees of valgus (Table 4).⁵

Heel Valgus	<21° (n = 16)	> 21° (n = 8)
Good Outcomes	15	4

Table 4. Postoperative Outcomes for Heel Valgus <21° and >21°.

Arthrodesis

Triple arthrodesis with the fusion of talocalcaneal, talo-navicular, and calcaneo-cuboid joints

had been indicated for symptomatic tarsal coalitions.¹⁰ A retrospective study by Klerken et al. on 83 patients with triple arthrodesis was followed-up at 3-year, 7.5year, and again at 15-year to assess the long-term functional outcomes. A total of 35 patients were followed for longer than 15 years, and 48 patients were followed-up at 15 years or less. Radiographic studies were taken at each of the follow-up visits. From the group of 48 patients, only 38 qualified for data analysis due. From the total of 10 disqualified patients, 3 withdrew consent, 3 passed away between follow-up visits due to other medical problems, 3 could not be reached, and 1 patient had transportation issues. From the 3 failures, 1 underwent ankle arthroplasty and 2 underwent ankle arthrodesis. From the group of 35 patients, 8 had malalignment on lateral view radiograph, and 27 on dorsal plantar view. From the group of 73 patients (10 lost between follow-ups), 16 developed osteoarthritis secondary to the arthrodesis according to their radiographs. Foot function index pain score decreased from 58 right after surgery to 20.90 at the 15-year follow-up. However, the AOFAS score between follow-up visits showed no statistical difference.11

In a retrospective study by Mann et al. on isolated subtalar arthrodesis in 44 patients with an average follow-up of 59.5 months, 93% reported as either very satisfied or satisfied. There were 7% of all patients reported as unsatisfied with the procedure. To break the data down further, 58% reported with excellent results, 28% with good results, 7% with fair results, and 7% with poor results. The AOFAS Hindfoot score for this group was reported at 89 at the final follow-up visit. There were 3 cases of calcaneal fractures and 3 cases of malpositions from the surgery. However, union was achieved in all cases, except for 1 case where the patient experienced calcaneal fracture. Unfortunately, there were 40% reported with decreased transverse tarsal motion, 30% with decreased dorsiflexion, and 9% with decreased plantarflexion. Additionally, there were 36% cases of arthrosis of the ankle, and 41% of the transverse tarsal joint. Due to the limited range of motion postoperatively, 22 patients experienced difficulty walking on uneven terrain, stairs, and inclines. In terms of activity limitations, 21 patients reported a mild decline, and 1 had severe limitations.¹²

Discussion

The resection technique is indicated for tarsal coalitions with either anterior, middle facets, or greater than 50% of facet involvement. Despite some disadvantages such as potential nerve injury and revision surgeries due to failure, the resection procedure has good results, according to the AOFAS, the AOFAS Ankle Hindfoot score, and the UCLA

activity scores.^{7,8,9} Additionally, ROM improves in the majority of the patients postoperatively.⁹ Even though 2 patients required additional surgeries due to recurrent coalitions, and 11 due to mal-alignment, all had good outcomes according to AOFAS scores.⁹

Unfortunately, severity of hindfoot valgus does play a role in postoperative outcomes. In the study by Mahan et al., hindfoot valgus of greater than 16 degrees results in a slight decrease in UCLA activity score, despite nearly identical AOFAS score. This perhaps indicates that a greater degree of hindfoot valgus leads to a decrease in postoperative activity level.⁸ Additional studies in a meta-analysis by Kothari and Masquijo support this claim. Their study found that greater than 21 degrees of hindfoot valgus reported worse outcomes compared to patients with less than 21 degrees of hindfoot valgus.⁵ Another factor to consider when assessing postoperative functional goals is preoperative activity restrictions due to pain. Patients that endorsed activity restrictions due to pain prior to the resectional surgery reported a lower AOFAS and UCLA activity scores than those without restrictions.7,8

The triple arthrodesis procedure has been indicated as a salvage procedure for tarsal coalition due to the high risk of osteoarthritis in the long run. Although, because of the patient's old age, osteoarthritis could be due to an independent process. As a result, there are limited studies done for this procedure and only reserved for failed resectional surgery.7 In contrast, patients reported decreased pain postoperatively and during the 15 years follow-up. Additionally, AOFAS does not fluctuate over time.¹¹ However, AOFAS score does go down between the 24-month follow-up and the 2-year follow-up in patients with resectional surgeries.^{7,9} Despite the fact that AOFAS score in the arthrodesis group being constant over time, Mann et al. retrospective study on STJ arthrodesis demonstrates restriction ankle range of motion on dorsiflexion and plantarflexion, as well as the transverse tarsal motion. Additionally, almost ¹/₃ of all cases reported with ankle arthrosis and nearly half reported with transverse tarsal arthrosis postoperatively. Furthermore, the restricted ankle range of motion leads to ankle instability and many patients reported imbalance when walking on uneven surfaces. As a result, arthrodesis surgeries should not be the primary operative treatment due to its severe decrease in functional outcomes and daily activities.¹²

A population-based study by Jackson et al. discusses that primary arthrodesis is an independent factor associated with the need for subsequent surgery in tarsal coalitions. Especially in the pediatric population, growth plates would be disturbed and joint fusion would not provide good quality of life for the patient post op. With reoperation rates being higher in patients treated with arthrodesis, resection is recommended as the primary treatment of tarsal coalitions in adolescent patients.¹³ However, there are exceptions with the primary form of treatment depending on foot type of the adolescent patient. In a study by Li and Myerson describing the rationale for excision of a middle facet tarsal coalition, it is noted that success of coalition resection is based on hindfoot rigidity and presence of a flatfoot deformity. A rigid and flatfoot make resection less likely to be successful, making arthrodesis favorable in rigid tarsal coalitions.¹⁴

For the adult population, symptomatic coalitions that are arthritic are better treated with arthrodesis for full pain relief. Thorpe and Wukich describe that patient with absent subtalar motion and normal hindfoot alignment warrant in situ fusion of the subtalar joint. Patients with greater than 15 degrees of valgus hindfoot malalignment while weight bearing or adjacent joint arthrosis warrant triple arthrodesis with or without a medial displacement osteotomy of the calcaneus.⁶

Despite how common tarsal coalitions are, several limitations continue to exist that deem difficult to determine the superiority of one technique over the other. Although the AOFAS scores between the resectional surgery and the arthrodesis procedures were similar postoperatively, they are isolated studies with data on one technique or the other, and not directly compared the two techniques. When the techniques are directly compared, the sample size for patients undergoing arthrodesis are very limited in many articles. This can be attributed to arthrodesis not being a primary form of treatment for tarsal coalitions. A small sample size could skew results one way or the other. Future studies should incorporate a bigger sample size for patients receiving arthrodesis as primary treatment to avoid potential bias and to strengthen the conclusion drawn from the data.

Conclusion

Tarsal coalitions are congenital fusions of two or more tarsal bones that begin symptoms of foot pain in the ages of 8-12. The majority of research suggests that surgical resection is a better form of primary treatment in pediatric and non-arthritic patients when compared to arthrodesis. Arthrodesis is used as a salvage procedure with subsequent surgery. Multiple surgeries are not ideal for the pediatric population. It is intuitive that arthrodesis has higher rates of complications due to the fusion of joints in a growing adolescent. Growth plates would be disturbed. Thus, resection is the ideal form of treatment for tarsal coalitions in adolescents, with arthrodesis only being viable as the last resort. However, arthrodesis would be recommended if the coalitions present as rigid with adjacent arthritic changes, being more common in the adult population.

References

1. Lemley F, Berlet G, Hill K, Philbin T, Isaac B, Lee T. Current Concepts Review: Tarsal Coalition. *Foot & Ankle International*. 2006;27(12):1163-69.

2.Kulik SA, Clanton TO. Tarsal Coalition. Foot & Ankle International. 1996;17(5):286-96.

3. Andrea D. Cass, Craig A. Camasta, A Review of Tarsal Coalition and Pes Planovalgus: Clinical Examination, Diagnostic Imaging, and Surgical Planning, The Journal of Foot and Ankle Surgery, Volume 49, Issue 3, 2010, Pages 274-93,

4. Edmonds WB, Wiley K, Panas K, Technique Article: Tarsal Coalition Resection Using Kirschner Wires Across the Subtalar Joint in a Two-Incision Approach, The Journal of Foot and Ankle Surgery. 2019;58(2):337-40.

5. Kothari A, Masquijo J. Surgical treatment of tarsal coalitions in children and adolescents. *EFORT Open Rev.* 2020;5(2):80-89.

6. Thorpe SW, Wukich DK. Tarsal coalitions in the adult population: does treatment differ from the adolescent? Foot Ankle Clin. 2012;17(2):195-204. 7.Docquier PL, Maldaque P, Bouchard M. Tarsal coalition in paediatric patients. Orthopaedics & Traumatology: Surgery & Research. 2019;105(1):123-31.8. Mahan ST, Spencer SA, Vezeridis PS, and Kasser JR. Patient-reported outcomes of tarsal coalitions treated with surgical excision. *Journal of Pediatric Orthopaedics*. 2015; *35*(6):583-88.

9. Gantsoudes GD, Roocroft JH, and Mubarak SJ. Treatment of talocalcaneal coalitions. *Journal of Pediatric Orthopaedics*. 2012;*32*(3):301-07.

10.Soni JF, Valenza W, Matsunaga C. Tarsal coalition, Current Opinion in Pediatrics. 2020;2(1): 93-99.

11. Klerken T, Kosse NM, Aarts CAM, Louwerens JWK. Longterm results after triple arthrodesis: Influence of alignment on ankle osteoarthritis and clinical outcome. Foot Ankle Surg. 2019;25(2):247-50.

12. Mann RA, Beaman DN, Horton GA. Isolated subtalar arthrodesis. Foot Ankle Int.1998;19(8):511-19.

13. Jackson TJ, Mathew SE, Larson AN, Stans AA, Milbrandt TA. Characteristics and reoperation rates of paediatric tarsal coalitions: a population-based study. J Child Orthop. 2020; 14(6): 537-543.

14. Li S, Myerson MS. Excision of a Middle Facet Tarsal Coalition. JBJS Essent Surg Tech. 2020;10(1):1-14.

Kirschner Wire Fixation versus Implants for Proximal Interphalangeal Joint Arthrodesis

Jonathan Ibanez, B.S., Alex Dang, B.S., and Rahul Natarajan, B.S.

ABSTRACT

Objective: To compare and contrast Kirschner wire (K-wire) fixation versus implants for proximal interphalangeal joint (PIPJ) arthrodesis.

Methods: A PubMed search on relevant research pertaining to the interventional techniques for arthrodesis was reviewed. This included data from multiple studies detailing and comparing the use of surgical equipment for implementation of arthrodesis.

Results: In this comparative study, it was observed that K-wire fixation and intramedullary implants for PIPJ arthrodesis are both commonly used hardware for the management of digital contracture deformities. Both forms of hardware implemented in arthrodesis offer similar levels of patient satisfaction. However, it is noted that implants have greater incidence of fusion and fewer complications when compared to K-wire fixation. Thus, the research indicates a preference for intramedullary implants in PIPJ arthrodesis as long-term management of hardware is crucial for correction of digital contracture deformities.

Conclusion: Both forms of hardware have benefits and risks with their usage. When considering which to use, it is based on surgeon preference for the situation, long term patient satisfaction, and incidence of complications.

Introduction

Lesser toe deformities are one of the most common complaints among patients who present to foot and ankle specialists. One survey conducted by Dunn et al found that amongst patients in a multiethnic population of adults over the age of 65 years old, hammertoe deformities accounted for 34.5% of foot and ankle complaints.¹ Hammertoe deformities can cause significant pain around the dorsal proximal interphalangeal joint which can manifest in the form of calluses, corns, or ulcerations. Interventions for these deformities initially involve a conservative approach which include padding around pressure points, accommodative footwear, and supportive insoles with a metatarsal pad. When conservative measures fail, an extensive assortment of operative treatment modalities are available which can be distilled into two broad categories, arthrodesis with kirschner wire fixation and arthrodesis utilizing proximal interphalangeal joint implant. This study will examine both categories of arthrodesis and compare the benefits and limitations of each fixation method. Through discussion of these approaches to proximal interphalangeal joint arthrodesis this article will present surgeons and patients with information that may be valuable in the preoperative planning stage.1

An understanding of the etiology of hammertoes is essential to understanding the different approaches offered for surgical correction. The most common is an imbalance in intrinsic and extrinsic musculature in the foot, most commonly causing flexion at the proximal interphalangeal joint which is coupled in some cases with flexion at the distal interphalangeal joint. The types of imbalance can be categorized as flexor stabilization, extensor substitution, or flexor substitution, which reflect the muscle groups responsible for the deformity. Other causes of hammertoes include hallux valgus, inflammatory arthritis, and neuromuscular abnormalities driven by diabetes. A hammertoe deformity can eventually progress to a plantar plate rupture which may cause more pain and would require a different surgical approach. It is therefore important to understand the treatment pathway for hammertoes and the advantages, risks, and constraints that each surgical approach carries.¹

Methods

Relevant articles were found through PubMed and other educational sources to analyze the benefits and limitations of both K-wire fixation and PIPJ implants for the purpose of arthrodesis. Inclusion criteria includes discussion of both procedures for various foot pathologies utilizing arthrodesis for treatment. Exclusions in the study include blogs, opinions, or commentary. Search terms included "K-wire vs. PIPJ implant for arthrodesis" and "arthrodesis techniques."

Results

Rothermel et al. performed a study on 12 cadaveric second toe pairs to compare K-wires to two types of implants, the X Fuse and Smart Toe. One group of six patients was used to compare Kwires to X Fuse, while the other group used the remaining six patients to compare K-wires to Smart Toe. For the first group, six second toe pairs were split evenly so that six proximal interphalangeal (PIP) joints were stabilized with K-wires, the six contralateral PIP joints were stabilized with X Fuse. For the other six second toe pairs, six PIP joints were stabilized with K-wires, and the last six PIP joints with Smart Toe. The study found that the average K-wires failure force was 91.0 newtons, while the failure force for X Fuse and Smart toe were 63.3 newtons and 53.3 newtons, respectively. Additionally, the stiffness for Kwire was 21.3 N/mm, while Smart Toe was 14.4 N/mm. One other element that the study found was that both the K-wises and SmartToe implants failed when the cortical bone was breached. However, the X Fuse implant failed upon pulling out for the joint. The study also found that bending K-wires will also cause it to fail.²

Angirasa et al. conducted a similar comparative study on 28 patients with hammer toe contractures. In this study, patients were followed-up six times, at day 7,14,21,28, 56, and again at day 180 to assess for pain, complications, and return to work status. Out of the total of 28 patients, 15 patients received K-wire fixation, the remaining 13 patients were fixated with SmartToe implants. All patients were mobilized in CAM boot for the first four weeks, and regular shoes afterward. At 7 day follow-up, the study found that K-wire had an average of 7 VAS score with a standard deviation of 1.60, while SmartToe had an average score of 6.83 with a standard deviation (std) of 1.34. At 6-month follow-up, K-wire had an average VAS score of 1.60 with 1.84 std, while SmartToe at 0.33 and 0.78 std. On a scale of 0-10 for patient satisfaction, with 10 being the most satisfied, Kwire received a score 7.93 with 2.31 std, while SmartToe received a 8.83 with 1.47 std at 7 days follow-up. At 6month follow-up, K-wire group slightly decreased to 7.6 with an std of 1.92, while SmartToe significantly increased to 9.83 with 0.29 std. The average return to normal activities for the K-wire group was 37.33 days with 7.79 days std, while the SmartToe group was 29.19 days with 5.02 days std. For the PIPJ arthrodesis integrity assessment, radiographs were taken at day 28, day 56, and 6-month post-operatively. Data found 40% of the Kwire group achieved arthrodesis at the 28-day follow-up, 13.33% at 56-day, 6.67% at 6-month, and 40% never achieved end-to-end arthrodesis. On the other hand, all 100% of SmartToe patients were able to achieve arthrodesis. Lastly, eight different post-op complications were found among the K-wire group, most common ones were digit deviation, failure to achieve arthrodesis as noted in 40% of the population, contracture, joint pain, bent pin, second digit excessive widening, and revision surgeries due to broken K-wires. On the other hand, the SmartToe group did not report any sign of implant failure, excessive pain, loss of correction, or digit deviation.3

Another comparative study by Scholl et al. on SmartToe versus K-wire arthrodesis on 117 digits with hammer toe deformity. The study went on from 2007 to 2010 with average follow-up ranging from 94 to 1130 days with a mean of 388.6 days and an std of 285.9 days. The total of 31 digits were excluded in the final data analysis process due to the lack of a 90day radiographic follow-up. Of the remaining 86 digits, 48 were on the right foot and 38 were on the left foot. Unlike the previous study by Angrisa et al. who analyzed only 2nd digits, this study included 54 second digits, 24 third digits, and 8 fourth digits. The total of 58 digits were fixated with SmartToe, the remaining 28 digits were with K-wires. When evaluating on radiographs during follow-up appointments, 87.9% of the SmartToe group and 85.7% of the K-wires group showed between 0 to 10 degrees angulation in the transverse plane to indicate good position. Similarly, osseous unions on radiographs were observed in 68.9% of the SmartToe group and 82.1% of the K-wires group. Complications such as fracture of the internal fixation were observed in 20.7% of the implants, and 7.1% of the K-wires group. Additionally, revision surgeries occurred in 8.6% of the SmartToe group, and 10.7% of the K-wires group due to asymptomatic malunion and nonunion observed on radiographs during follow-ups.⁴

In a randomized controlled trial by Jay et al., post op outcomes for lesser digital hammertoe correction were compared using either K-wire or 2piece intramedullary implant for fixation of the PIPJ. Of the 91 participants in the study, 46 (50.55%) were randomly placed in the K-wire group and 45 (49.45%) in the intramedullary implant group. It was found in regards to footrelated Quality of Life (QOL) that the baseline Bristol Foot Score (BFS) had a mean of 43.49 for the K-wire group and 46.47 for the intramedullary implant group (p = 0.2308). The baseline composite Foot Function Index (FFI) score was a mean of 98.68 for the K-wire group and 99.95 for the intramedullary implant group (p = 0.8844). For radiographic findings demonstrating incidence of fusion for the PIPJ post op, union was noted in 16.28% of participants for the K-wire group and 84.44% of participants for the intramedullary implant group after a 6 month period (p < 0.0001). Approximately 98% of the PIPJ fusions stabilized with K-wire showed fibrous pseudoarthrosis at 6 weeks and 3 months post op, and about 84% at 6month follow-up radiographic inspection. For the intramedullary implant, about 42% revealed fibrous pseudoarthrosis at the 6-week follow-up and about 16% at the 3- and 6-month follow-up inspections.⁵

In a retrospective review of hammertoe correction by Richman et al., post op outcomes were compared between usage of K-wire fixation and a novel intramedullary fusion device (CannuLink). With a total of 99 patients, 60 experienced K-wire fixation and 39 experienced fusion with the CannuLink implant. The K-wire group noted 16 patients (27%) to be symptomatic after about a 1 year follow-up. About 9.5% of patients had recurrent deformities, 3% developed late infections due to the deformities, and 1% developed partial numbness. About 5.3% required revision surgery. For the intramedullary implant group, 3 patients (7.7%) remained symptomatic at the 1 year follow-up and were all associated with a complication. No patients had hardware failure or required revision surgery.⁶

Discussion

The main argument of this article details the best method to fixate a hammer toe contracture, one of the most common podiatric conditions in the elderly population.⁷ Historically, K-wire has been widely used as the traditional method to fixate the PIPJ.8 However, recent technological advances have shifted the trend towards implants to eliminate the external wire exposure of K-wires that inherently lead to potential postoperative complications.9 Numerous studies have been published over the years to compare different types of implants to K-wires. One study by Angrisasa et al. comparing Kwires to SmartToe does show a preference for SmartToe due to increased pain relief, higher patient satisfaction, quicker rate of returning to normal activities, higher rate of achieved end-to-end arthrodesis, and no postoperative complications.³ However, the patient satisfaction score is difficult to accurately measure since it is subjective and multiple factors could contribute to the overall satisfaction.¹⁰ Similarly, study by Scholl et al. supported study by Angrisasa et al. on SmartToe as a more preferred fixation method due to lower incidence of osseous union, lower rate of revision surgeries, higher rate of good positioning on post-op radiographs. Although there is a higher rate of fractured internal fixation in the SmartToe group, multiple factors could contribute such as the patient's non-compliant early weight bearing.⁴

Given the data from multiple studies that prefer implants over K-wires, Rothermel et al. hypothesize that implants such as SmartToe and X Fuse would be stronger and stiffer than K-wires. Interestingly, their data shows the opposite.² Despite the advantages implants offer, Kwires come out on top as a more stable device of the two options. As a result, K-wires might be a more viable option for patients that are non-compliant and tend to weight-bare premature post-operatively. Additionally, the data found in this study play a role in explaining data in Scholl el al. where a higher rate of internal fixation fracture found in the SmartToe group compared to the Kwires group. However, when all advantages and disadvantages are taken into consideration, implants such as SmartToe are by far the more superior option of the two.⁴ Unfortunately, there should be cooperation of a bigger sample size and the long term follow-up to increase the validity and credibility of the study, and to fully assess the performance of each type of fixation.

In the randomized controlled trial by Jay et al., qualitative factors of patient satisfaction were used to assess the two fixation techniques post op. The Bristol Foot Score (BFS) is calculated from a self-reported questionnaire by the patient focusing on foot-related quality of life and daily activities. The Foot Function Index (FFI) score is also another self-reported questionnaire, but is divided into 3 subcategories: pain, disability, and activity limitation. This measures foot pain and difficulty ambulating in various situations. Composite (total) and subcategory scores are then calculated.5 Though the BFS and FFI score were slightly higher for intramedullary implants, there were not statistically nor clinically significant differences between the treatment groups. This shows that there is not much difference between the two techniques subjectively speaking for a patient's quality of life post op and short term. However, the statistically significant difference between the techniques for observed union of the PIPJ, being about five times greater for the intramedullary implant group than the K-wire group, shows that intramedullary implants provide greater stability for the joint than K-wires long term. Those in the intramedullary implant group also experienced persistent fibrous pseudoarthrosis about five times less than the Kwire group at the 6-month follow-up inspection. This portrays that intramedullary implants have lower post op complication rates compared to Kwires. Thus, in terms of practical applications for a PIPJ arthrodesis, a greater incidence of fusion with lower chances of developing post op fibrous pseudoarthrosis makes intramedullary implants more ideal to use over K-wire fixation for long term management of hammer toe contractures.

In the retrospective review of hammertoe correction by Richman et al. comparing post op outcomes between K-wire fixation and the CannuLink intramedullary fusion implant, it was found that the intramedullary implant resulted in fewer complications overall, with only 1 recurrent deformity and no revision surgeries compared to the K-wire group (Richman et al.). This shows that long term management of arthrodesis in digital contracture deformities would benefit more with intramedullary implants as they provide fewer complications and revision surgeries compared to K-wire fixation.⁶

Conclusion

The purpose of this comparative study is to list the advantages and disadvantages of K-wires

and implants so that patients can make an informed decision when it comes to fixating a digital contracture deformity. Most studies suggest that implants are a more viable option as they offer a higher incidence of union, patient satisfaction, and fewer revisions and complications long term. Further research is required to determine the most ideal patient outcome. However, it is up to the surgeon for hardware choice in arthrodesis based on the situation, long term patient satisfaction, and risk of post op complications.

References

 Dunn JE, Link CL, Felson DT, Crincoli MG, Keysor JJ, McKinlay JB. Prevalence of foot and ankle conditions in a multiethnic community sample of older adults. Am J Epidemiol. 2004;159(5):491-98.

2. Rothermel SD, Aydogan U, Roush EP, Lewis GS. Proximal InterphalangealArthrodesis of Lesser Toes Utilizing K-Wires Versus Expanding Implants: Comparative Biomechanical Cadaveric Study. Foot Ankle Int. 2019;40(2):231-36.

3. Angirasa AK, Barrett MJ, Silvester D. SmartToe® implant compared with Kirschner wire fixation for hammer digit corrective surgery: a review of 28 patients. J Foot Ankle Surg. 2012;51(6):711-13.

4. Scholl A, McCarty J, Scholl D, Mar A. Smart toe® implant versus buried Kirschner wire for proximal interphalangeal joint arthrodesis: a comparative study. J Foot Ankle Surg. 2013;52(5):580-83.

5. Jay RM, Malay DS, Landsman AS, Jennato N, Huish J, Younger M. Dual-Component Intramedullary Implant Versus Kirschner Wire for Proximal Interphalangeal Joint Fusion: A Randomized Controlled Clinical Trial. J Foot Ankle Surg. 2016; 55: 697-708.

 Richman SH. Siqueira MB, McCullough KA, Berkowitz MJ.
Correction of Hammertoe Deformity With Novel Intramedullary PIP Fusion Device Versus K-Wire Fixation. Foot Ankle Int. 2017; 38(2): 174-180.

7. Albright RH, Waverly BJ, Klein E, Weil L Jr, Weil LS Sr, Fleischer AE. Percutaneous Kirschner Wire Versus Commercial Implant for Hammertoe Repair: A Cost-Effectiveness Analysis. J Foot Ankle Surg. 2018;57(2):332-38.

 Hendrick SE, Kannegieter E. SmartToe, ToeGrip and buried k-wire versus percutaneous k-wire fixation for 2nd PIPJ arthrodesis: A comprehensive review of outcomes. The Foot. 2020;45(1):101692
Wei RX, Ling SK, Lui T, Yung PS. Ideal implant choice for proximal interphalangeal joint arthrodesis in hammer toe/claw toe deformity correction: A systematic review. Journal of Orthopaedic Surgery. 2020;28(1):1-9.

10. Obrador C, Losa-Iglesias M, Becerro-de-Bengoa-Vallejo R, Kabbash CA. Comparative Study of Intramedullary Hammertoe Fixation. Foot Ankle Int. 2018;39(4):415-25.

Pes Planus: Prevalence, Complications, and Treatment in Athletes

Alexander Carrillo-Kashani B.S., Sean Nguyen B.S., Asad Siddiqi M.S.

ABSTRACT

Objective: The goal of this article is to determine the prevalence of pes planus deformity in athletes in various sports, the complications that can arise from having pes planus deformity, and a potential method of treatment. **Methods:** Articles from the NCBI database that discussed the prevalence, complications, and treatment methods of pes planus were reviewed.

Results: The incidence of an overpronated forefoot (decreased medial longitudinal arch) is higher in athletes when compared to the normal population. Some complications seen in athletes include stress fractures, subsequent malalignments in the spine, and an overall elevated risk of injury to the lower extremity. Treatment methods involve orthoses, however their effectiveness is debated.

Conclusion: Pes planus deformity is prevalent among athletes. The complications have been shown to vary dependent on the sport. Orthoses are a method of treatment, though more research is required regarding their effectiveness.

Introduction

Pes planus, commonly known as "flat foot," is a pathology in which the medial longitudinal arch of the foot is lost. The condition has multiple etiologies often delineated between congenital or acquired. Congenital flexible pes planus is typically seen in young children and can be resolved without treatment.¹

Acquired pes planus, more often seen in the adult population, is a result of injuries to surrounding structures in the foot. The biomechanics behind this deformity involves the forefoot inverting on the rearfoot, resulting in subtalar joint pronation, forefoot supination, and an everted calcaneus. This leads to sequelae including compensation injuries of the lower leg, fractures to the navicular, tears of the plantar calcaneonavicular ligament, and posterior tibial tendon dysfunction.

Acquired pes planus due to posterior tibial tendon dysfunction is categorized using the Johnson and Strom classification system.² Johnson and Strom classification uses the clinical examination to stage the severity of pes planus deformity. The staging system guides treatment options for physicians in clinical practice.

While it's estimated that 20-37% of the US population have some degree of pes planus¹, there is no reliable data on the percentage of athletes with a pes planus deformity. Athletes across sports exert repeated forces on their feet, such as running and jumping. A result of pes planus is flexible, unstable feet that require excessive compensatory muscle activity which can lead to injuries. Thus, pes planus may have a noticeable effect on the health, availability and performance of athletes. The purpose of our study is to analyze the prevalence and complications related to pes planus in athletes as well as a potential treatment option.

Methods

This study utilized articles from the NCBI database. Articles were searched for with keywords such as "pes planus", "athletes", "NFL (National Football League)", "MLB (Major League Baseball)", and "NBA (National Basketball Association)". Articles that included background, prevalence, complications of pes planus, as well as treatments related to athletes were included.

Results

In a study performed by Bernasconi et al.,³ the foot type of National Football League (NFL) players (n=36) was compared to a control group from the general population (n=10). NFL players were found to have a neutrally aligned hindfoot, and normal subtalar morphology when compared to the controls. However, the medial longitudinal arch (forefoot arch angle, FAA) was decreased (p=0.03), with the navicular/medial cuneiform closer to the floor (p=0.03, p=0.01) in NFL players vs. the control group.

Bhosale et al. compared the feet of sub-elite (non-professional) athletes from various sports such as football, basketball, and hockey.⁴ The study found that the frequency of pes planus deformity differed in the respective sports. Football players were found to have the highest prevalence of flat foot amongst the three at 33% (n=15/46). Basketball players were recorded at 22% presenting with a flat foot (n=10/46), and hockey at 7% (n=3/46).

This data leads to questions of what complications these competitors face. Major League Baseball (MLB) players were found to be negatively impacted.⁵ Feigenbaum et al. observed that baseball players, specifically pitchers, with a pes planus deformity in their stance foot (vs. lunge foot) during a pitch had the highest odds ratio (3.7) of requiring shoulder surgery. An example of these actions is

lordosis, an inward curvature of the spine, due to the compensation of the flexible flat foot.⁵ An excessive lordosis compensation causes hyperabduction and hyper-external rotation of the shoulder during a pitch. This increases the force required to throw the ball, whilst increasing the risk of injury.

Ho et al. reflected on an already established athletic pes planus, and how the most common treatment method of orthoses plays a role in performance.⁷ Their research analyzed 26 basketball players, 11 of whom were diagnosed with flat feet. Those 11 were found to have decreased ankle plantarflexion in the toe-off phase of gait. Additionally, this subsection was found to have greater ankle muscle strength and less hip joint power. In regards to their treatment, Ho et al. found that the use of orthoses resulted in ankle eversion while jumping in the flat-footed group. This mechanism reduced ground reactive forces and ankle movement during the toe-off phase. Ho et al. ultimately cited insufficient evidence to assert that orthoses benefit flat-footed basketball players in their overall performance.

Discussion

Pes planus is a condition in which the longitudinal arch of the foot has flattened due to muscle weakness, genetic deficits, or a multifactorial etiology. Though differing on specifics of their definition of pes planus, the reported articles inherently agree on this definition. Bernasconi et al. demonstrated that players in the NFL generally had an over-pronated foot with a decreased medial longitudinal arch. Moreover, Bhosale et al. purported that a substantial portion of football, basketball, and hockey players experienced varying degrees of pes planus. It is a significant finding that could be the explanation for certain injuries on the field, court, and rink due to excessive compensatory muscle actions Identifying this and other foot-related injuries. phenomenon across sports could lead to improved management of players, ultimately resulting in fewer games missed and enhanced overall performance.

The correlation to specific injury remains to be seen in this subsection of athletes. More studies examining this topic further can lead to successful prevention strategies and initiatives to mitigate the risk of injury. It is clear that pes planus seems to affect athletes across sports and often leads to further injury if left untreated. This finding can guide the development of effective treatment options.

In the article written by Feigenbaum et al., there was a measurable increase in odds of injury to the shoulder or elbow in MLB pitchers with an abnormal foot arch. Pes planus has been determined to lead to subsequent malalignments in the spine, more specifically increases in lumbar lordosis. Increases in lumbar lordosis have been shown to cause hyperabduction and hyper–external rotation of the shoulder during the pitching motion, creating increases in forces at the shoulder and elbow. Again, more research is required, though this finding should be significant enough to promote the risk of shoulder injury in flat-footed pitchers and encourage injury prevention programs.

Lastly, the study by Ho et al. reviewed how pes planus affects athlete performance, and how orthoses can play a role in affecting said performance. Their conclusion that there is insufficient evidence to assert that orthoses benefit flat-footed basketball players puts into question how and when basketball players should be treated. It could be considered that orthotic treatment may only be indicated for certain sports. Furthermore from his conclusion, to extend beyond nonsurgical treatment options for flat-footed players to surgical intervention such as flat foot reconstruction would be unwarranted. Future research could examine another therapeutic approach such as surgery for cases of debilitating pes planus deformity in athletes.

This analysis had several limitations. The studies chosen were not fully comprehensive and the results varied from sport to sport. There is a scarcity of data on pes planus in athletes, their complications, and treatment. There is also a conflicting conclusion from Michelson as to if pes planus in athletes should be treated.⁸ However, his conclusion fails to include the reported evidence of complications in pes planus deformity. The data accumulated in this study demonstrates an underlying relationship between pes planus in athletes and numerous complications. Specific studies differentiated by the type of athlete would help definitively determine if a causation relationship exists. Such further studies would also lead to enhanced treatment options and proper risk management for athletes. This would benefit the athletes' availability and performance in their respective sports which additionally benefits their leagues 'financial viability and future growth.

Conclusion

Our paper aimed to review pes planus in athletes. The prevalence and complications varied depending on the sport. It was found that pes planus affects a large population of athletes with potentially debilitating complications. However, sufficient research discussing the causation of injuries is not available. This likely is due to the complexities of professional sports and the different factors that lead to injury. With the limited research available, it can be difficult to blame pes planus deformities as the cause of prospective injury. Treatment has been limited to orthosis with conflicting results. Thus, further research would benefit healthcare professionals and athletes in the most effective treatment strategy.

References

- 1. Raj MA, Tafti D, Kiel J. Pes Planus. StatPearls. Published August 3, 2021. Accessed January 11, 2022.
- Abousayed, Mostafa M, et al. "Classifications in Brief: Johnson and Strom Classification of Adult-Acquired Flatfoot Deformity." *Clinical Orthopaedics and Related Research*, Springer US, Feb. 2016.
- Bernasconi A, Cesar C, Roberts L, et al. Foot Alignment in Symptomatic National Football League (NFL) Athletes: A Weightbearing CT Analysis. *Acta Ortop Bras.* 2021;29(3):118-123.
- 4. Bhosale N, Nadala P. Prevalence of flexible flat foot in athletes. *Kesari Mahratta Trust.* 2021; 1(1).
- Feigenbaum LA, Roach KE, Kaplan LD, Lesniak B, Cunningham S. The association of foot arch posture and prior history of shoulder or elbow surgery in elite-level baseball pitchers. J Orthop Sports Phys Ther. 2013;43(11):814-820.
- Ho M, Kong PW, Chong LJ, Lam WK. Foot orthoses alter lower limb biomechanics but not jump performance in basketball players with and without flat feet. *J Foot Ankle Res.* 2019;12:24. Published 2019 Apr 23.
- Michelson JD, Durant DM, McFarland E. The injury risk associated with pes planus in athletes. *Foot Ankle Int.* 2002;23(7):629-633.

Klippel-Trenaunay Syndrome: a review of management and treatment of lower extremity vascular malformations

Victoria Starzyk B.S

ABSTRACT:

Objective: Klippel-Trenaunay Syndrome (KTS) is a rare congenital condition with no well-defined, established mode of treatment. This study reviews current options for the management of the lower extremity vascular malformations of KTS.

Methods: This review identified literature since April 31, 2016, using the PubMed and Google Scholar databases. The following search strategy was used: *Klippel-Trenaunay Syndrome OR vascular malformations OR lower extremity complications*.

Results: Symptomatic treatment is the primary method of management for KTS. Operational treatments are based on symptomatic improvement for severe or refractory cases.

Conclusion: Further research on the management of KTS must be done to improve the quality of life of patients with this rare disorder.

Introduction:

Klippel-Trenaunay Syndrome (KTS) is a rare complex vascular congenital malformation that typically affects a unilateral lower extremity.¹ The syndrome is characterized by a triad of venous insufficiency secondary to extremity varicosities, cutaneous vascular malformations (port-wine stains), and hypertrophy of soft tissues and bone resulting in leg length discrepancy. The diagnosis is clinical and may be supported with imaging. Duplex ultrasound, MRI, and CT may demonstrate venous and lymphatic malformations and tissue hypertrophy. KTS is associated with significant comorbidities such as pain, edema, ulcerations, and pruritus. The severity of vascular malformations requires a multidisciplinary team's care.² Primary treatment is based on nonoperative management. Refractory cases may require vascular surgery. The objective of this literature review is to evaluate current treatment options for KTS.

Methods:

This review identified literature since April 31, 2016, using the PubMed and Google Scholar databases. The following search strategy was used: *Klippel-Trenaunay Syndrome OR vascular malformations OR lower extremity complications*. A primary focus on English language literature was used in this search.

Results:

A review of the medical literature revealed that symptomatic treatment is the primary method of management for KTS.³ Symptomatic treatment includes lifestyle modification, local wound care, orthotics, extremity elevation, and compression. Due to the rarity and complexity of KTS, a multidisciplinary team should be involved early in patient care.² Operational treatments are based on the symptomatic improvement of severe refractory cases.¹

Recent studies have investigated the effectiveness of vascular operations such as vein stripping, and thoracic duct decompression.^{4,5,6} Vein stripping is used to remove or tie off a large varicose vein.⁵ In a longitudinal study, Malgor et al. found that stripping the great saphenous and small saphenous veins for management of KTS resulted in 50% reporting significant pain relief. Thoracic duct decompression redirects lymphatic flow to restore the lymphatic system integrity.⁶ In a retrospective study, Wen et al. reviewed the utilization of lymphoscintigraphy to assess candidacy for thoracic duct decompression and found that in the four patients with post-surgery follow-up, three achieved significant, measurable symptomatic relief.

Emerging targeted immune therapies such as sirolimus or alpelisib are nonsurgical options for the management KTS. In an open-label study across three centers, Parker et al. evaluated the safety and efficacy of low-dose sirolimus in reducing tissue overgrowth among 30 patients.⁷ Sirolimus resulted in a moderate decrease in mean percentage total tissue volume. However, 72% of patients in this study experienced at least one adverse event, with infection being the most common. In an experimental study on alpelisib conducted with 19 patients, Wen et al. demonstrated improvements in vascular malformation size although side-effects included hyperglycemia and oral ulceration were common.⁸

No consensus has been reached on the proper management of KTS and the role of immunotherapy.⁹ Ashgar et al., in reviewing the literature, suggest utilizing a conservative approach directed at symptomatic treatment with noninvasive measures and consideration of surgical options when inadequate.

Discussion:

There is no known cure for KTS, and symptomatic treatment is directed at improving quality of life.³ KTS complications include pain, swelling, lymphedema, bleeding, psychological disturbance, abnormal walking posture, superficial thrombophlebitis, and deep vein thrombosis.

Primary treatment is nonoperative based on symptom alleviation through medical management akin to chronic venous disorders.¹ In addition, consideration may be given to the possibility of deep venous agenesis, which makes remaining superficial vessels vital for lower extremity flow. The presence of hand or foot malformations in KTS may predict the presence of deep venous system abnormalities.⁷

Medical management includes lifestyle modification, local wound care, orthotics, extremity elevation, and compression.¹ Limb edema may be managed by a regimen of elevation and compression stockings with a pressure of 20 to 40 mm Hg.³ Psychological support and pain management are also mainstays of therapy. Intermittent pneumatic compression can be a helpful adjunct in reducing edema. Orthopedic treatment is directed at the management of uneven limb lengths. Heel inserts or compensatory shoes are appropriate for leg length discrepancies <1.5 cm. If the discrepancy is >2 cm, osteotomy surgical intervention with or epiphysiodesis may be more appropriate.

Minimally invasive procedures include pulsed laser, embolization, sclerotherapy, and radiofrequency or laser ablation.¹ Laser therapy may treat port-wine stains or ulceration. ³ Endovenous laser therapy on the greater saphenous veins may aid in managing varicosities. Sclerotherapy with foam-based agents may effectively reduce symptoms with an acceptable rate of complications.⁴ Radiotherapy has been reported to induce regression of hemangiomas slowly.

Symptom progression or more severe CEAP (clinical, etiological, anatomical, pathophysiological) classification of venous disorders (greater than class 2 with symptoms or class 3) may warrant operative intervention.¹ Relative indications for intervention include pain, functional impairment, swelling, limb asymmetry, or cosmetic reasons. Absolute indications include hemorrhage, infections, refractory ulcers, or acute thromboembolism.³ In these circumstances, surgical treatments such as vein stripping and thoracic

duct decompression for KTS may be warranted. Vein stripping that utilizes CT findings and thoracic duct decompression that utilizes lymphoscintigraphy findings have both been found to provide significant pain relief for KTS patients.^{5,6} DVT, PE, and nerve palsies were the main surgical complications of these procedures. However, many authors have reported worsening symptoms following procedures such as multiple ligations and stripping.³ Surgical intervention may be viewed as a viable option in management of vascular malformations after medical management and pain management options have been optimized.⁹

Targeted immune therapies such as sirolimus or alpelisib are emerging treatments for KTS that do not yet have a clear role in management.^{7,8} By targeting mTOR and PIK3CA respectively, sirolimus and alpelisib inhibit the cell proliferation and angiogenesis involved in KTS. Although both sirolimus and alpelisib show promise, further trials are needed to evaluate its use in patients with KTS.

A limitation of this study is that KTS is a rare disease and there are few articles in the literature devoted to assessing the efficacy of KTS treatment modalities. Some of these studies focused on other diseases of vascular malformation. Most of the studies specifically focused on KTS had limited evidence in the format of small case studies and retrospective studies.

Conclusion:

Studies on the management of KTS have been conducted with a limited number of patients due to its rarity. The literature suggests various ways of management without an established standard of treatment. Available case reports and retrospective studies suggest that medical management is preferred as first-line therapy with the option to incorporate surgical intervention for refractory symptoms and cases of greater severity. Open operative management with vein stripping or thoracic duct decompression options may be worth considering when conservative management is inadequate. A promising new alternative to symptomatic and operative management is immune therapy with sirolimus or alpelisib. Further research on the application of these medications to KTS is needed to confirm therapeutic efficacy with the goal of improving the quality of life of patients with this rare disorder.

References:

- Wang SK, Drucker NA, Gupta AK, Marshalleck FE, Dalsing MC. Diagnosis and management of the venous malformations of Klippel-Trénaunay syndrome. *J Vasc Surg Venous Lymphat Disord*. 2017;5(4):587-595. doi:10.1016/j.jvsv.2016.10.084
- John PR. Klippel-Trenaunay Syndrome. Tech Vasc Interv Radiol. 2019;22(4):100634. doi:10.1016/j.tvir.2019.100634
- Asghar F, Aqeel R, Farooque U, Haq A, Taimur M. Presentation and Management of Klippel-Trenaunay Syndrome: A Review of Available Data. Cureus. 2020;12(5):e8023. Published 2020 May 8. doi:10.7759/cureus.8023
- Markovic JN, Nag U, Shortell CK. Safety and efficacy of foam sclerotherapy for treatment of low-flow vascular malformations in children. J Vasc Surg Venous Lymphat Disord. 2020;8(6):1074-1082. doi:10.1016/j.jvsv.2019.11.023
- Malgor RD, Gloviczki P, Fahrni J, et al. Surgical treatment of varicose veins and venous malformations in Klippel-Trenaunay syndrome. *Phlebology*. 2016;31(3):209-215. doi:10.1177/0268355515577322
- Wen Z, Tong G, Liu Y. Potential Utilization of Lymphoscintigraphy in Patients With Klippel-Trenaunay Syndrome. *Clin Nucl Med.* 2021;46(1):25-30. doi:10.1097/RLU.000000000003361
- Parker VER, Keppler-Noreuil KM, Faivre L, et al. Safety and efficacy of low-dose sirolimus in the PIK3CArelated overgrowth spectrum. *Genet Med.* 2019;21(5):1189-1198. doi:10.1038/s41436-018-0297-9
- Venot Q, Blanc T, Rabia SH, et al. Targeted therapy in patients with PIK3CA-related overgrowth syndrome [published correction appears in Nature. 2019 Apr;568(7752):E6]. *Nature*. 2018;558(7711):540-546. doi:10.1038/s41586-018-0217-9
- Asghar F, Aqeel R, Farooque U, Haq A, Taimur M. Presentation and Management of Klippel-Trenaunay Syndrome: A Review of Available Data. *Cureus*. 2020;12(5):e8023. Published 2020 May 8. doi:10.7759/cureus.8023

Unmasking Acral Lentiginous Melanoma

Alysia Gregg B.S., Lauryn Orsillo B.S., Hanna Shulte B.S.

ABSTRACT

Objective: Acral lentiginous melanoma (ALM) is a rare subtype of malignant melanoma diagnosed in higher proportion among people of color. In this article, we will explore the clinical presentations of ALM, and how it may contribute to delays in diagnosis and treatment.

Methods: A literature review was performed using the PubMed search engine and Google Scholar. Keywords and terms that were used in the search included "acral lentiginous melanoma", "ALM", and "cutaneous melanoma." Literature was examined for clinically relevant information concerning the clinical presentation and diagnosis of acral lentiginous melanoma.

Results: ALM accounts for two to three percent of new melanoma and thirty-three to 36% of total diagnosed cutaneous malignant melanoma (CMM) in Blacks, 18 to 23% in Asians/Pacific Islanders, and 9%t in Hispanic Whites, versus only 1% in non-Hispanic Whites. It often mimics benign lesions leading to misdiagnosis, which is the most common cause for delayed treatment and can reduce the 5-year survival rate up to 68.9%.

Conclusion: Health care providers should be familiar with the presentation of ALM, particularly in patients of color for which it accounts for ¹/₃ of melanoma diagnoses. Early diagnosis and intervention plays a vital role in improving patient outcomes, so high clinical suspicion and close evaluation of suspicious acral lesions with dermatoscopy and biopsy is imperative.

Introduction

Cutaneous malignant melanoma (CMM) is the most lethal form of skin cancer, and is estimated to be the fifth most commonly diagnosed cancer in 2021, according to NIH SEERS database. Acral lentiginous melanoma (ALM) is a rare subtype of malignant melanoma that primarily presents on the palms, soles, and nailbeds. It is responsible for a higher proportion of malignant melanomas in Blacks and Asian/Pacific Islanders and is associated with poor prognosis. Low survival rates are proposed to be multifactorial, but are frequently related to late diagnosis and atypical clinical morphologies.

Epidemiology

ALM accounts for 2-3% of all new melanomas. The average age of diagnosis is 62.8, and males and females are equally affected. ALM disproportionately affects people of color. Previous population based studies in the United States have demonstrated that ALM accounts for 33-36% of total diagnosed CMM in Blacks, 18-23% in Asians/Pacific Islanders, and 9% in Hispanic Whites, versus only 1% in non-Hispanic Whites.¹ The 5 year melanoma specific survival rates for ALM are significantly lower than CMM (80.6% vs 93%, respectively). Furthermore, the 5 year survival rates were shown to be highest in non-Hispanic whites at 84.3%, lower in Asian/Pacific Islanders at 72%, and lowest in Blacks at 66.9%.1 When controlled for stage, a more recent study found differences in survival between non-Hispanic whites and Blacks in patients with Stage I and Stage III disease. Another study found no significant difference in melanoma specific

survival rates when controlled for Breslow depth of invasion. $\ensuremath{^{12}}$

Clinical Presentation

ALM is responsible for 60% of melanomas affecting the palms, soles, and subungual regions of the distal extremities.³ Previous studies show similar acral lesion patterns with 45-80% of acral lesions being attributable to ALM.⁴⁵ The majority of ALM lesions affect the lower extremity, and affect the palmoplantar vs subungual surfaces at a 3:2 ratio.⁶⁷

ALM is most often an acquired lesion, only arising from pre-existing nevi in less than 11% of cases.^s The lesion typically presents as a macule or patch with variegated brown pigmentation and irregular borders that follow the ridges of the dermatoglyphics. It may progress to become blueblack colored, nodular, or ulcerated as the tumor invades further. Due to the irregular nature and frequently missed diagnosis of ALM, it was proposed that the classical "ABCDE" acronym for melanoma be replaced with "CUBED" when examining acral surfaces: Colored lesions where any part is variegated, Uncertain diagnosis, Bleeding lesions, Enlargement of lesions, and Delay in healing beyond 2 months.⁹

ALM can also affect the nails as subungual ALM, with the thumb and great toe most frequently affected in up to 92% of cases.¹⁰ Subungual ALM can have variable presentations including diffuse pigmentation of the nail, a pigmented streak of nail, or ulceration. When pigment extends into the adjacent proximal or lateral nail fold, it is called "Hutchison's Sign" and is a worrisome clinical feature often associated with ALM. Additionally, extension further from the nail fold into the adjacent glabrous skin is a common feature amongst more advanced subungual ALM. $^{\scriptscriptstyle 10}$

Methods

A literature review was performed using the PubMed search engine and Google Scholar. Key words and terms that were used in the search included "acral lentiginous melanoma", "ALM", and "cutaneous melanoma." Literature was examined for clinically relevant information concerning the clinical presentation and diagnosis of acral lentiginous melanoma. Publication language was limited to English. There were no limitations put on the date published.

Results

A multitude of misdiagnoses of ALM have been found in the literature including: non-healing ulcers, verrucae, nevi, onychomycosis, tinea, and trauma.¹¹ In a study published by Albreski et al. in 2009, 22 case reports of unusual ALM presentations were evaluated. Of these reports, it was found that the majority of misdiagnosed cases included "ulcerations", "verrucous lesions", and "tinea." ⁶

Consistent with these findings are two recent case reports by Mansur et al. and Suarez et al. The 2015 paper by Mansur et al. details an 87-year-old woman with a 2.5 year history of a non-healing diabetic foot ulcer. The ulcer's failure to heal ultimately led to amputation of the toe, at which time histopathologic diagnosis of ALM was made. ¹²

A 2019 case report by Suarez et al. outlines a similar story of a 67-year-old man with 1 pack per day smoking history, as well as history of hypertension, diabetes, and dyslipidemia. He was referred to a vascular clinic for intermittent claudication and a left heel ulcer refractory to conservative treatment for 12 months. He underwent surgical intervention with femoropopliteal bypass with recovery of his distal pulses, but unfortunately, the ulcer worsened. Wound biopsy was ultimately performed and revealed ALM.

Furthermore, Markinson et al. outlines 3 cases in a 2019 case series with delayed diagnosis of subungual ALM in the great toe. In the first case, a 50-year-old man sustained trauma to the great toe 2 years prior, and regarded the ongoing appearance of the toe to be a direct result of the trauma. The patient was ultimately referred for biopsy and found to have features consistent with ALM. In the second case, a 52-year-old man was treated for paronychia for 4.5 months without resolution. The lesion initially presented amelanotic, however, on later examination the lesion had developed multiple adjacent pigmented streaks of unknown duration. Nail bed biopsy

ultimately revealed a deeply invasive ALM. And finally, in the third case, a 64-year-old man was treated for onychomycosis with subungual bleeding for several months, presumed to be related to the irritation of the thickened, dystrophic nail as it rubbed in his shoe. Biopsy was ultimately performed revealing ALM.¹¹



Figure 1: Acral lentiginous melanoma of the great toe that was treated as a diabetic foot ulcer for more than 1 year.⁶

Diagnosis

Given the wide range of mimicry seen with ALM, establishment of clear criteria for the evaluation of morphologic clinical features is of the utmost importance. Two methods have been proposed to assess acral lesions on dermoscopy. The first, by Koga and Saida, states the most important finding of ALM seen on dermoscopy is a parallel ridge pattern (PRP), a pigmentation running parallel with the ridges of the skin. Secondly, there is a lack of typical acral melanocytic nevi features such as fibrillar patterns (filamentous, parallel, fine streaks in slanted directions), parallel-furrow patterns (pigmentation along the furrows), and/or lattice-like patterns (linear pigmentation crossing the furrows).^{10,14}

The second method, by Lallas et al., uses the acronym BRAFF to assess six dermatoscopic findings in the diagnosis of ALM: Four positive findings (Blotches, Ridge pattern, Asymmetry, and colors), and two negative findings (Fibrillar pattern and Furrow pattern). Despite the clinical appearance and dermoscopy findings, lesions greater than 7 mm in diameter should be biopsied, and all lesions greater than 9 mm are likely to be melanoma.¹⁰ Overall, the histologic features of ALM can be fairly subtle, thus, it is essential to consider both clinical presentation along with dermoscopic findings for ALM diagnosis.

Treatment

Like other melanoma subtypes, wide local excision with margins based on tumor thickness is the primary treatment for ALM. Per the AAD and AJCC, current Breslow depth guidelines include:¹⁰

- In-situ lesions: 0.5 to 1 cm margins
- Breslow depth < 1 mm: 1 cm margin
- Breslow depth 1.01 2 mm: 1- 2 cm margin

Breslow depth > 2 mm: 2 cm clinical margin Primary closure, skin grafting, and secondary intention healing are performed following excision. For subungual melanomas, a more conservative, wide local excision without removal of bone, followed by a full-thickness skin graft is currently being studied for better functional and cosmetic outcomes. Immune stimulators may improve the function of checkpoint inhibitors in metastatic ALM therapy. Topical imiquimod monotherapy can prevent progression and even regression of ALM but its effects may be limited by the thick stratum corneum of acral skin.10 Genotyping may help triage for targeted therapy with KIT inhibitors given the increased KIT mutations in ALM. Lastly, radiation therapy is often only used as adjuvant treatment or in recurrent disease due to the low radiosensitivity of melanocytes.10

Discussion

ALM is associated with a worse prognosis than CMM, which is proposed to be related to late diagnosis and atypical clinical morphologies.

This delay in diagnosis has proven to be a major issue and is most often caused by misdiagnosis. The extensive differential diagnosis for ALM includes other melanocytic neoplasms such as congenital acral nevi, lentigo, and acquired acral nevi. The nonmelanocytic lesions that can mimic ALM are: vascular ulcers, chronic wounds, bacterial and fungal infections, calcaneal petechiae, terra firma-forme dermatosis, verrucae, and other pigmented skin cancers such as squamous cell carcinoma or porocarcinoma. For subungual ALM, the differential includes ethnic pigmentation, subungual haematoma, lentigo, and nevi. Previous studies by Mansur et al., Suarez et al., and Markinson et al. have confirmed this mimicry. Mistaking ALM for one of these similar presenting lesions can have adverse consequences such as delaying accurate treatment up to 12 months, increasing tumor thickness over time, and reducing the 5-year survival rate up to 68.9%.12 For this reason, early diagnosis of ALM is imperative. Prompt evaluation of abnormal acral lesions with dermoscopy, biopsy, and histology should be utilized in order to provide a more accurate and expedited clinical diagnosis of ALM, with the most important defining characteristic being parallel ridge pattern. Early diagnosis and intervention is necessary for better

prognosis; thus, physicians should have a high index of suspicion when examining new or abnormal appearing lesions in the extremities of patients of color in which it accounts for one third of the melanoma diagnoses.

Conclusion

ALM is an unusual subtype of melanoma that often presents on the soles of the feet, palms of the hands, or subungual region. It accounts for a disproportionate amount of melanomas diagnosed in darker skinned individuals and has a unique pathophysiology that gives it a predilection for sun-protected areas of the body. This is in contrast to other cutaneous melanocytic lesions in which we know UVB exposure is a significant risk factor.

Early diagnosis of and intervention in ALM may play a vital role in improving patient outcomes. Multiple studies have shown that misdiagnosis, as well as lack of knowledge of melanoma risk factors among minority populations, decreased access to care, decreased observation of the soles of the feet by elderly patients, and many other cultural factors may delay prompt treatment and subsequent survivability. By understanding the social barriers and being aware of the signs and potential mimicry of ALM, patients and physicians can help in expediting care to increase survival rates. Overall, physician training, public awareness, and patient education could decrease the delay in diagnosis seen for ALM and, thus, lead to a more favorable outcome for patients.

References:

- Bradford PT, Goldstein AM, McMaster ML, Tucker MA. Acral Lentiginous Melanoma: Incidence and Survival Patterns in the United States, 1986-2005. Arch Dermatol.2009;145(4):427–434. doi:10.1001/archdermatol.2008.609
- Huang, K., Fan, J., & Misra, S. (2020). Acral Lentiginous Melanoma: Incidence and Survival in the United States, 2006-2015, an Analysis of the SEER Registry. *The Journal* of surgical research, 251, 329–339.
- Kuchelmeister, C., Schaumburg-Lever, G., & Garbe, C. (2000). Acral cutaneous melanoma in caucasians: clinical features, histopathology and prognosis in 112 patients. *The British journal of dermatology*, 143(2), 275–280.
- Feibleman, C. E., Stoll, H., & Maize, J. C. (1980). Melanomas of the palm, sole, and nailbed: a clinicopathologic study. *Cancer*, 46(11), 2492–2504.
- Jimbow, K., Takahashi, H., Miura, S., Ikeda, S., & Kukita, A. (1984). Biological behavior and natural course of acral malignant melanoma. Clinical and histologic features and prognosis of palmoplantar, subungual, and other acral malignant melanomas. *The American Journal of dermatopathology*, 6 Suppl, 43–53.
- Albreski, D., & Sloan, S. B. (2009). Melanoma of the feet: misdiagnosed and misunderstood. *Clinics in dermatology*, 27(6), 556–563.
- Phan, A., Touzet, S., Dalle, S., Ronger-Savlé, S., Balme, B., & Thomas, L. (2006). Acral lentiginous melanoma: a

clinicoprognostic study of 126 cases. The British journal of dermatology, 155(3), 561–569.

- Pampena, R., Kyrgidis, A., Lallas, A., Moscarella, E., Argenziano, G., & Longo, C. (2017). A meta-analysis of nevus-associated melanoma: Prevalence and practical implications. *Journal of the American Academy of Dermatology*, 77(5), 938–945.e4.
- 9. Bristow, I.R., de Berker, D.A. Development of a practical guide for the early recognition for malignant melanoma of the foot and nail unit. *J Foot Ankle Res* 3, 22 (2010)
- Hall KH, Rapini RP. Acral Lentiginous Melanoma. 2021 Jul 28. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan–. PMID: 32644539.
- Markinson, B. C., Stowers, J. M., Black, A., Saccomanno, R., & Desman, G. (2019). The misdiagnosis of acral lentiginous melanoma: Three case presentations. *Journal of the American Podiatric Medical Association*, 109(2), 166– 171. https://doi.org/10.7547/17-038
- Mansur, A. T., Demirci, G. T., Ozel, O., Ozker, E., & Yıldız, S. (2015). Acral melanoma with satellitosis, disguised as a longstanding diabetic ulcer: A great mimicry. *International Wound Journal*, *13*(5), 1006–1008. https://doi.org/10.1111/iwj.12481
- Suarez Gonzalez LA, Del Canto Peruyera P, Cerviño Alvarez J, Alvarez Fernandez LJ. Misdiagnosed Malignant Tumor on an Ischemic Limb. Wounds. 2019 Feb;31(2):E12-E13. PMID: 30730300.
- Nakamura Y, Fujisawa Y. Diagnosis and Management of Acral Lentiginous Melanoma. Curr Treat Options Oncol. 2018 Jun 27;19(8):42. doi: 10.1007/s11864-018-0560-y. PMID: 29951919.

Comparing and contrasting peripheral nerve blocks and spinal anesthesia in lower extremity surgery

Aye Chan Moe, B.S., Vivian Chan, and Htet Aung Khant, B.S.

ABSTRACT

Objectives: To compare and contrast peripheral nerve blocks and spinal anesthesia in surgeries of the lower extremity, particularly in foot and ankle.

Methods: A PubMed and Google Scholar search was conducted on comparative studies investigating peripheral nerve blocks and spinal anesthesia in foot and ankle surgeries.

Results: Peripheral nerve blocks have been shown to significantly prolong postoperative analgesia and have lower risks of perioperative complications as compared to spinal anesthesia. Positive outcomes are also associated with ultrasound guidance in regional anesthetic practice.

Conclusion: Additional comparative studies are in demand to make a definitive assessment, but there is sufficient evidence in the current literature for using peripheral nerve blocks over spinal anesthesia in foot and ankle surgeries.

Introduction

In the United States, regional anesthesia methods have been widely utilized in lower extremity procedures over the conventional use of general anesthesia. Regional anesthesia methods include central blocks - consisting of spinal and epidural anesthesia - as well as peripheral nerve blocks, where anesthetics are targeted locally. Regional anesthesia is associated with a significant reduction in postoperative cardiac arrhythmias and pulmonary complications.¹ Additional benefits include the ability to reach target areas, faster postoperative recovery, and lower overall hospital costs. With regards to foot and ankle surgeries, moderate to severe postoperative pain often cannot be managed by oral pain medications alone.² Regional anesthesia has been shown to effectively reduce postoperative pain in surgeries of foot and ankle and require less perioperative opioids.^{3,4} In fact, peripheral nerve block in the foot and ankle region is found to reduce pain intensity during the immediate postoperative period and prolong analgesia.5

In the past, continuous spinal anesthesia blocks were the preferred mode of anesthesia during lower extremity procedures.⁶ Administered into the lumbar cerebrospinal fluid to anesthetize spinal nerves, spinal anesthesia prolongs sensory and motor block without significant adverse effects or the biochemical and metabolic consequences of general anesthesia. With continuous medical advancements, use of neuraxial blocks have become less enticing

because of possible side effects such as arterial hypotension, vomiting, late respiratory depression, and other neurological consequences.^{7,8} Therefore, peripheral nerve blocks have become more widely supported and used due to lower incidences of postoperative pulmonary complications and cardiac complications.¹

Despite the increasingly popular and common usage of peripheral nerve blocks, especially those guided by ultrasound, few studies have investigated the possible advantages of this technique to spinal blocks.⁹ Though many studies have examined the usage and efficacy of each block individually, comparative studies are much more scarce. As such, this review aims to compare and contrast peripheral nerve blocks and spinal anesthesia in surgeries of the lower extremity, particularly in the foot and ankle.

Methods

A PubMed and Google Scholar search was conducted with the keywords "spinal anesthesia" "peripheral nerve block," "lower limb surgery," "nerve blocks," and "postoperative analgesics" for papers published within 2010-2020. The literature was perused for studies specifically comparing the two analgesic techniques and measuring the respective perioperative outcomes in foot and ankle surgeries specifically. The excluded criteria restricted non-English-language publications, articles individually investigating each analgesic technique without comparison, and studies that performed more than one analgesic technique for each comparison.

Results

Urfalioglu et al. (2015) conducted a study regarding a retrospective comparison of spinal blocks and ankle blocks in lower extremity surgery, specifically open wounds to the foot, debridement of the foot, and toe amputation. To conduct their study, the patient population consisted of those who were suffering from open wounds of the foot secondary to diabetes or cardiac diseases. Two groups were created; one that received a spinal block and the other received an ankle block. Demographic data, such as age, gender, height, average blood pressure, and heart rate were recorded. Both groups showed a decrease in hemodynamic parameters, with a significantly more pronounced effect in the subarachnoid block group. More specifically, the average blood pressures 60 minutes after analgesic administration were 82.43 ± 10.43 and 101.20 + 12.91 for the spinal anesthesia and ankle block groups respectively. The heart rate for the spinal anesthesia group 60 minutes after administration was 70.10 + 11.02, while the same measurement was 82.94 ± 11.14 in the ankle block group. The study concluded that the group with peripheral nerve blocks had lower neurological and cardiac side effects when compared to spinal anesthesia. Furthermore, this study suggested that patient populations such as diabetics or cardiacassociated disease patients should preferably use an ankle block as the prefered anesthetic method.¹⁰

Singh et al. (2016) was a randomized prospective study that assessed the hemodynamic stability and recovery of patients who underwent elective foot surgery. The investigators performed analgesics of either subarachnoid block, also known as spinal block or ankle block, which is a common peripheral nerve block. In this study, patients were randomly divided into two groups: subarachnoid group and ankle block group. Demographic data was collected, including variables age, sex, weight, average blood pressure, and heart rate. It was found that among the group of patients that received subarachnoid anesthesia, one patient developed hypotension, one patient developed a headache that

lasted three days, three patients experienced gastrointestinal symptoms of nausea and vomiting, and one patient developed urinary retention.¹¹ In the ankle block group, only one patient was reported having an episode of nausea and vomiting and no other postoperative complications were found. These findings supported the notion as set by numerous other studies that the ankle block provides a positive intraoperative hemodynamic profile as well as a faster recovery when compared to a subarachnoid block. This is largely due to the fact that ankle block is an area specific analgesic that does not overlap with the sympathetic system of the patient. Overall, the findings from this study advocate for the use of ankle blocks especially in at-risk patient populations because of the decrease in hemodynamic variations, minimal pain relief and postoperative complications.¹¹

Protić et al. (2010) examined the efficacy of invasive ultrasound-guided regional minimal anesthesia and its postoperative analgesia duration for ankle surgery, and compared them with corresponding measures of spinal anesthesia.12 Two groups of 20 adult patients with bimalleolar fracture were randomly assigned to either receive the ultrasound-guided femoro-popliteal block (US-FPB) or a spinal anesthesia (SA). The numbers of patients who completed the study were 18 and 19 respectively, as regional anesthesia failed in two patients from the US-FPB group while there was one unsuccessful spinal in the SA group. There were no significant differences in the levels of anesthesia in both groups, but duration of postoperative analgesia was significantly higher in the US-FPB group than in the SA group. However, onset of complete sensory motor block was significantly faster in the SA group in comparison to the US-FPB group.¹² Given that significantly longer postoperative analgesia was achieved with minimal invasive US-FPB provided, the authors concluded that this analgesic method was more preferable to SA for ankle surgery in regards to postoperative comfort of the patients.12

Karaarslan et al. (2016) also compared the ultrasonography-guided popliteal sciatic nerve block with spinal anesthesia across multiple quantitative and qualitative measures. This randomized controlled trial divided 60 patients scheduled for hallux valgus correction surgery into two groups: the spinal anesthesia group received unilateral spinal block while the popliteal block group received popliteal sciatic nerve block with nerve stimulator and ultrasonography guidance. The recorded measures were efficacy, postoperative pain scores, adverse effects, additional analgesic requirements, and patient satisfaction scores in both groups enrolled in the big toe realignment surgery. Adverse effects for the spinal anesthesia group included hypotension, bradycardia, postdural puncture headache, and urinary retention while the popliteal block group exhibited none.¹³ Additional significant findings in the popliteal block group consisted of: lower pain magnitude at the second, fourth, sixth, and twelfth hours, longer postoperative first analgesic requirement times, and higher pain satisfaction scores.¹³ Specifically, the visual analog scale (VAS) superficial pain scores for the spinal group were 6, 3, 5, 5, 3 at the second, fourth, sixth, twelfth, and twenty-fourth hours post-operation, and 2, 2, 0, 2, 2 in the popliteal group; only the twenty-fourth hour measure was not statistically significant. Moreover, the time of first analgesic use in hours was 3 + 1 in the spinal group and 13 + 6 in the popliteal group. Finally, 17 patients in the spinal group indicated "Satisfied" or "Very Satisfied" on the pain satisfaction ratings compared to twenty four participants in the popliteal group. Therefore, the authors' recommendation for hallux valgus correction surgeries was peripheral nerve blocks instead of spinal anesthesia.13

Discussion

Karaarslan et al., Singh et al., and Urfalioglu et al. all recorded significantly lower visual analogue scale (VAS) pain scores at certain postoperative intervals (second, fourth, sixth, and twelfth hours; second, fourth, and sixth hours; sixth, twelfth, and twenty-fourth hours respectively)^{10,11,12} in the peripheral nerve block group compared to the spinal block group; Protić et al. did not measure VAS in their study. Karaarslan et al. also noted significantly higher pain satisfaction scores among patients in the popliteal block group than the spinal anesthesia group.¹³ This suggests that peripheral nerve blocks provide better pain control than spinal blocks.

Furthermore, all four studies observed more prominent or frequent hypotension as well as headaches in the spinal anesthesia group than in the peripheral nerve block group.^{10,11,12,13} The drop in blood pressure from baseline, postoperative nausea, and vomiting were significantly decreased in the peripheral nerve block groups in studies conducted by Singh et al. and Urgalioglu et al.^{10,11} Another common adverse effect - urinary retention - was observed in both Karaarslan et al. and Singh et al.^{11,13} Hence, the hemodynamic, neurological, gastrourinary side effects were consistently seen at higher rates or more commonly in spinal anesthesia compared to peripheral nerve blocks.

In particular, both randomized controlled trials by Protić et al. and Karaarslan et al. compared ultrasound-guided peripheral nerve blocks to spinal anesthesia (SA). Protić et al. recruited adult patients aged 18-66 with bimalleolar fracture while Karaarslan et al. enrolled patients of ages 18-60 who were scheduled for hallux valgus correction surgery. Both studies found the duration of postoperative analgesia measured using the first postoperative analgesic request and earlier analgesic requirements - to be longer with ultrasound-guided peripheral nerve blocks than with SA.^{12,13} In the SA group, Protić et al. recorded significantly faster onset of complete sensory motor block while Karaarslan et al. noted significantly shorter time until initiation of surgery, signifying that the SA group of both studies experienced the full effects of anesthesia earlier than the ultrasound-guided peripheral nerve blocks group.^{12,13}

Regarding the imaging modality used as accompaniment to the peripheral nerve blocks in the two studies above, it should be noted that such ultrasound guidance in regional anesthetic practice is rising and linked to improved success rates for various regional anesthetic techniques.¹⁴ In addition to the positive outcomes observed in Proticé et al. and Karaarslan et al. a 2021 retrospective study showed favorable clinical results with high efficacy in lowerextremity surgeries under ultrasound-guided nerve block.¹⁵ Ultrasound usage in nerve blocks has also been shown to reduce the required volume of local anesthetic solution and decrease procedural times.^{16,17}

All four studies endorse peripheral nerve blocks as a viable - and at times, even better alternative to spinal anesthesia in foot and ankle surgeries.^{10,11,12,13} Nonetheless, there exist several limitations to the regional anesthetic technique. A retrospective comparative study in 2013 by van Geffen et al. did not find significant mortality benefits in using regional blocks for lower extremities amputations instead of spinal blocks or general anesthesia.¹⁶ However, it is suggested that a patient's preoperative comorbidities may be a strong confounder in the association between the risks of mortality and the type of perioperative anesthesia administered.¹⁶ Moreover, common side effects related to peripheral nerve block procedures include incomplete block, infection, localized hematoma resulting in ischemic injury, and direct neuronal injury.¹⁸

Conclusion

Peripheral nerve blocks have been shown to significantly prolong postoperative analgesia and have lower risks of perioperative complications, including postoperative hemodynamic, gastrourinary, gastrointestinal, and neurological side effects, as compared to spinal anesthesia.^{10,11,12,13} Positive outcomes are also associated with ultrasound guidance in regional anesthetic practice. Admittedly, peripheral nerve blocks are not yet the gold standard for lower extremity surgery, which can be attributed to the lack of training. However, there is a general interest and a positive attitude towards learning more about peripheral nerve blocks. Given their advantages in foot and ankle surgeries over spinal anesthesia, peripheral nerve blocks are anticipated to increase in usage during surgical procedures of the lower extremity in the coming years.

References

- Chery J, Semaan E, Darji S, Briggs WT, Yarmush J, D'Ayala M. Impact of regional versus general anesthesia on the clinical outcomes of patients undergoing major lower extremity amputation. Ann Vasc Surg. 2014;28(5):1149-1156.
- Samuel R, Sloan A, Patel K, Aglan M, Zubairy A. The efficacy of combined popliteal and ankle blocks in forefoot surgery. J Bone Joint Surg Am. 2008;90(7):1443-1446.
- Shah S, Tsai T, Iwata T, Hadzic A. Outpatient regional anesthesia for foot and ankle surgery. Int Anesthesiol Clin. 2005;43(3):143-151.
- Singelyn FJ. Single-injection applications for foot and ankle surgery. Best Pract Res Clin Anaesthesiol. 2002;16(2):247-254.
- Stéfani KC, Ferreira GF, Pereira Filho MV. Postoperative Analgesia Using Peripheral Anesthetic Block of the Foot and Ankle. Foot Ankle Int. 2018;39(2):196-200.
- Lux EA. Continuous spinal anesthesia for lower limb surgery: a retrospective analysis of 1212 cases. Local Reg Anesth. 2012;5:63-67.
- Rodziewicz TL, Patel S, Garmon EH. Lower Extremity Blocks. In: StatPearls. Treasure Island (FL): StatPearls Publishing; September 8, 2021.

- Semenikhin AA, Shumatov VB, Mazaev VP, Rybakova LA. Oslozhneniia i pobochnye éffekty spinal'noĭ anestezii [Complications and side effects of spinal anesthesia]. Anesteziol Reanimatol. 1991;(4):59-62.
- Lin R, Hingorani A, Marks N, et al. Effects of anesthesia versus regional nerve block on major leg amputation mortality rate. Vascular. 2013;21(2):83-86.
- Urfalioglu A, Gokdemir O, Hanbeyoglu O, et al. A comparison of ankle block and spinal anesthesia for foot surgery. Int J Clin Exp Med. 2015;8(10):19388-19393. Published 2015 Oct 15.
- Singh AP, Singh B, Bhardwaj A, Singh I, Kaur P. Comparative Analysis of Unilateral Subarachnoid Block with Ankle Block for Elective Foot Surgery. International Journal of Medical and Dental Sciences. 2016 Jul 1;5(2):1150-5.
- Protić A, Horvat M, Komen-Usljebrka H, et al. Benefit of the minimal invasive ultrasound-guided single shot femoro-popliteal block for ankle surgery in comparison with spinal anesthesia. Wien Klin Wochenschr. 2010;122(19-20):584-587.
- Karaarslan S, Tekgül ZT, Şimşek E, et al. Comparison Between Ultrasonography-Guided Popliteal Sciatic Nerve Block and Spinal Anesthesia for Hallux Valgus Repair. Foot Ankle Int. 2016;37(1):85-89.
- Neal JM. Ultrasound-Guided Regional Anesthesia and Patient Safety: Update of an Evidence-Based Analysis. Reg Anesth Pain Med. 2016;41(2):195-204.
- Kang C, Hwang DS, Song JH, et al. Clinical analyses of ultrasound-guided nerve block in lower-extremity surgery: A retrospective study. J Orthop Surg (Hong Kong). 2021;29(1):2309499021989102.
- van Geffen GJ, van den Broek E, Braak GJ, Giele JL, Gielen MJ, Scheffer GJ. A prospective randomised controlled trial of ultrasound guided versus nerve stimulation guided distal sciatic nerve block at the popliteal fossa. Anaesth Intensive Care. 2009;37(1):32-37.
- Danelli G, Fanelli A, Ghisi D, et al. Ultrasound vs nerve stimulation multiple injection technique for posterior popliteal sciatic nerve block. Anaesthesia. 2009;64(6):638-642.
- Jeon YT. Peripheral nerve block for anesthesia in patients having knee arthroplasty. Korean J Anesthesiol. 2012;62(5):403-404.
- Zewdie A, Debebe F, Azazh A, Salmon M, Salmon C. A survey of emergency medicine and orthopaedic physicians' knowledge, attitude, and practice towards the use of peripheral nerve blocks. Afr J Emerg Med. 2017;7(2):79-83.
- Vadivelu N, Kai AM, Maslin B, Kodumudi V, Antony S, Blume P. Role of regional anesthesia in foot and ankle surgery. Foot Ankle Spec. 2015;8(3):212-219.

Comparing Local Perioperative Methods and Antibiotic Prophylaxis in Surgical Site Infection Prevention

Sravani Sai Alla, B.S., Jessica Trujillo Landeros-Arnold, B.S., Anushka Sunil Ramnani, B.S.

ABSTRACT

Objectives: Surgical site infection prevention is a key component of medicine that can be used to prevent morbidity and mortality. This literature review aims to compare local modalities with a baseline modality of antibiotic prophylaxis in terms of efficacy and benefit to the patient.

Methods: A PubMed search was conducted on relevant clinically- based research articles from the years 1986-2019. Each method was analyzed in its respective setting.

Results: Perioperative oxygenation and antimicrobial irrigation have shown to have promising results in lowering the rates of SSIs while triclosan-loaded sutures, which also lower the rates of SSIs (OR 0.72, 95% CI 0.59-0.88), may be better suited for higher risk surgical procedures. Perioperative antibiotics yield little to no difference in preventing SSIs.³² 1.6% of patients who received antibiotics acquired a postoperative infection versus 1.4% who did not receive antibiotics acquired a postoperative infection.³²

Conclusion: In conclusion, the literature indicates that there are various methods that can aid in preventing surgical site infections including local perioperative measures as well as antibiotic prophylaxis. While antibiotic prophylaxis is not recommended routinely in clean, uncomplicated surgeries, it may be recommended to use local modalities in concert with antibiotic prophylaxis. However, further research is necessitated.

Introduction

Surgical site infection (SSI) is defined by The Centers for Disease Control and Prevention (CDC) as, a post-operative infection at the specific surgical location/body part.1 Both the patient and their healthcare team play vital roles in the prevention of SSIs. There are a variety of ways one can develop SSIs such as patient-related factors, surgical risk factors, and physiological states. Additionally, surgical risk factors that can increase the risk of developing an SSI include an unanticipated increase in length of procedural duration and poor surgical scrub technique from the operating team members.² Physiological states that can increase the risk of developing SSI are. traumatic injury, transfusion of blood products, low body temperature, low blood oxygen levels, and high blood glucose.²

The use of perioperative oxygenation remains controversial, research has been inconsistent showing both benefit and patient deterioration.³ Research supports middle-aged patients receiving oxygen therapy but there is more risk involved for both patients that are young and elderly.⁴The risk of oxygen therapy is due to a resultant collapse of alveoli and airway narrowing.⁵ Healthcare providers may consider oxygen therapy to reduce the risk of SSI on an individualized basis.

Povidone-iodine irrigation is a widely used practice used prior to wound closure. It has been shown to be used as an inexpensive, and safe

procedure that removes microbes from the wound site. The World Health Organization (WHO) and Centers for Disease Control (CDC) recommend the use of povidone-iodine irrigation for the prevention of SSI in prophylactic incisional wound irrigation.⁶

The use of antimicrobial coated sutures has been shown to be a useful tool in preventing SSI. A specific antimicrobial-coated suture, triclosan-coated sutures (TCS) have been shown to be effective in the prevention of SSI.⁷ The TCS was found to be effective against both Gram-positive and negative bacteria as well as methicillin-resistant *Staphylococcus aureus*.⁸

The use of properative antibiotic prophylaxis is a common practice in certain surgical cases. The specific antibiotic given is dependent on the anatomical region of the operative site, however, the three most widely used perioperative antibiotics are cefazolin, clindamycin, and vancomycin.⁹ Important considerations include the dosage and timeframe of the prophylactic antibiotics.⁹ Not every surgical procedure requires the use of prophylaxis antibiotics but it is important to consider on a case-by-case basis.

question arises on which type of antibiotics are best as prophylaxis for surgery. Studies suggest that narrowspectrum antibiotics, directed at treating Staphylococcus aureus, are most often used19. Cefazolin is ideal due to its coverage of normal skin flora, lower risk of type 1 (immediate) hypersensitivity, and bioavailability.10 However, in patients with a β -lactam allergy, clindamycin or vancomycin may be used. Vancomycin should be administered slowly over the hour to avoid vancomycin infusion syndrome.¹⁰ Clindamycin is used more often as it has limited drug reactions and no kidney issues when compared to vancomycin, in addition to the vancomycin infusion syndrome.10 Besides a β -lactam allergy, vancomycin may be used if there is an increased risk of MRSA in the given patient subgroup.¹⁰ However, as vancomycin is not as effective as cefazolin for methicillin-sensitive Staphylococcus aureus (MSSA), some clinicians suggest that both antibiotics may be given prophylactically for these patients.¹⁰

This review aims to compare local modalities with antibiotic prophylaxis in terms of efficacy and benefit to the patient.

Methods

A PubMed search was conducted on relevant research pertaining to local perioperative methods as well as antibiotic prophylaxis in preventing postoperative infection. Nine studies from the years 1986-2019 were identified and included in this review. Some phrases that were used for our search included: postoperative infection control, intraoperative infection control, surgical antibiotic prophylaxis, postoperative infection prophylaxis, lower extremity, and orthopedic surgery. Studies that discussed various infection control modalities but did not specifically mention lower extremity surgery were included. This was done with hopes that these modalities could be extrapolated and potentially used in podiatric procedures. Studies that mentioned holistic interventions for infection control were excluded.

Results

Perioperative Oxygenation

The World Health Organization (WHO) recommended that all adult patients undergoing surgery who are placed under general anesthesia with endotracheal intubation should be given an 80% fraction of inspired oxygen (FiO2) intraoperatively. Furthermore, this should be continued from 2 to 6 hours postoperatively. It was found that this method would reduce the risk of SSIs.¹¹ Through the administration of 80% FiO2, more oxygenation will be delivered to the surgical incision. Simultaneously, oxygen will also be delivered to infected tissue as it has a lower oxygen tension when compared to healthy

tissue. This oxygen delivery is thought to increase oxygen-dependent killing via neutrophils.¹² In 2016. Allegranzi et. al. conducted a meta-analysis of 11 randomized controlled trials (RCTs) to evaluate the effect of the administration of perioperative increased FiO2 (80%) compared to perioperative standard FiO2 (30-35%) in preventing SSIs. Criteria for measuring efficacy included measuring the rates of surgical site infection within a defined amount of postoperative days.¹⁰ In this meta-analysis, patients under general anesthesia with mechanical ventilation and endotracheal administration were included. It was found that the administration of perioperative 80% FiO2 was more beneficial in reducing SSIs when compared to perioperative 30-35% FiO2 (odds ratio 0.72, 95% CI 0.55-9.4).¹¹ Furthermore, Allegranzi et. al. suggest that the 80% FiO2 should also be continued in the 2-6 hour postoperative period as the benefits of perioperative oxygenation can only be observed when 80% FiO2 is used both in the perioperative period, via intubation, and immediate postoperative periods, via high-flux mask.¹¹

Antimicrobial Irrigation

Perioperative wound irrigation is described as the cleansing of an open wound with an aqueous solution. This is a widely used method in order to reduce the risk of SSIs.^{13,14,15} In 2016, Allegranzi et.al. conducted a meta-analysis of 21 randomized controlled trials comparing the use of wound irrigation vs. no wound irrigation in various surgical patients, with the criteria of efficacy measuring a significant reduction in infection rates. Within this meta-analysis, there were four RCTs using a saline solution to irrigate the wound. From these studies, there was a moderate to low quality of evidence.¹¹ However, it was found that saline solution irrigation using pulse pressure or forced application showed a larger benefit in the reduction of SSIs.¹¹ Moreover, this meta-analysis contained 7 RCTs that showed a significant benefit of the use of surgical wound irrigation with an aqueous povidone-iodine solution of differing concentrations when compared to a saline solution-based irrigation (Odds Ratio 0.31, 95% CI 0.13-0.73, p = 0.07).¹¹ A meta-analysis of 5 RCTs indicated that there was no significant difference in reduction of SSIs with antibiotic irrigation of the wound, saline solutionbased irrigation of the wound, and no irrigation of the wound (Odds Ratio 1.16, 95% CI 0.64-2.12, p = 0.63).11 Therefore, the WHO suggests incisional wound irrigation with an aqueous povidone-iodine solution before wound closure, especially in clean and clean-contaminated wounds. However, the WHO found that there is insufficient evidence to recommend saline solution-based irrigation of surgical wounds

before closing the wound in reducing the risk of SSIs. 11

Antimicrobial Coated Sutures

Antimicrobial coated sutures were developed with the goal of preventing the colonization of microbes within suture material in surgical incision sites. Animal studies showed a reduction in the number of bacteria as well as a lower incidence of wound infections when triclosan-coated sutures were used for wound closure. A similar result was seen in clinical studies as well.^{16,17,18}

In 2016, Allegranzi et. al. conducted a metaanalysis of 13 RCTs and 5 Cohort Studies which studied triclosan coated sutures in a majority adult population, as only one of these studies focused on the pediatric population.¹⁰ The results of this metaanalysis showed that there is a significant reduction in SSIs in surgical patients whose wounds were closed with antimicrobial-coated sutures when compared to non-coated sutures (RCTs: OR 0.72, 95% CI 0.59-0.88; Observational studies: OR 0.58, 95% CI 0.40-0.83).¹⁰ With this evidence, the WHO suggests the utilization of triclosan-coated sutures perioperatively to reduce the risk of SSIs.

Antibiotic Prophylaxis

Antibiotics are paramount for the prevention of surgical site infections (SSI) and reducing adverse drug reactions, leading to overall better clinical outcomes.¹⁸ In a clean, elective foot and ankle surgery, the rate of SSI is 0.26% to 2% with 5% of patients experiencing a postoperative infection, 1.3% - 10.1% in clean-contaminated, 10.2%-21.9% in contaminated, and 10%-40% in dirty wounds according to the Healthcare Cost and Utilization Project (HCUP) Statistical Brief.^{10,,20} The goal of antibiotic prophylaxis is to prohibit the proliferation of microbes in a usually sterile site and prevent contamination by external organisms.²¹ While prophylaxis is now warranted in most surgeries, the discussion of the importance is crucial.¹⁹

In orthopedic surgery, antibiotic prophylaxis is the standard of care for hip and knee arthroplasty, including fractures.¹⁹ and trauma. open Recommendations for prophylactic use surround patient presentation at the time of surgery as well as the type of procedure.¹⁰ Antibiotics are recommended for elective surgeries, surgeries that involve bone, patients taking medications that may predispose them to a higher risk for infection, and any implants or hardware.¹⁹ However, there are no clear guidelines accounting for the length of the procedure, with research suggesting that two half-lives of the antibiotic(s) used must be completed before administering another dose.¹⁰ There are also no clear guidelines for soft tissue procedures, such as tendon excisions. $^{10}\,$

Antibiotics should be administered 60 minutes prior to the first incision, with antibiotics that require longer infusion times, like vancomycin, administered 120 minutes before the surgery.¹⁰ However, a recent study by Tantigate et. al. revealed that there was no difference in the rate of SSI if antibiotics were administered less than 15 minutes prior to the first incision versus 15 to 60 minutes before the first incision.^{22,19} In this study of 1569 procedures, a priori power analysis was used to detect a 4% absolute increase in infection rate.²² A higher rate of SSIs was found in patients who received antibiotics more than 60 minutes before the surgery.²²

Comparing Local Modalities With Antibiotic Prophylaxis

Knighton et al conducted a study to evaluate the effects of inspired oxygen in comparison with antibiotics to reduce bacterial clearance in vivo. 9 groups with oxygenation ranging from 12% -45% fraction of inspired oxygen (FiO₂) was evaluated without antibiotics, in conjunction with antibiotics infused at the same time as the oxygenation, and antibiotics given 2 hours after the instigation of oxygenation were evaluated to see a change in lesion size and reduction in *E.coli* in the wound. ²³This study showed that oxygenation with 45% FiO₂ raised PO₂ levels from 10 to 40 mmHg, which is sufficient for bacterial killing by neutrophils. The results showed that while 45% FiO₂ alone did reduce lesion size, a combination with ampicillin significantly reduced lesion size (p<0.0001). ²³

In a 2019 study by Poilvache et al, methicillin-sensitive Staphylococcus aureus (MSSA) and methicillin-resistant Staphylococcus aureus (MRSA) biofilm strains were grown in vitro. Pulse lavage (PL) alone resulted in a reduction of bacterial counts (CFU) from 3-4 log₁₀ and reduce the biomass of MRSA and MSSA by 81.7% and 98% respectively.24 Flucloxacillin reduced CFU of MSSA by 3log₁₀ and biomass by 70% while vancomycin had no effects on MRSA.24 However, when used in combination with pulse lavage, with vancomycin for MRSA strains and flucloxacillin for MSSA strains, there was a statistically significant (p<0.0001) reduction in CFU and biomass in both strains, signifying that there is a greater effect on reducing bacterial count when pulse lavage and antibiotics are used in combination.24

In 2016, Karip et al. conducted a study to evaluate the potential of both antibiotic prophylaxis and antimicrobial coated sutures in preventing postoperative complications in patients who received surgical management for pilonidal sinus disease. In this study, the primary goal was to compare the incidence of early infections in patients who did and didn't receive antibiotic prophylaxis.²⁵ This goal was prematurely terminated, as the rate of infectious complications was too great in the group of patients that did not receive antibiotic prophylaxis.²⁵ The second goal of this study was to compare the rates of early infection between a group that received both antibiotic prophylaxis and triclosan coated sutures and a group that received antibiotic prophylaxis with conventional sutures.²⁵ The rate of micro-organism growth in the group who received triclosan coated sutures was 65.8% whereas the rate of micro-organism growth in the group who received conventional sutures was 75%.²⁵ Furthermore, both groups had similar occurrences of wound dehiscence.²⁵ Despite the slightly lower rate of infection in the group that received triclosan coated sutures, it was found that there was not a statistically significant difference between both groups.²⁵ Therefore, it was concluded in this study that only antibiotic prophylaxis was needed in this population.²⁵

Discussion

Surgical site infections can have a debilitating effect on the patient and an immense financial impact on the healthcare system. Therefore, it is increasingly important to methods to decrease the risks of SSIs.

A few ways to decrease the risk in the intraoperative setting are through perioperative oxygenation, antimicrobial irrigation, and antibiotic-coated sutures. Prophylactic antibiotics, given perioperatively, have been a standard of care for most podiatric surgeries.¹⁰

Local modalities, such as perioperative oxygenation and povidone-iodine irrigation, are frequently used in surgeries, but not often supported in literature. Perioperative oxygenation has been widely analyzed in the literature, especially when discussing abdominal surgeries. Since orthopedic and podiatric surgeries often indicate the use of a tourniquet during the procedure and have a different pathogenic and opportunistic flora, perioperative oxygenation may not translate the same effects when it comes to reducing SSIs. However, it has been found that in high-energy lower extremity fractures, such as pilon fractures, the use of perioperative oxygenation has been shown to be a safe and cost-effective measure to significantly decrease the rate of SSIs.28 Furthermore, when perioperative oxygenation is used in combination with antibiotics, further reduction of bacterial bioburden is achieved.²³ This suggests that even though perioperative oxygenation is more widely practiced in non-lower extremity surgeries, there is a high likelihood that this method of controlling surgical site infections would still be highly valuable in lower extremity surgeries.

Pulse lavage with povidone-iodine has been shown to be a great tactic in reducing bacterial load substantially. When comparing the effects of solely using perioperative antibiotics and using perioperative pulse lavage, antibiotics are shown to only minimally reduce bacterial load. This occurs because antibiotics alone are unable to penetrate biofilms that are created by both MSSA and MRSA. When both methods are used simultaneously, there is a considerable reduction in bacterial load, since pulse lavage with povidoneiodine has a higher ability to penetrate through biofilms. However, the utilization of pulse lavage with povidone-iodine can have a negative effect on thyroid function, although this was reported to be in a very minor number of patients and no serious harm has occurred.²⁹ Therefore, pulse lavage with povidoneiodine solution has been contraindicated in those with iodine sensitivity, burns, thyroid irrigation, and renal disease.²⁹ However, since the risk profile of povidoneiodine pulse lavage is limited and affects only a small portion of the study, it is still beneficial in reducing infection when used in combination with perioperative antibiotics in prosthetic joint implants, such as those used in arthrodesis procedures.

Antimicrobial sutures, which are often embedded with triclosan, have been demonstrated to have little to no adverse effects.^{30 31} Triclosan coated sutures have been shown to decrease periincisional pain (p<0.01) and edema when compared to nonantimicrobial coated sutures, and do not have an adverse effect on wound healing. 3º Given Triclosan's gram positive and gram negative coverage, it makes it efficacious against many organisms that are vastly prevalent throughout lower extremity pathology. Given the antibiotic properties within these sutures, there is a concern regarding the potential they carry to create resistance patterns among some significant pathogens. However, recent studies have demonstrated that the long term expose to triclosan, through measuring minimum inhibitory concentration, there was neither creation of antibiotic resistance nor diminishing antimicrobial activity.³⁰ Therefore, the use of triclosan coated sutures is indicated when there is a higher perceived risk of infection via contamination of patient's own skin flora or intraoperative aerosols. One of the major limitations to this form of controlling SSIs is their cost, as antimicrobial sutures often cost much more than noncoated sutures. Furthremore, it has been evidenced that when comparing the use of regular sutures in conjunction with antibiotic prophylaxis and triclosancoated sutures, there is no statistically significant reduction in SSIs between both methods.^{27,30} Therefore, the utilization of triclosan-coated sutures is

most highly warrated in very high risk surgeries taking place in large, urban, multicenter hospitals, and is not necessitated in everyday surgical use.

Surgical site infections remain as one of the most damaging complications.²⁷ Local modalities such as perioperative oxygenation, antimicrobial irrigation, and the use of antimicrobial sutures provide promising results in helping prevent these complications. While currently the standard of care in most procedures, antibiotic prophylaxis is not recommended in clean, elective surgery.¹⁹ If any metallic hardware is required, it is up to the surgeon's preference whether to use prophylactic antibiotics.¹⁹ It may be recommended to use local modalities in concert with antibiotic prophylaxis. However, further research is necessitated.

Some limitations to this study are that not all local modalities were discussed, such as adhesive taping, vancomycin powder, use of powderless gloves, preparation of the surgical site, operating room traffic, and surgical hand sepsis.²⁷ These modalities have a contributing factor in SSI prevention. Factors such as patient ASA score and inpatient duration were also not exclusively accounted for in this study.

Conclusion

In conclusion, the literature indicates that there are various methods that can aid in preventing surgical site infections including local perioperative measures as well as antibiotic prophylaxis. Overall, it was found that most local modalities, such as perioperative oxygenation and pulse lavage with povidone-iodine, are best used in conjunction with antibiotic prophylaxis to maximize the reduction in surgical stie infections.^{23,28,29} The use of triclosan coated sutures is not necessitated in every day surgical procedures, as it does not relay a significant reduction in SSIs.^{27,30} Future studies can be centered around the impact of patient-related factors, such as ASA status, on the efficacy of local modalities.

References

- Centers for Disease Control and Prevention. (CDC). Surgical site infection (SSI). Atlanta, GA: CDC; 2010. https://www.cdc.gov/hai/ssi/ssi.html. Accessed August 22, 2019.
- Cheadle WG. Risk factors for surgical site infection. Surg Infect (Larchmt). 2006;7 Suppl 1:S7-S11.
- Morkane, C.M., McKenna, H., Cumpstey, A.F. *et al.* Intraoperative oxygenation in adult patients undergoing surgery (iOPS): a retrospective observational study across 29 UK hospitals. *Perioper Med* 7, 17 (2018).
- D. Martin, M. Grocott, Recommendations for perioperative oxygenation, *BJA: British Journal of Anaesthesia*, Volume 115, Issue 5, November 2015, Page 802,
- Habre W, Peták F. Perioperative use of oxygen: variabilities across age. Br J Anaesth. 2014;113 Suppl 2:ii26-ii36.

- Goswami, K., & Austin, M. S. (2019). Intraoperative povidone-iodine irrigation for infection prevention. *Arthroplasty today*, 5(3), 306–308.
- Onesti MG, Carella S, Scuderi N. Effectiveness of antimicrobial-coated sutures for the prevention of surgical site infection: a review of the literature. *Eur Rev Med Pharmacol Sci.* 2018;22(17):5729-5739.
- Bustamante Montalvo M, Cainzos M, Prieto Carreiras L, et al. Evaluation of the effect of triclosan coated sutures in the prevention of surgical site infections in a Spanish hospital setting: A prospective, observational study. *Infect Prev Pract.* 2021;3(3):100154. Published 2021 Jun 7. doi:10.1016/j.infpip.2021.100154
- Crader MF, Varacallo M. Preoperative Antibiotic Prophylaxis. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; July 18, 2021.
- Boyd J, Chmielewski R. Prevention of Infection in Foot and Ankle Surgery. *Clin Podiatr Med Surg.* 2019;36(1):37-58. doi:10.1016/j.cpm.2018.08.007
- 11. Allegranzi B, Zayed B, Bischoff P, et al. New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: an evidence-based global perspective. *Lancet Infect Dis.* 2016;16(12):e288-e303.
- Hopf HW, Hunt TK, Rosen N. Supplemental oxygen and risk of surgical site infection. *JAMA* 2004; 291: 1956.
- Whiteside OJ, Tytherleigh MG, Thrush S, Farouk R, Galland RB. Intra-operative peritoneal lavage—who does it and why? *Ann R Coll Surg Engl* 2005; 87: 255– 58.
- Diana M, Hübner M, Eisenring MC, Zanetti G, Troillet N, Demartines N. Measures to prevent surgical site infections: what surgeons (should) do. *World J Surg* 2011; 35: 280–88.
- Pivot D, Tiv M, Luu M, Astruc K, Aho S, Fournel I. Survey of intraoperative povidone-iodine application to prevent surgical site infection in a French region. *J Hosp Infect* 2011; 77: 363–64
- Marco F, Vallez R, Gonzalez P, Ortega L, de la Lama J, Lopez-Duran L. Study of the efficacy of coated Vicryl plus antibacterial suture in an animal model of orthopedic surgery. *Surg Infect (Larchmt)* 2007; 8: 359– 65.
- 17. Rothenburger S, Spangler D, Bhende S, Burkley D. In vitro antimicrobial evaluation of Coated VICRYL* Plus Antibacterial Suture (coated polyglactin 910 with triclosan) using zone of inhibition assays. *Surg Infect (Larchmt)* 2002; **3** (suppl 1): S79–87.
- Storch ML, Rothenburger SJ, Jacinto G. Experimental efficacy study of coated VICRYL plus antibacterial suture in guinea pigs challenged with *Staphylococcus aureus*. Surg Infect (Larchmt) 2004; 5: 281–88.
- Modha MRK, Morriss-Roberts C, Smither M, Larholt J, Reilly I. Antibiotic prophylaxis in foot and ankle surgery: a systematic review of the literature. *J Foot Ankle Res.* 2018;11:61. Published 2018 Nov 15.
- Steiner CA, Karaca Z, Moore BJ, Imshaug MC, Pickens G. Surgeries in Hospital-Based Ambulatory Surgery and Hospital Inpatient Settings, 2014: Statistical Brief #223. In: *Healthcare Cost and Utilization Project (HCUP) Statistical Briefs.* Rockville (MD): Agency for Healthcare Research and Quality (US); May 2017.
- Deacon JS, Wertheimer SJ, Washington JA. Antibiotic prophylaxis and tourniquet application in podiatric surgery. J Foot Ankle Surg. 1996;35(4):344-349.
- Tantigate D, Jang E, Seetharaman M, et al. Timing of Antibiotic Prophylaxis for Preventing Surgical Site Infections in Foot and Ankle Surgery. *Foot Ankle Int.* 2017;38(3):283-288.

- Knighton DR, Halliday B, Hunt TK. Oxygen as an antibiotic. A comparison of the effects of inspired oxygen concentration and antibiotic administration on in vivo bacterial clearance. *Arch Surg.* 1986;121(2):191-195.
- Poilvache H, Ruiz-Sorribas A, Sakoulas G, Rodriguez-Villalobos H, Cornu O, Van Bambeke F. Synergistic Effects of Pulsed Lavage and Antimicrobial Therapy Against *Staphylococcus aureus* Biofilms in an *in-vitro* Model. *Front Med (Lausanne)*. 2020;7:527. Published 2020 Sep 17.
- Karip AB, Çelik K, Aydın T, et al. Effect of Triclosan-Coated Suture and Antibiotic Prophylaxis on Infection and Recurrence after Karydakis Flap Repair for Pilonidal Disease: A Randomized Parallel-Arm Double-Blinded Clinical Trial. Surg Infect (Larchmt). 2016;17(5):583-588.
- Katarincic JA, Fantry A, DePasse JM, Feller R. Local Modalities for Preventing Surgical Site Infections: An Evidence-based Review. J Am Acad Orthop Surg. 2018;26(1):14-25.
- Bosco JA 3rd, Slover JD, Haas JP. Perioperative strategies for decreasing infection: a comprehensive evidence-based approach. Instr Course Lect. 2010;59:619-28. PMID: 20415410.
- Stall A, Paryavi E, Gupta R, Zadnik M, Hui E, O'Toole RV. Perioperative supplemental oxygen to reduce surgical site infection after open fixation of high-risk fractures: a randomized controlled pilot trial. *J Trauma Acute Care Surg.* 2013;75(4):657-663.
- Chundamala J, Wright JG. The efficacy and risks of using povidone-iodine irrigation to prevent surgical site infection: an evidence-based review. *Can J Surg.* 2007;50(6):473-481.
- Edmiston CE, Seabrook GR, Goheen MP, et al. Bacterial adherence to surgical sutures: can antibacterial-coated sutures reduce the risk of microbial contamination?. J Am Coll Surg. 2006;203(4):481-489. doi:10.1016/j.jamcollsurg.2006.06.026
- Storch M, Perry LC, Davidson JM, Ward JJ. A 28-day study of the effect of Coated VICRYL* Plus Antibacterial Suture (coated polyglactin 910 suture with triclosan) on wound healing in guinea pig linear incisional skin wounds. *Surg Infect (Larchmt)*. 2002;3 Suppl 1:S89-S98.
- Zgonis T, Jolly GP, Garbalosa JC. The efficacy of prophylactic intravenous antibiotics in elective foot and ankle surgery. J Foot Ankle Surg. 2004;43(2):97-103.
- Dounis, E. Tsourvakas, S, Kalyvas L et al. Regional intravenous versus systemic intravenous prophylactic administration of third-generation cephalosporins (ceftazidime and ceftriaxone) in elective foot surgery. *The Foot* 5.3 (1995): 133-136

Examining the Overall Efficacy of the Addition of an Interspace Between the Popliteal Artery and Capsule of the Posterior Knee (iPACK) Block to an Adductor Canal Block in the Setting of Major Knee Surgery, a General Review

Todd Hinsch B.S., B.S.N., R.N. and Alexander Jonson B.S.

ABSTRACT

Objective: This paper aims to examine the general analgesic efficacy of the addition of the iPACK block to the adductor canal block versus the adductor canal block alone in the setting of major knee surgery.

Methods: A search was conducted using PubMed, Embase, Elsevier, and Google Scholar using the keywords "interspace between the popliteal artery and the capsule of the posterior knee block," "iPACK pain control and efficacy," and "addition of iPACK block to adductor canal block."

Results: The study done by Vichainarong et al. suggests the iPACK block offers no analgesic benefit when administered in the setting of surgeon-administered local infiltration analgesia, which was subsequently confirmed by the systematic review done by D'Souza et al. and the meta-analysis completed by Hussain et al.^{13,17,18} However, Vichainarong et al. did demonstrate that iPACK recipients had increased mobility and decreased overall length of hospital stay.¹⁷ This coincides with the results of the study by D'Souza et al. that found a decreased pain with movement score in those patients that received an iPACK block.¹⁸

Conclusion: With the varied outcomes of the studies included, the current literature does not support the use of the iPACK block for post-operative pain control. Specifically, it is not indicated for pain control when administered with an adductor canal block in the setting of surgeon administered local infiltration analgesia during major knee surgery. Based on the analysis of the included studies, the authors do not recommend the utilization of the iPACK block in standard peri-operative management of patients undergoing major knee surgery.

Introduction

Post-surgical pain is common and expected after invasive procedures, yet prognostic of a patient's outcome. The amount of pain experienced by a patient in the peri-operative and recovery period had been implicated in both recovery time and surgical outcomes. These undesired effects of pain have been linked to the stress response initiated by the body. In short, the greater amount of pain experienced often results in longer recovery times and poor patient outcomes.¹ This need for quality analgesia has driven the creation and utilization of new methods of pain management in the peri-operative period including nerve blocks to limit the use of opioids. This paper looks to examine the efficacy of one of the most recently developed nerve blocks, the interspace between the popliteal artery and the capsule of the posterior knee (iPACK) block in the setting of major knee surgery.

Traditionally, post-operative pain was managed with opioids. Common side effects of postoperative opioids include sedation, dizziness, nausea, vomiting, constipation, tolerance, and most applicable for immediate post-surgical care, respiratory depression.² Additionally, it has been demonstrated that individuals receiving outpatient procedures who take more opioids after surgery experience greater pain and less satisfaction with their pain relief.³ Due to these adverse outcomes, the multimodal approach to surgical pain control has grown in popularity amongst surgical and anesthesia providers. This approach to pain control includes the use of pharmacological agents such as oral and IV non-steroidal antiinflammatory drugs (NSAIDS), oral and IV opioids, epidural administration of opioids and anesthetics, and regional anesthesia injections.⁴ One of the most widely used and effective modalities included in this approach to pain control is the peripheral nerve block.⁵ This technique has gained favor due to its opioid-sparing effects and its ability to decrease the reliance on general anesthesia.⁴ Nerve blocks have a wide variety of applications for surgical pain control and have become a common practice for many orthopedic

procedures including the total knee arthroplasty (TKA).

Proper recovery from a TKA requires robust pain control while still preserving the ability for early patient mobilization. Considering this requirement, the addition of a peripheral nerve block to the TKA has become standard practice.⁶ Once widely used, the femoral nerve block (FNB) has lost favor due to muscular branch involvement, resulting in muscle weakness of the quadriceps.⁷ In response to this, the adductor canal block (ACB) was developed to aid in sparing the quadricep muscle function while retaining the analgesic benefit.^{8,9} Subsequently the ACB has emerged as a comparable replacement in major knee surgeries.^{10,11}

While these techniques have become the standard for post-operative pain control following major knee surgery, additional blocks have been developed to supplement their effects and increase pain coverage and further spare muscular involvement. Specifically, the use of regional tissue infusions of local anesthetics is being examined as a possible adjunct to both the ACB and the FNB.¹² The adjunctive block that has gained some notoriety of late is the iPACK block.¹³ This is a site-specific tissue infusion of local anesthetic injected behind the knee using ultrasound guidance. Its aim is to provide analgesia to the posterior capsule of the knee while preserving lower extremity motor function by sparing the main trunks of the sciatic nerve.¹⁴ Though the iPACK block was first described by Dr. Sanjay Sinha and his colleagues from St. Francis Hospital and Medical Center in Connecticut in 2012 as a potential improvement on past techniques, it was not until 2019 in which Tran et. al evaluated the injectate spread in both proximal and distal approaches in a cadaveric study.¹⁵ It was found at this time that there was coverage of the posterior genicular branch of the obturator nerve, superior medial genicular nerve, superior lateral genicular nerve, and anterior branch of the common fibular nerve.¹⁶ This paper aims to give a general summary and review regarding the general efficacy of adding the iPACK block to an ACB in the setting of major knee surgery.

Methods

A search was conducted using PubMed, Embase, Elsevier, and Google Scholar using the keywords "interspace between the popliteal artery and the capsule of the posterior knee block," "iPACK pain control and efficacy," and "addition of iPACK block to ACB." The literature was searched for studies that emphasized the addition of an iPACK block to an ACB for major knee surgery and its efficacy at providing pain control with highest consideration given to meta-analysis and randomized control trials. Both inpatient and outpatient studies were included in the review. The literature review was limited to English language papers. No restrictions were placed on publication date, but preference was given to those articles published in the last five years. Any article that did not address the iPACK blocks' efficacy at pain control in the post-operative period was excluded along with any article that did not involve the simultaneous use of an ACB.

Results

Vichainarong et al. examined the efficacy of adding an iPACK block to a continuous ACB with surgeon-administered local infiltration analgesia to improve pain control following a TKA. The study was conducted as a double-blind randomized control trial with 72 patients. The iPACK block was randomly assigned to different patients to examine if morphine utilization varied between groups in the first 24 hours after surgery. The group that received only the ACB and local infiltration anesthesia with no iPACK block had an average morphine utilization of 1.31mg +/-1.8mg. Whereas the group that received the iPACK block had a morphine utilization of 0.61+/- 1.25mg with a p-value of 0.08, indicating no significant statistical correlation between iPACK block administration and morphine utilization. The paper concluded that adding the iPACK block to the continuous ACB with local infiltration analgesia showed no significant difference in patient reported pain scores or in morphine utilization in the first 24 hours after surgery between the group that received the iPACK block and the group that did not. However, the group that received the iPACK block had increased post-surgical mobilization as evidenced by lower Timed Up and Go (TUG) scores on post-operative days one and two. The TUG test measured the time in seconds it took for a patient to stand up from a wheelchair, walk three meters, turn around, walk back, and sit back down in the same chair. The iPACK group showed a mean TUG score significantly lower than the control group with a mean post-operative day one difference of -30.3 seconds (p-value = 0.008) and mean post-operative day two difference of -38.9 seconds (p-value = 0.001).¹⁷

D'Souza et al. conducted a systemic review of randomized control trials comparing the effectiveness of analgesia delivered by the addition of the iPACK block against surgical pain control strategies that did not contain an iPACK block for TKA. This study looked at eight randomized control trials with a total of 777 patients included in the review. Bias, quality of each study, and outcome examined were evaluated using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) guidelines and software giving each outcome examined a GRADE score. GRADE scores are assessed based on the hierarchy of evidence provided and possible sources of bias in each article selected. A GRADE score of "high" indicates that the true effect lies close to the estimated effect. A GRADE score of "moderate" indicates that the effect is likely close to the estimated effect but could be inaccurate. A GRADE score of "low" indicates that the confidence in the estimated effect is limited. The primary outcome examined was post-operative opioid consumption in either the post anesthesia care unit (PACU) or during post-operative day one (POD1). Seven of the eight studies met this criterion, totaling 606 patients. Only one out of these seven studies showed a decrease in opioid use in patients that received the iPACK block. Five showed no significant difference in opioid utilization between patients that received the iPACK block and those that did not. One study showed an increase in opioid utilization in patients that received the iPACK block versus patients that did not. This primary outcome received a GRADE score of moderate. The secondary outcome examined postoperative pain score with movement in the PACU or during POD1. Five studies looked at this outcome totaling 389 patients. In three of these studies, patients who received the iPACK block reported decreased pain with movement in the PACU and on POD1. The remaining studies reported no statistical difference in pain with movement scores in the PACU or during POD1. This outcome received a GRADE score of low. In summation, this study showed that iPACK block administration was correlated with similar opioid use after 24 hours compared to without the addition of the iPACK block. The iPACK block group also showed a decreased movement pain score but similar or higher overall pain scores after a 24-hour period.¹⁸

Hussain et al. conducted a meta-analysis looking to evaluate the efficacy and analgesic benefit of adding the iPACK block to the ACB with surgeon administered local infiltration analgesia versus ACB alone for TKA. The main outcome examined in their study was pain severity at six hours in the post-surgical period. The secondary outcomes included opioid consumption at 24 hours, functional recovery and complications arising from the iPACK block itself. In total, 14 randomized control trials were analyzed with a total patient count of 1,044. For the main outcome of pain control of the iPACK block in the setting of ACB and local infiltration anesthesia, four trials were included with a total of 273 patients. These studies showed that adding the iPACK block to the ACB in the setting of surgeon administered local infiltration analgesia did not improve pain control or decrease recovery time. However, eight trials totaling 631 patients that received the ACB and the iPACK block without local infusion anesthesia were examined for pain control at six hours post-op. These studies showed that adding the iPACK block to the ACB reduced pain by a weighted mean difference of -1.33cm with a confidence interval of 95% and a pvalue of less than 0.00001.¹³

Discussion

The study done by Vichainarong et al. suggests the iPACK block offers no analgesic benefit when administered in the setting of surgeonadministered local infiltration analgesia. This was subsequently confirmed by the systemic review done by D'Souza et al. and the meta-analysis completed by Hussain et al.^{13,17,18} However, Vichainarong et al. did demonstrate that iPACK block recipients had increased post-operative mobility and decreased overall length of hospital stay.17 This coincides with the results of the study by D'Souza et al. that found a decreased pain with movement score in those patients that received an iPACK block.18 However this evidence was given a GRADE score of "low" indicating that confidence in the effect estimate is limited and the true effect of it is likely to be substantially different from the estimated effect.¹⁷

The primary limitation of this study is the limited available literature on the iPACK block itself. The iPACK block is a new local anesthesia modality, and its use is not widespread. Finding high quality evidence-based studies that specifically addressed our desired outcomes was limited in comparison to other well established nerve block techniques. Another limitation is the general structure of this review. The goal was to provide a summary of the available literature regarding the utilization of the iPACK block in the setting of major knee surgery. As such, no formal or systematic review process was utilized. Rather, a summation of relevant literature was found and used to formulate the conclusion and recommendations. Finally, this study only included outcomes related to pain control, opioid utilization, and post-operative mobility after major knee surgery. While these are good indicators of overall efficacy of the block many other outcomes could be examined such as length of hospital stay, rate of post-surgical recovery, or range of motion.

The results of this review have given some contradictory evidence to the addition of an iPACK block as an adjunctive mechanism for recovery from major knee surgery. All studies examined concluded that overall pain severity scores were not affected by the addition of the iPACK block when administered concurrently with surgeon administered localinfiltration analgesia. However, it was demonstrated to have a positive effect on post-operative pain control in the absence of surgeon administered local-infiltration analgesia.¹³ There was also evidence presented suggesting the iPACK block helps specifically with pain that occurs during movement in the immediate post-surgical period.^{10,17,18}

These findings can help guide and determine the proper avenue for further study and implementation of the iPACK block. The effects of the iPACK block and local infiltration analgesia need to be examined against each other to accurately assess which provides superior pain control and better postsurgical outcomes. Secondly, the decreased pain in motion experienced with iPACK block recipients, while not directly contributing to the overall pain control ratings, could contribute to the findings that patients that received iPACK blocks on average spent less time in the hospital post-surgery compared to those that did not. This correlation needs to be expanded upon in further studies to determine the role of the iPACK block in this outcome given the low GRADE score given by the researchers.¹⁷

Additionally, early mobilization in the postsurgical period following TKA has been demonstrated to increase pain control, decrease length of hospital stay, and increase positive surgical outcomes.¹⁹ The study by Vichainarong et al. provided data that may suggest a decreased time to first mobilization based on the mentioned differences in TUG scores.¹⁷ This could be a further area of investigation into the usefulness of the iPACK block. Lastly, any ultrasound-guided invasive peripheral nerve block carries some inherent risk. Given this risk, there is a need for investigation into the risk-to-benefit ratio of providing an iPACK block specifically for the purposes of pain control during movement and excluding it all together.

Conclusion

With the varied outcomes of the studies included, the current literature does not support the use of the iPACK block for post-operative pain control.

Specifically, it is not indicated for pain control when administered with an ACB in the setting of surgeon administered local infiltration analgesia during major knee surgery. Based on the analysis of the included studies, the authors do not recommend the utilization of the iPACK block in standard peri-operative management of patients undergoing major knee surgery.

References

- Kampitak, W., Tanavalee, A., Ngarmukos, S., & Tantavisut, S. (2020). Motor-sparing effect of iPACK (interspace between the popliteal artery and capsule of the posterior knee) block versus tibial nerve block after total knee arthroplasty: a randomized controlled trial. *Regional Anesthesia and Pain Medicine*, 45(4), 267–276.
- Benyamin, R. (2014). Opioid Complications and Side Effects Biologics for Back Pain View project Clinical Outcomes of Epidural Steroid Injections View project.
- Nota, S. P. F. T., Spit, S. A., Voskuyl, T., Bot, A. G. J., Hageman, M. G. J. S., & Ring, D. (2015). Opioid Use, Satisfaction, and Pain Intensity After Orthopedic Surgery. *Psychosomatics*, 56(5), 479–485.
- Kehlet, H., & Wilmore, D. W. (2002). Multimodal strategies to improve surgical outcome. *The American Journal of Surgery*, 183(6), 630–641.
- Lavie, L. G., Fox, M. P., & Dasa, V. (2016). Overview of Total Knee Arthroplasty and Modern Pain Control Strategies. *Current Pain and Headache Reports*, 20(11), 1–5
- Lavie, L. G., Fox, M. P., & Dasa, V. (2016). Overview of Total Knee Arthroplasty and Modern Pain Control Strategies. *Current Pain and Headache Reports*, 20(11), 1–5.
- Ganapathy S, Wasserman R, Watson J, et al. (1999) Modified continuous femoral three-in-one block for post-operative pain after total knee arthroplasty. *Anesthesia & Analgesia*, 89, (1197–1202).
- Kapoor R., Adhikary S.D., Siefring C., McQuillan P.M. (2012) The saphenous nerve and its relationship to the nerve to the vastus.medialis in and around the adductor canal: An anatomical study. *Acta Anaesthesiologica Scandinavica*, 56 (3), 365-367.
- Perlas A, Kirkham KR, Billing R, Tse C, Brull R, Gandhi R, Chan VW. (2013) The impact of analgesic modality on early ambulation following total knee arthroplasty. *Regional Anesthesia and Pain Medicine*. 2013 Jul-Aug, 38(4), 334-9.
- Qin, L., You, D., Zhao, G., Li, L., & Zhao, S. (2021). A comparison of analgesic techniques for total knee arthroplasty: A network meta-analysis. *Journal of Clinical Anesthesia*, 71, 110257.
- Yu, R., Wang, H., Zhuo, Y., Liu, D., Wu, C., & Zhang, Y. (2020). Continuous adductor canal block provides better performance after total knee arthroplasty compared with the single-shot adductor canal block? *Medicine*, 99(43), e22762.
- Kampitak, W., Tanavalee, A., Ngarmukos, S., & Amarase, C. (2019). Opioid-Sparing Analgesia and Enhanced Recovery After Total Knee Arthroplasty Using Combined Triple Nerve Blocks With Local Infiltration Analgesia. *The Journal of Arthroplasty*, 34(2), 295–302.
- Hussain, N., Brull, R., Sheehy, B., Dasu, M., Weaver, T., & Abdallah, F. W. (2021). Does the addition of iPACK to adductor canal block in the presence or absence of periarticular local anesthetic infiltration improve analgesic and functional outcomes following total knee arthroplasty? A systematic review and meta-analysis. *Regional Anesthesia and Pain Medicine*, 46(8), 713–721.

- 14. Clint E. Elliott, Salman Thobhani, The adductor canal catheter and interspace between the popliteal artery and the posterior capsule of the knee for total knee arthroplasty, Techniques in Regional Anesthesia and pain Management, 2014: 18(4):126-129.
- 15. Vlessides, M. New regional technique controls post-TKA
- pain, Anesthesiology News, 38 (2012), p. 1216. Tran J, Giron Arango L, Peng P, Sinha SK, Agur A, Chan V. Evaluation of the iPACK block injectate spread: a cadaveric study. Regional Anesthesia & Pain Medicine. 2019;44(7):689-694
- 17. Vichainarong, C., Kampitak, W., Tranavalee, A., Ngarmukos, S., Songborassame, N. (2020). Analgesic efficacy of infiltration between the popliteal artery and capsule of the knee (iPACK) block added to local infiltration analgesia and continuous adductor canal block after total knee arthroplasty: a randomized clinical trial. Regional Anesthesia and Pain Medicine, 45(11), 872-879.
- 18. D'Souza, R. S., Langford, B. J., Olsen, D. A., & Johnson, R. L. (2021). Ultrasound-Guided Local Anesthetic Infiltration Between the Popliteal Artery and the Capsule of the Posterior Knee (IPACK) Block for Primary Total Knee Arthroplasty: A Systematic Review of Randomized Controlled Trials. Local and Regional Anesthesia, Volume 14, 85-98.
- 19. Wang, F., Ma, W., & Huang, Z. (2021). Analgesia effects of IPACK block added to multimodal analgesia regiments after total knee replacement. Medicine, 100(22), e25884.

Evaluation of Similarities and Discrepancies in International Podiatry

Jacob Abjelina, B.S. and Chanelle Mariano, B.S.

ABSTRACT

Objective: The purpose of this study is to summarize the available information regarding podiatric education and scope of practice internationally. This study compared the requirements in education and scope of practice internationally among the 198 countries.

Methods: Google search engine was used to query the above categorical information for the 198 countries currently recognized by the Office of the Historian, United States Department of State. Only information from verified government websites, educational establishments, national Podiatric associations, and primary sources found on PubMed/NCBI were included.

Results: The findings of the study indicate diverse training, education, and practice across 28 countries that had reliable information available.

Conclusions: Inconsistencies of what defines podiatry as a medical field create confusion in regard to the importance of the practice.

Introduction

The beginnings of professional foot care can be traced to Ancient Egypt and became a more established profession in the 1800s.¹ In 1911, the first podiatry school in the United States opened, known as The New York School of Chiropody.² During this time, the prerequisite for admissions was one year of high school education. As the demand for podiatrists continued to expand, so did the need for medical knowledge in orthopedics, general medicine, and surgery.³ Other countries have adopted different programs for aspiring podiatrists, propelling the field of podiatry forward in society on an international level. With the aging population, the demand for podiatrists has increased. This demand for podiatry is being met in the United States through the nine podiatric colleges as well as the eligibility to perform surgery on patients.

This may not be the case in other countries, so there is a need to evaluate podiatric schooling and practice on an international level. Due to this lack of data, the purpose of this study is to provide a compilation of similarities and discrepancies between podiatric education and scope of practice around the world.

Methods

The investigated education and practice standards were modeled after the milestones required to achieve the title of Doctor of Podiatric Medicine (DPM) in the United States and were categorized into the following segments:

- Presence of a national podiatry association
- Degree requirements
- Prerequisite courses

- Admissions tests
- Length of medical school education
- Residency or continued education requirement
- Ability to perform surgery

The presence of a national podiatry association was included as a marker of a country's recognition of podiatry as a healthcare profession in that respective country. Criteria for the presence of a national podiatry association was the identification of a national body of podiatrists, a representing board, and/or an official website. Minimum degree requirements, prerequisite courses, admissions tests, and length of medical school education data were collected from national podiatry association websites and university admission websites.

Minimum degree requirement was defined as the successful acquisition of a required degree prior to attending a podiatric medical program. This was designated by minimum degree required: high school diploma, undergraduate diploma, or no requirement (none). Prerequisite courses were defined as successful completion of specific subject matter classes prior to admission to podiatric training. Admissions tests were interpreted as the successful passing of any pre-medical exam, like the MCAT or the specific country's equivalent, necessary for application. Length of medical education was measured in years. When calculating the average years of podiatric medical school, the upper limit of given ranges were used. In cases when the queried resource presented information in terms of semesters, one semester is reported as equivalent to half of one year.

Residency or equivalent training information was collected from national podiatry association websites as well as websites for individual educational programs within a specific country. The criteria for residency or equivalent training was defined as any mandatory clinical training program prior to licensing for approved medical practice.

Lastly, scope of surgical practice data was acquired from national podiatry association websites. Surgical practice was further subdivided into three scopes: full, which indicates that podiatrists have surgical privileges within their anatomical scope of practice; limited, which are those that can perform nail procedures and selective skin procedures; and none, which indicates that podiatrists of that country are not granted surgical privileges. "Full*" indicates surgical rights achievable with additional training beyond residency or equivale

Google search engine was used to query the above categorical information for the 198 countries currently recognized by the Office of the Historian, United States Department of State. Only information from verified government websites, educational establishments, national podiatric associations, and primary sources found on PubMed/NCBI were included. The keywords searched included the title of each category by country as well as alternate terms such as, "foot and ankle specialists", "podiatrists", "chiropody", "national organization", "podiatry schools", "requirements", and "programs". Sources in the English language or those that could be translated to English via Google Translate were included.

Results

Country [Reference]	National Association	Minimum Degree Requirements	Prerequisite Courses	Admissions Test	Length of Medical Education	Residency or Equivalent	Surgery
Argentina [4]	None	High School Diploma	-	-	3 Years	Yes	Limited
Australia [5, 6]	Yes	High School Diploma or Undergraduate Degree	Yes	Yes	3 years	Yes	Full
Belgium [7, 8]	Yes	High School Diploma	-	None	3 Years	None	None
Brazil [9, 10, 11]	None	Undergraduate Degree	-	-	3.5 Years	-	-
Brunei [12]	None	-	Yes	-	3-4 Years	-	Limited
Canada [13]	Yes	Undergraduate Degree	Yes	None	4 Years	None	Full
China [14]	None	-	-	-	-	-	Full
Denmark [15, 16]	Yes	High School Diploma	Yes	None	1.5 years	None	None
Finland [17]	Yes	High School Diploma	Yes	None	3.5 Years	None	None
France [18]	Yes	High School Diploma	Yes	None	3 Years	Yes	None
Germany [19, 20, 21]	None	Undergraduate Degree	Yes	-	2-4 Years	Yes	-

Iceland [22]	Yes	High School Diploma	Yes	None	1.5-2 Years	None	Limited
Ireland [23, 24]	Yes	High School Diploma	Yes	None	3-4 Years	-	Limited
Israel [25]	None	-	Yes	-	-	-	Full
Italy [26]	Yes	High School Diploma	Yes	Yes	3 Years	None	None
Malta [27]	Yes	Undergraduate Degree	Yes	None	4 years	None	Limited
The Netherlands [28]	Yes	High School Diploma	Yes	None	3 Years	None	None
New Zealand [29]	None	Undergraduate Degree	Yes	None	3 Years	None	Limited
Norway [30]	Yes	High School Diploma	Yes	None	1.5 years	None	None
Poland [31]	None	Undergraduate Degree	Yes	-	2 Years	-	None
Portugal [32]	Yes	High School Diploma	Yes	None	4 Years	Yes	None
South Africa [33, 34]	Yes	Undergraduate Degree	Yes	None	1-3 Years	-	-
Spain [35]	None	Undergraduate Degree	Yes	None	4 Years	None	Full
Sweden [36, 37, 38, 39]	Yes	High School Diploma	Yes	None	1.5 Years	None	None
Switzerland [40]	Yes	High School Diploma	Yes	None	3 Years	None	Limited
United Kingdom [41, 42, 43]	Yes	High School Diploma or Undergraduate Degree	Yes	-	3-4 years	-	Full*
United States [44]	Yes	High School Diploma	Yes	Yes	4 Years	Yes	Full
Uruguay [45]	None	High School Diploma	Yes	None	3 Years	None	None

Table 1: Summarized Data for the 28 included countries

Of the 198 countries currently recognized by the Office of the Historian, information regarding podiatric medical schooling and practice could be found for 28 countries. The results of the search are compiled in Table 1. For the 170 countries that are not included in Table 1, no reliable resources or insufficient data could be found regarding the categories investigated.

Of the 28 countries included in Table 1, 64% have a nationally recognized podiatric society.

For the majority of the included countries (54%), the minimum degree requirement for entry into

a podiatric training program is a high school degree. 29% require a form of undergraduate education and 7% are offered a choice to begin schooling after high school or after university education. No information could be found for the remaining 11%.

In terms of the requirement to take prerequisite courses prior to entering podiatric schooling, 86% require taking certain classes before entering. Information regarding the remaining 14% could not be found. Regarding the requirement to take an admissions test, 43% required an admissions test,
25% did not require one, and no information could be found in the remaining 32%.

With reference to length of schooling, most podiatric education is completed after 1.5 - 4 years. 26 countries had information for this category, requiring an average of 3.1 years of schooling.

With regards to residency requirements, only 21% required a formal residency program or postgraduate training. 50% did not require a residency program or an equivalent and no information could be found for the remaining 29%.

Of the 28 countries included in Table 1, practicing podiatrists are eligible to perform surgery in 25% within their anatomical scope of practice. 25% have limited surgical privileges, 39% are not able to perform any type of surgery, and no info could be found for 11%.

Discussion

Exploring the different avenues and requirements in the education and training of all podiatric physicians is a necessary first step to evaluating the status and perception of the profession not just domestically but globally. Although this investigation compares medical schooling between unequivocal medical systems, summarizing and general differentiation assists in preliminary indexing of education requirements and training that can act as the foundation of future detailed investigations and comparisons.

The summarized findings of Table 1 reveal the significant diversity of podiatric medicine across multiple countries due to the wide range of training requirements and scope of practice. As all fields of healthcare are subjected to increased globalization, this diversity may pose a challenge to international podiatric collaboration, as the discrepancies in training and/or clinical and surgical experience can create communication and cooperation conflicts despite being of the same profession.

When compared to the training of podiatric physicians and surgeons in the United States, podiatry in other countries is more limited in scope and training, with the notable exceptions of Australia and the United Kingdom. In terms of degree requirements, prerequisite courses, training and scope of practice, Australia and the United Kingdom can be viewed as more similar to the United States than most other countries.^{7, 8, 42, 43, 44}

The difference in status is reflected in title differences, like podiatrists being technicians and not practitioners in some countries such as Uruguay, as well as in practical privileges, like in Belgium where podiatrists are restricted from performing major surgeries and are only subject to referral from orthopedists, neurosurgeons, vascular surgeons, etc.⁹,

10, 45 The benefits of podiatric services are well demonstrated in domestic literature and growing internationally. The perceived lack of benefit of podiatric services in other countries may be lagging until recently due to the allocation of these services to other specialties like orthopedics and dermatology as well as the differences in practice between American podiatry and podiatry of other countries. However, growth is apparent as seen in the recognition that a need for podiatrists exists in countries such as the United Kingdom which offers incentives, such as dedicated support scholarships and stipends, for those who do choose to become a podiatrist.⁴² Additionally, countries such as Canada are expanding their medical education requirements to imitate the rigor of training in the United States.15

The lack of podiatry programs across the world and thus the unfamiliarity with the profession has also limited the number of potential students. To combat further misinformation and unfamiliarity, it is important for those aspiring podiatrists to understand the field of podiatry and what type of practice is offered in each country. This summary may present interested parties an introduction to the available options for podiatric education internationally. Additionally, in an age of growing interest in studying abroad and world travel, this data can be used by aspiring podiatrists interested in learning more about how to gain licensure for practice in specific countries, including the different limitations of practice and educational requirements, as well as by travelers as a means of comparing their home country's podiatric standards and scope to that of the country of injury.

Internet web search restrictions and language barriers acted as limitations to the potential breadth of information that could be included in this study. Due to the restriction of English language sources, searches for certain policies were limited, and, despite translation applications, some sources were not deemed reliable enough to be included in the data pool due to translation inconsistencies. Therefore, those countries not included in the results do not necessarily lack podiatry as a profession, but rather keywords for online searches could not be accurately produced due to language differences or were overlooked due to the unavailability of the resource in English. Additionally, clarification for certain inconsistencies was difficult to obtain in order to appropriately summarize the available data. For example, Brunei and Ireland consider podiatry a surgical practice, but practitioners within those countries are limited to nail and skin procedures.^{14, 25} Additionally, podiatric schools in the United Kingdom have different requirements for admission, but not necessarily common prerequisites.43 The lack of standardization of prerequisites and training between countries and even

within training programs of the same country poses challenges to allocation of data for this investigation.

Conclusion

The summarized data was compiled to evaluate the opportunities for propelling podiatry forward amongst societies around the world through collaboration and standardization. This data may also serve as a reference when considering medical services if studying or traveling abroad as well as summarized data for aspiring students. Future investigative studies could explore the professional and societal perceptions of podiatry as a medical and surgical specialty due to the limited training and requirements needed to become licensed in foreign countries.

References:

- Advanced Foot and Ankle Center. 2019. The History of Podiatry - Advanced Foot and Ankle Center. https://afacutah.com/the-history-of-podiatry/ Accessed 5 July 2021.
- Nycpm.edu. n.d. New York College of Podiatric Medicine. https://www.nycpm.edu/history.asp Accessed 5 July 2021.
- Levy, L., 2020. Podiatry and the Exploding Growth of the Aging Population. *Podiatry Management*. https://podiatrym.com/pdf/2019/12/Levy120web Accessed 5 July 2021.
- Podologia.fmed.uba.ar. 2021. PODUBA Escuela Universitaria de Podología. http://www.podologia.fmed.uba.ar/ Accessed 5 July 2021.
- Podiatry.org.au. 2021. About Australian Podiatry Association Ltd. https://www.podiatry.org.au/about/podiatry-career
- Accessed 5 July 2021.
 Podiatry.org.au. 2021. Australian Podiatry Association - Find a podiatrist near me.
- https://www.podiatry.org.au/ Accessed 5 July 2021.
- Podologie.be. 2021. Home Belgische Vereniging der Podologen. https://www.podologie.be/ Accessed 5 July 2021.
- Ejustice.just.fgov.be. 2021. LOI WET. http://www.ejustice.just.fgov.be/cgi_loi/change_lg.pl?la nguage=fr&la=F&cn=2016030713&table_name=loi Accessed 5 July 2021.
- I-fab.org. 2021. *iFAB International Foot and Ankle Biomechanics Community (i-FAB)*. http://www.i-fab.org/ Accessed 5 July 2021.
- Universidade Anhembi Morumbi. 2021. PODOLOGIA | Universidade Anhembi Morumbi. https://portal.anhembi.br/graduacao/cursos/podologia/# sobre Accessed 5 July 2021.
- Portal.anhembi.br. 2021. https://portal.anhembi.br/wpcontent/uploads/2020/08/Podologia_PPC-Resumido-Mooca.pdf Accessed 5 July 2021.
- Moh.gov.bn. 2021. Ministry of Health Podiatrist. http://www.moh.gov.bn/SitePages/Podiatrist.aspx Accessed 5 July 2021.
- Podiatrycanada.org. 2021. FAQs Canadian Podiatric Medical Association. https://www.podiatrycanada.org/faqs/ Accessed 6 July 2021.

- Puhuahospital.com. 2021. Podiatry | Beijing Puhua International Hospital. http://puhuahospital.com/departments/podiatry Accessed 6 July 2021.
- Fodterapeut.dk. 2021. Danske Fodterapeuter | Danske Fodterapeuter © 2021. https://www.fodterapeut.dk/ Accessed 6 July 2021.
- Netvaerksportalen.dk. 2021. LasF Landsforeningen af statsautoriserede Fodterapeuter | Netværksportalen -Vejen til nye netværk! Foreninger og netværk i Danmark. http://www.netvaerksportalen.dk/lasflandsforeningen-af-statsautoriserede-fodterapeuter Accessed 6 July 2021.
- Sjjl.fi. 2021. TERVETULOA! Suomen Jalkojenhoitaja- ja Jalkaterapeuttiliitto ry. https://www.sjjl.fi Accessed 6 July 2021.
- 18. Fnp-podologues.fr. 2021. https://www.fnp-podologues.fr/ Accessed 6 July 2021.
- PodiatryInternational.com. 2021. Podiatry in Germany

 PodiatryInternational.com.
 https://podiatryinternational.com/podiatry-in-germany/ Accessed 6 August 2021.
- Gesetze-im-internet.de. 2021. PodG Gesetz über den Beruf der Podologin und des Podologen. https://www.gesetze-iminternet.de/podg/BJNR332010001.html Accessed 6 July 2021.
- Podo-Deutschland. 2021. Ausbildung. https://www-podo--deutschland-de.translate.goog/derberuf/ausbildung? x_tr_sl=auto&_x_tr_tl=en&_x_tr_hl =en-US Accessed 6 July 2021.
- 22. Fotur.is. 2021. Fótur.is FÍF. https://www.fotur.is/ Accessed 6 July 2021.
- 23. Nuigalway.ie. 2021. *Programmes NUI Galway*. https://www.nuigalway.ie/podiatricmedicine/programm es/ Accessed 6 July 2021.
- SCPI. 2021. About SCPI. https://www.podiatryireland.ie/about-us/ Accessed 6 August 2021.
- Nefesh B'Nefesh. 2021. Podiatry. https://www.nbn.org.il/aliyahpedia/employmentisrael/degrees-licensing/podiatry/ Accessed 6 July 2021.
- Associazionepodologi. 2021. Associazione Podologi. https://www.associazionepodologi.it/ Accessed 6 July 2021.
- Podiatry.org.mt. 2021. APM | Association of Podiatrists Malta. https://www.podiatry.org.mt/ Accessed 6 July 2021.
- De podotherapeut, de specialist in de voetengezondheidszorg. 2021. De podotherapeut, de specialist in de voetengezondheidszorg - NVvP. https://www.podotherapie.nl/ Accessed 6 July 2021.
- Aut.ac.nz. 2021. Study Podiatry Bachelor of Health Science - AUT. https://www.aut.ac.nz/study/studyoptions/health-sciences/courses/bachelor-of-healthscience-in-podiatry Accessed 6 July 2021.
- Fot og Helseakademiet. 2021. Utdanning i fotterapi med ortopediteknikk VG2/3. https://www.fotoghelseakademiet.no/vg2vg3-fotterapimed-ortopediteknikk/ Accessed 6 July 2021.
- Wsbinoz.edu.pl. 2021. Rodzaje studiów podyplomowych - WSBiNoZ Łódź. https://www.wsbinoz.edu.pl/oferta-ksztalcenia/studiapodyplomowe/rodzaje-studiow-podyplomowych Accessed 6 July 2021.
- 32. APP | Associação Portuguesa de Podologia. 2021. APP. https://appodologia.com/ Accessed 6 July 2021.

- Podiatry Association of South Africa. 2021. Podiatry Association of South Africa. https://podiatrist.co.za/ Accessed 6 July 2021.
- Uj.ac.za. 2021. Podiatry Master in Health Sciences Podiatry. https://www.uj.ac.za/faculties/health/Podiatry/Pages/M

aster-in-Health-Sciences-Podiatry-.aspx Accessed 6 July 2021.

- Unileon.es. 2021. Grado en Podología | Universidad de León. https://www.unileon.es/estudiantes/ofertaacademica/grados/grado-en-podologia Accessed 6 July 2021.
- Fotförbundet. 2021. Fotförbundet Hitta närmaste fotvård. https://sverigesfotterapeuter.com/ Accessed 6 July 2021.
- Medlemmar.fotforbundet.com. 2021. https://medlemmar.fotforbundet.com/wpcontent/uploads/2021/06/UTBILDNINGAR-2.pdf Accessed 6 July 2021.
- Norrlands Yrkeshögskola. 2021. Hem Norrlands Yrkeshögskola. https://www.nyhs.se/ Accessed 6 July 2021.
- 39. Yrgo. 2021. Yrgo, högre yrkesutbildning Göteborg. https://www.yrgo.se Accessed 6 July 2021.
- Schweizerischer Podologen-Verband SPV. 2021. Schweizerischer Podologen-Verband SPV - Podologie Schweiz. https://www.podologie.swiss/ Accessed 6 July 2021.
- College of Podiatry. 2021. Training to become a podiatrist. https://cop.org.uk/become-a-podiatrist/ Accessed 6 July 2021.
- 42. Healthcentre.org.uk. 2021. UK Schools of Podiatry. https://www.healthcentre.org.uk/podiatry/uk-schoolsof-podiatry.html Accessed 6 July 2021.
- College of Podiatry. 2022. Becoming a Podiatric Surgeon. https://rcpod.org.uk/become-apodiatrist/career-opportunities-and-scope/podiatricsurgeon#:~:text=There%20are%20currently%20two%2 0MSc,by%20the%20University%20of%20Huddersfield Accessed 3 March 2022
- 44. The American Association of Colleges of Podiatric Medicine (AACPM). 2021. Becoming a Podiatric Physician - The American Association of Colleges of Podiatric Medicine (AACPM). [online] Available at: https://aacpm.org/becoming-a-podiatric-physician/ Accessed 6 July 2021.
- 45. Portal Udelar. 2021. *Portal Udelar*. https://udelar.edu.uy/portal/ Accessed 6 July 2021.

Podiatric Physician Perspective on the use of Cannabidiol (CBD) in the Treatment of Foot and Ankle Pathology

Harsh Varshney, B.S. and Douglas Weng, B.S.

ABSTRACT

Objective: With the growth of alternative medicines and ongoing legalization of marijuana, cannabidiol products are becoming increasingly popular as a treatment modality. Pre-existing research has found implications for the use of CBD in pain management which warrants additional research into its application in the field. The aim of this study was to learn about physician views towards CBD and its potential role for pain management, specifically in the field of podiatric medicine.

Methods: Data was collected utilizing a Qualtrics survey platform. Questionnaire answers were collected through optional participation via electronic mail and data was stored through the Qualtrics platform. The study was designed with anonymous participation to reduce influence of bias. Question content is included in the data and discussion sections below.

Results: Quantitively, a total of 46 responses were recorded for this study. From a qualitative standpoint, the survey design included an open response section from participants which also allowed important considerations for potential future research taking into account different forms of CBD products and their administration. **Conclusion:** The data suggests that there is a positive shift towards the perception of CBD use in podiatric practice. Further research needs to be conducted on the long-term effects of CBD as well as how CBD plays into context-

specific pathologies as they pertain to the field of podiatric medicine.

Introduction

Chronic pain is an ever growing pandemic across the globe. In Europe, debilitating chronic pain affects 1 in 4 people in elderly populations.¹ In Australia, over 80% of patients in nursing homes suffer persistent pain.² In the United States (US), 20% of adults have chronic pain with 8% having pain that limits at least one major life activity.³

Pain management is a growing field in the practice of medicine as well as the various modalities used to mediate pain. As of December 2020, 36 states in the U.S. have legalized cannabis use for medicinal purposes. Clinical evidence suggests that Cannabidiol (CBD) produces therapeutic benefits in certain conditions and improves quality of life. In recent years, the use of CBD has also gained significant attention due to its therapeutic effects being free from psychoactive effects associated the with tetrahydrocannabinol (THC).4 This study focuses on one aspect in particular: Cannabidiol and the endocannabinoid system, specifically in the field of podiatric medical care.

Background

CBD is termed a phytocannabinoid as the compound originates from the *Cannabis* genus of plants.⁵ CBD is less known compared to its more mainstream counterpart tetrahydrocannabinol, better known as THC which is also derived from *Cannabis* and known for its psychoactive inducing effects.

In 1988, Howlett et al⁶ discovered the first cannabinoid receptor (CB1) and in 1993, Munro⁷ discovered a second (CB2). Both were seven domain G protein coupled receptors affecting cyclic AMP in areas related to nociceptive pain along the central and peripheral nervous system.⁸

In 2006, Mackie⁹ performed a study that showed CB2 as an important mediator for suppressing both pain and inflammatory responses. Similar sentiments were produced by Wade in 2003.¹⁰ Even with these studies, however, no endocannabinoids had been clinically administered to humans yet, possibly due to legalities, patentability issues and commercial feasibility at the time. These issues have led to "black market" CBD products that can be viewed as having hindered the progression of CBD products into legal market as non-FDA approved products are pushed with less care towards mislabeling and contamination issues, FDA 2020.¹¹

However, as of 2018, the US Hemp Farming Act legalized the cultivation and refinement of hemp and its constituents, thus starting a trend of mass marketing for CBD products.4 This has further lead to a marked increase in its use and viability as a treatment option.9 As commercial use of CBD is still relatively limited, there have been few studies looking into the practical benefits of CBD use in general or practice specific settings, leading to this study on provider perspectives on its use in podiatric medicine. There are also few studies on side-effects and potential overuse of CBD products, though exploration in recent literature has noted some potential hazards that may include teratogenicity in offspring of pregnant women and contamination with other chemicals.^{11,12,13} It is worth noting that the lack of peer reviewed overviews may contribute to the lack of widespread use among practicing physicians.

The current scientific data has shown that the use of CBD is context-specific and cannot be universally applied yet.⁴ Thus, the question of how the use of CBD is perceived by podiatric physicians in practice today was formulated. The objective of this study was to learn about physicians' attitudes and views towards CBD and its potential role in pain management, specifically in the field of podiatric medicine.

Methods

A survey was designed to measure provider opinions and consisted of a total of 14 questions. The first question included a consent request. The following questions were designed to collect data as it pertains to the objective. Qualtrics was used to administer this survey and responses were anonymously collected. The survey was designed to understand how podiatric providers perceive the use of CBD products in practice and was sent out to practicing podiatric physicians in the state of California. After receiving IRB approval to conduct this study, funding for this project was granted through the WesternU Office of Research and Biotechnology. There was no conflict of interest for this study and no funding was received from the CBD industry.





Figure 1.1 How often do patients inquire about CBD products?



Figure 1.2 Have you read medical literature on CBD?



Figure 1.3 Has your reading of medical literature affected your opinion on the use of medical CBD?



Figure 1.4 I believe there is adequate SAFETY data for routine use of CBD in podiatric settings



Figure 1.5 I believe there is adequate EFFICACY data for routine use of CBD in podiatric settings



Figure 1.6 I feel I need more information/guidance regarding the use of CBD products in medicine



Figure 1.7 I feel confident advising patients regarding the use of CBD products



Figure 1.8 What reason/s leads to reservations on advising patients regarding CBD?



Figure 1.9 Do you currently recommend CBD products to your patients?



Figure 1.10 How likely are you to suggest CBD for the following?



Figure 1.11 Do you believe the use of CBD products is a public health concern?



Figure 1.12 Do you believe CBD products contain some chemicals that may cause long term effects?



Figure 1.13 Do you believe CBD products should be regulated by the FDA?

Discussion

The survey first considered how often patients inquire about CBD products. Of the 46 participants, 90% of responses indicated some level of inquiry. This is correlated to the survey question in which all providers agreed they need more information on its use. This led to the understanding that a patient pool that is more prone to ask questions about CBD would lead to providers who would want to be more educated on its efficacy. The survey also showed that providers who had already read existing medical literature, tended to provide a more positive outlook on the use of medical CBD.

Figure 1.2 shows 54% of the pool indicated they had read medical literature on the use of CBD and of that group, 80% indicated that their own readings had positively impacted their perception on its use whereas the other 20% indicated that their readings had neither positive nor negative impact. These results suggest that education on the topic leads to a more positive outlook on the use of CBD. When this same pool of participants was asked about the safety and efficacy of CBD use, 64% had positive views on its efficacy in routine use within a podiatric setting as shown in Figure 1.5. However, it should be noted that with 64% of practicing physicians having a positive view on the efficacy of CBD, only 52% agreed that there was adequate literature on safety in routine use.

However, data showed that a positive perception of CBD does not translate to actual use. Distribution of data seen in Figure 1.7 led us to understand that there was a split between those who did and did not feel confident advising the use of CBD products to patients with 39% confident, 44% not confident and 17% unsure. Figure 1.8 shows the most common reason for hesitation amongst those who did not feel as confident was the lack of sufficient research conducted and not enough personal knowledge. Research suggests that there are a lack of studies performed on the use of CBD in practice, specifically as it applies to podiatric medicine and the efforts to discuss the long-term complications of CBD use are still lacking and require more attention in order to provide a shift in the use of CBD in practice.⁴

When asked about four specific pathologies, data in Figure 1.10 shows a similar pattern of distribution in regard to how likely the provider would suggest the use of CBD with a slight increase in "neither likely nor unlikely." The data suggests that although providers feel more comfortable advising on the products, it was indicated that they would still like more research on them. Figure 1.10 also showed providers being more likely to advise CBD for nerve pain and arthritic pain and less for post operative pain.

As previously noted, Aviram and Samuelly-Leichtag 2017¹⁴ showed the use of CBD in medicine being context-specific and preclinical/clinical studies having indicated a potential benefit of CBD use in chronic pain associated with multiple conditions. Serpell et al¹¹ conducted a study that demonstrated the ability of CBD to reduce neuropathic pain. Furthermore. CBD has demonstrated antiinflammatory effects in conditions including arthritis through the interaction of cannabidiol products with the body's endocannabinoid system.¹⁵ Subsequently, this has been the focus of research into possible arthritis therapies.

In addition to the anonymous quantitative questions provided in the survey study, participants were provided an open response section. Multiple providers indicated a preference for topical over oral administration. In conjunction with the data presented in Figures 1,7,11,12, these additional responses suggest that lack of research and insufficient personal education leads to increased caution with oral medication. Additionally, it was noted that CBD use amongst some podiatric providers received recommendations of its use from providers in other specialties, including anesthesiologists. This data may lead to future studies further examining provider recommendations for its use in specific pathologies over others.

When considering the potential to be a public health concern, Figure 1.11 shows 61% of participants

indicated they do not consider it a public health concern. However, Figure 1.13 shows 57% of participants indicated that its use should be regulated by the FDA. With the increase in legalization of CBD products across the country and subsequent increase in sales of these products in the commercial market, it is important to have a regulatory system in place to provide for the safe dissemination of these products.

Our study mirrors the current climate of CBD use as a treatment modality in the medical field. There is an increase in patient curiosity as the products become more commercially recognized alongside an increase in provider inquiries about the efficacy in its use. Data in this study confirms the need for increased research in this field and suggests continued education amongst providers is needed if CBD products are to be a more commonly used modality in podiatric settings. Future studies showing increased efficacy over current treatment options may lead to increased comfortability in provider recommendations. In addition, CBD use as a form of adjunct treatment in podiatric practice has yet to be explored. CBD's potential role in the multimodal approach to pain management is a branch that requires further research as its unique pathway has not yet been addressed by other analgesics.

Limitations in this study included the data collection process. The original data collection process was to be done in person at the Western Foot and Ankle Conference. Due to pandemic limitations changing the conference to a virtual platform, data collection procedures needed to be modified which inevitably led to changes in the potential study sample size. Data collection was also altered as sample pools became geographically isolated. It is recognized that the results extrapolated from data collected may be skewed to the cultural views of a specific geographic area and may differ provided a wider sample size. In addition, it is understood that legislation surrounding the use of CBD products in California may vary from other regions across the country.

Conclusion

Overall, the data showed a neutral-to-positive shift toward the use of CBD products in podiatric practice. With developing research these products may have their place in treatment plans. In regard to education, the results from Figure 1.6 indicate that additional Continuing Medical Education courses could be implemented into the curriculum for providers. Further research can be conducted to examine the level of pain relief experienced, the types of pain and conditions that can be treated with CBD, and short to long term effects of these products.

References

- Frondini C, Lanfranchi G, Minardi M, et al. Affective behavior and cognitive disorders in the elderly with chronic musculoskeletal pain: the impact on an aging population. *Arch Gerontol Geriatr.* 2007;44(Suppl 1):167–71
- Gibson SJ, IASP global year against pain in older persons: highlighting the current status and future perspectives in geriatric pain. *Expert Rev Neurother*. 2007;7:627–35.
- Dahlhamer J, Lucas J, Zelaya C, Nahin R, Mackey S, DeBar L, Kerns R, Von Korff M, Porter L, Helmick C. Prevalence of chronic pain and high impact chronic pain among adults – United States, 2016. MMWR. 2018;67:1001-1006
- Argueta D, Ventura, C, Kiven, S, Sagi V, Gupta K. A Balanced Approach for Cannabidiol Use in Chronic Pain. *frontiers in Pharmacology*. April 2020;11: 561
- 5. Pate D. Chemical ecology of cannabis. *Journal of the International Hemp Association*. 1994;**2**:32–7.
- Howlett GM, Johnson MR, Melvin LS. Nonclassical cannabinoid analgetics inhibit adenylate cyclase: development of a cannabinoid receptor model. *GM Mol Pharmacol. 1988 Mar; 33(3):297-302.*
- Munro S, Thomas KL, Abu-Shaar M., Molecular characterization of a peripheral receptor for cannabinoids. *Nature*. Sep 21 993;365(6441):61-5.
- Fox A, Kesingland A, Gentry C, McNair K, Patel S, Urban L, James I. The role of central and peripheral Cannabinoid1 receptors in the antihyperalgesic activity of cannabinoids in a model of neuropathic pain. *Pain. 2001 May*; 92(1-2):91-100.
- Mackie K. Cannabinoid receptors as therapeutic targets. Annu Rev Pharmacol Toxicol. 2006; 46():101-22.
- Wade DT, Robson P, House H, Makela P, Aram JA. Preliminary Controlled Study to Determine Whether Whole-Plant Cannabis Extracts Can Improve Intractable Neurogenic Symptoms. *Clin. Rehabil.* 2003; 17(1): 21–29. doi: 10.1191/0269215503cr581oa
- 11. Report to the U.S. House "Sampling Study of the Current Cannabidiol Marketplace to Determine the Extent That Products are Mislabeled or Adulterated Report in Response to Further Consolidated Appropriations Act, 2020," FDA. Jul, 2020. https://hempindustrydaily.com/wpcontent/uploads/2020/07/CBD-Marketplace-Sampling RTC FY20 Final.pdf
- Serpell M, Ratcliffe S, Hovorka J, Schofield L, Tayle H, Lauder E. A double-blind, randomized, placebo-controlled, parallel group study of THC.CBD spray in peripheral neuropathic pain treatment. *European Journal of Pain* 2014;18(7):999-1012.
- Bonn-Miller MO, Loflin MJE, Thomas BF, Marcus JP, Hyke T., Vandrey R. Labeling Accuracy of Cannabidiol Extracts Sold Online. *JAMA* 318. 2017;318(17):1708–1709. doi: 10.1001/Jama.2017.11909
- 14. Aviram, J., Samuelly-Leichtag, G. (2017). Efficacy of Cannabis-Based Medicines for Pain Management: a

Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Pain Physician* 20 (6), E755–E796.

 Khaleghi M. New Arthritic Foundation Guideline on CBD Use Could be First of Many More to Come. *Alternative Therapies*. 2020;26(S1):1-4.

Atypical Presentation of a Plantar Ganglion Cyst: A Case Study

Jonathan Ibanez, B.S., Michael Amedeo, B.S., and Tanisha Minasian, B.A.

ABSTRACT

Objective: This paper will provide a case presentation of a patient with an atypical ganglion cyst.

Methods: The patient's chart including the subject's history of present illness, diagnostic tests, and imaging were collected from the provider. Informed consent was provided by the patient to have their case shared to advance medical knowledge. The case was then reviewed by the authors who identified components of the history, physical exam, and diagnostic tests that were critical in successfully treating the patient's ganglion cyst.

Results: A 45-year-old female presented to the clinic with a five-day history of pain on the plantar aspect of her right great toe. After conducting a thorough history and lower extremity-focused exam, the physician initially diagnosed the patient with an infection and prescribed a course of antibiotics for treatment. After the patient later presented to the clinic with no improvement in her symptoms, the physician ordered a series of Magnetic Resonance Imaging (MRI) to further investigate the pathology. The imaging studies determined that the patient had fluid consolidation in her toe consistent with that of a ganglion cyst, despite the atypical initial presentation.

Conclusion: Clinicians who encounter a similar case should specifically consider the location of the patient's pain, the history related to the pain, and the appearance of the region on physical exam and with standard imaging modalities available in the clinic. The uncommon presentation of this plantar ganglion cyst should encourage clinicians to thoroughly investigate a possible ganglion cyst pathology early in the patient presentation.

Introduction

A ganglion cyst is a soft tissue mass most commonly found on the hands and feet. Often confused with tumors, they are noncancerous and pose no health risk to the patient. Typically, a ganglion cyst results from fluid leaking from a tendon sheath or joint capsule into the surrounding subcutaneous space, which can present as a fluid-filled bump on the skin. Several factors have been noted to increase one's likelihood of developing ganglion cysts, including being a woman between the ages of 20 and 40 and having a history of osteoarthritis or joint injury.¹ Patients with ganglion cysts often experience a wide variety of symptoms, including tingling, burning, and aching at the affected area depending on the cyst's proximity to nerves and tendons.

When considering diagnosis of ganglion cysts, the provider will typically palpate the area to assess the mobility of the cyst or perform an aspiration to determine if there is fluid present. Another commonly used diagnostic tool for ganglion cysts is imaging such as MRI and X-Ray, which can provide the physician with details on the size, shape, location, and makeup of the cyst. These diagnostic tests are used to distinguish ganglion cysts from other common differential diagnoses, including lipomas and tenosynovitis.¹

If the mass is found to be a ganglion cyst, there are several different treatment modalities a provider can utilize depending on the presentation. In some cases, immobilization of the nearby joint is indicated due to activity being known to increase the size of ganglion cysts. Other common treatments include aspiration of fluid from the cyst as well as surgical removal.¹ While there are several tried-andtrue treatments for ganglion cysts, clinicians must be prepared for ganglion cyst presentations that do not align with what is classically described in the literature and may be more difficult to diagnose and treat.

Methods

The patient's chart including the subject's history of present illness, diagnostic tests, and imaging were collected from the provider, Dr. Arnold Ross, DPM. Informed consent was provided by the patient to have their case shared to advance medical knowledge. The case was then reviewed by the authors who identified components of the history, physical exam, and diagnostic tests that were critical in successfully treating the patient's ganglion cyst.

Case Report

A 45-year-old female initially presented to a podiatric outpatient clinic complaining of extreme pain under the right great toe for five days. She reported a possible incident of trauma to the toe, having remembered hitting her toe around the time the pain started. The patient reported minimal pain in the morning but that the pain worsened throughout the day. She noted that her family history was positive for gout. On exam, there was an area of tenderness under the right great toe with surrounding erythema and edema. A blood chemistry panel was ordered to assess for uric acid along with complete blood count and arthritis panel. The uric acid value at the time of initial presentation was 6.1 mg/dL. Radiographs were also initially taken of both the lateral right foot with the great toe dorsiflexed and a dorsal-plantar radiograph. A lateral radiographic view revealed a soft tissue prominence visible at the plantar surface and the dorsal-plantar radiographic view revealed a soft tissue prominence at the right great toe with some lateral deviation of the prominence into the first interspace. The provider and patient discussed possible etiologies of the pain including cellulitis, gout, and a fracture secondary to possible trauma. The patient was counseled on possible future need for advanced imaging, most likely an MRI, to adequately assess all possible etiologies. The patient was initially treated for a soft tissue infection of the great toe. She was prescribed 500 milligrams of cephalexin and a followup appointment was made for one week.



Figure 1. Lateral radiograph of right great toe taken at initial presentation (A). Dorsal-plantar radiograph of same day (B). Lateral oblique (C). Medial Oblique (D). Images obtained with permission of physician and patient.

Upon return to the office one week later, the patient began to complain of new numbness in addition to ongoing pain to the same right great toe and the adjacent second toe. During this visit, the patient and physician discussed the need for an MRI of the right foot to assess for possible etiologies of the pain and numbness. The patient then returned three weeks later to receive orthotics dispensed by the physician by which point the initial symptoms had still not resolved. The patient then returned three months later, still not having gotten the MRI and still complaining of pain. The patient obtained an MRI of the right foot four months later which showed "fluid signal interposed between medial and tibial and lateral fibular hallux sesamoids...lobulated fluid signal from mid-first proximal phalanx to distal first phalanx along plantar lateral aspect of the first digit consistent with large ganglion" according to the radiologist's impression. The fluid signal measured 4.1 cm by 2.4 cm. She presented to the original provider's office two weeks later with the MRI (Figure 4). At that visit, additional radiographs were taken of the right foot showing a soft tissue prominence at the plantar surface of the foot. The provider proceeded to perform an in-office incision and drainage of the plantar mass using which yielded serosanguinous fluid. The toe was dressed with gauze and coban. One week later, the patient presented to the office and had the right hallux mass incised and drained again. During this visit, the drainage was collected and sent for culture. The drainage from the mass yielded no growth on culture. The patient reported that the pain she initially presented with had completely subsided. Given the initial patient presentation and the subsequent imaging studies, labs, and treatment, the provider determined that this was a case of a plantar ganglion cyst. At one month follow-up the patient reported full resolution of symptoms.



Figure 2. Dorsal-plantar radiograph of right foot nine months after initial presentation, immediately prior to incision and drainage with mass marked. Images obtained with permission of physician and patient.



Figure 3. Lateral radiograph of right foot nine months after initial presentation, immediately prior to incision and drainage with mass marked. Image obtained with permission of physician and patient.



Figure 4. (A) T1 MRI of first metatarsophalangeal joint (B) T2 MRI of first metatarsophalangeal joint (C) T2 image of mass of distal hallux (D) T2 image of mass of distal hallux. Images obtained with permission of physician and patient

Discussion

The true mechanism of how a ganglion cyst forms is unclear. However, it is proposed that a ganglion cyst forms where soft tissue bulges out of a joint. Ganglion cysts are commonly seen in the wrists and hands but also occur in the ankles and feet. Rarely, ganglion cysts present at the first metatarsophalangeal joint of the foot.²

The patient presented to the clinic with localized pain in her right great toe. After some time, the patient remembered that she had trauma to her right great toe around the same time as her symptoms began. On physical examination, the patient presented with erythema and edema to the area. The patient also indicated a significant family history of gout. The symptoms reported by the patient combined with the clinical presentation give credence to several differential diagnoses. Based on the entire presentation, it is reasonable to include cellulitis and gout in the differential diagnosis list.

There were several factors that lead to cellulitis being included on the differential list. As was seen in the patient, cellulitis may present with erythema and edema.³ In addition, cellulitis is seen in the lower extremity unilaterally.³ Another differential diagnosis based on the clinical presentation may potentially be gout. The patient had uric acid levels of

6.1 mg/dL. Due to the previous history of gout, uric acid level, and the indicated area of pain, it would be reasonable to assume that the patient is experiencing an acute gout flare up. A typical gout flare up presents with pain at the first metatarsophalangeal joint, edema, and erythema.⁴ The patient presented with symptoms that could lead a physician to many different differential diagnoses, including but not limited to a ganglion cyst, cellulitis, or gout.

Imaging studies would be the appropriate next step to further distinguish between the differential diagnoses being considered by the physician. In this unusual case of a plantar ganglion cyst, imaging modalities were utilized to further understand the patient's case. Radiographs were the initial step to diagnosing this plantar ganglion cyst. Radiographs demonstrated a plantar prominence of the right foot into the first interspace in the dorso-plantar view. Plain radiographs are not typically able to provide visualization of the cyst. However, radiographs can help rule out differential diagnosis or any associated trauma that may be causing the patient's symptoms. In addition, radiographs are capable of supplying evidence of bone tumors and arthritis. Because of the lack of specificity that radiographs provide for ganglion cysts, the patient would require further advanced imaging. The next step to adequately assess the differentials for this patient's case would be to utilize MRI. MRI studies are optimal when treating soft tissue pathology. It has been noted that T2weighted images are better quality when assessing cysts.⁵ Typically, ganglion cysts are seen with welldefined margins and hypointense in T1 weighted images but hyperintense in T2 weighted images.⁵ This can be appreciated in the MRI images above. In figure 4A, a T1 image shows a hypointense image with a well-defined margin. In Figure 4B/C, a bright image along the first metatarsophalangeal joint can be appreciated. Both T1 and T2 weighted images demonstrate the findings of a plantar ganglion cyst in this patient's case.

There are various treatment options for patients who present with ganglion cysts. The course of their treatment typically depends on the severity of their clinical symptoms. Observation, aspiration, and surgical therapy are three of the most common treatment modalities. Observation of the ganglion cyst is an ideal first step if patients do not show any active symptoms such as pain. Previous reports of ganglion cysts indicate that in some cases, they may spontaneously resolve themselves if presented with no symptoms.⁶ Ganglion cyst aspiration is another treatment modality that usually provides some relief to patients that have bothersome symptoms. There has been some previous evidence of the recurrence of ganglion cysts within one year after aspiration.⁶ Different sized syringes are typically used depending on the estimated fluid volume. The patient noted in this report received two aspirations and reported a resolution of symptoms. The last common approach for ganglion cysts is surgical excision. This method is usually indicated for patients who have recurrent ganglion cysts and aspirations have been unsuccessful. However, it is important to note if the cyst is not removed in its entirety, recurrence is possible. With any surgery, complications may occur. There is always a risk for infection and neurovascular injury in surgical intervention. Ganglion cyst aspiration was the treatment modality that provided relief for the patient in this study. The patient reported symptom relief in a one-month follow up after the second aspiration was completed. Although the true mechanism behind ganglion cysts is still unclear, imaging studies and clinical manifestations may still provide the physician with enough clues to make a proper diagnosis.

Future providers who encounter a patient with a similar history and physical exam findings to those found in this case study will benefit from including a ganglion cyst in their initial list of differential diagnoses. This case demonstrates that while ganglion cysts more commonly present on the dorsal aspect of the foot and ankle, an atypical plantar presentation should be considered while all acute pathologies are ruled out.⁷ Providers who consider this uncommon presentation early on might be able to expedite the patient's diagnosis and treatment.

Conclusion

This atypical presentation of a ganglion cyst was unique in its clinical manifestation, which made it difficult to diagnose despite the various labs ordered and the standard radiographs taken. Clinicians who encounter a similar case should specifically consider the location of the patient's pain, the history related to the pain, the appearance of the affected area and utilize standard imaging modalities available in the clinic. The uncommon presentation of this plantar ganglion cyst should encourage clinicians to thoroughly investigate a possible ganglion cyst pathology early on in the patient presentation. Despite numerous confounding components, the result of the treatment was ultimately successful with the patient reporting no recurrence of the cvst and full resolution of the pain at one month follow-up.

References

 Suen M, Fung B, Lung CP. Treatment of ganglion cysts. *ISRN Orthop.* 2013;2013:940615. doi:10.1155/2013/940615
 Dyer SM, Simmons BP. The wrist and hand. In: Rheumatology, 6, Hochberg MC, Silman AJ, Smolem JS, et al (Eds), Mosby, St.Louis 2015. Vol 1, p.624. 3. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America.

Stevens DL, Bisno AL, Chambers HF, Dellinger EP, Goldstein EJ, Gorbach SL, Hirschmann JV, Kaplan SL, Montoya JG, Wade JC, Infectious Diseases Society of America

Clin Infect Dis. 2014;59(2):e10.

4. Raff AB, Kroshinsky D. Cellulitis: A Review. *JAMA*. Jul 19 2016;316(3):325-37.

doi:10.1001/jama.2016.8825

5. Hadler NM, Franck WA, Bress NM, Robinson DR. Acute polyarticular gout. *Am J Med.* May 1974;56(5):715-9.

doi:10.1016/0002-9343(74)90639-1

6. Nikolopoulos D, Safos G, Sergides N, Safos P. Deep peroneal nerve palsy caused by an

extraneural ganglion cyst: a rare case. Case Rep Orthop. 2015;2015:861697.

doi:10.1155/2015/861697

7. Zumrut M, Demirayak M, Kucukapan A. An Unusual Cause of Foot Drop: Peroneal

Extraneural Ganglion Cyst. *Pak J Med Sci.* 2016 Jul-Aug2016;32(4):1047-50.

doi:10.12669/pjms.324.9998

Fight Fungus Without Treatment Resistance



Terbinafine treatment can be an uphill battle.

Terbinafine resistance is on the rise globally and may occur in patients with terbinafine resistant strains of dermatophytic fungi.

The new terbinafine resistance test, only available at BakoDx, enables you to predict effectiveness before prescribing treatment.*

bako

Bako Diagnostics | 855-422-5628 | bakodx.com

*Available only as part of the Onychodystrophy PCR Test; Terbinafine resistance currently unavailable in NY.



Bako Diagnostics' PCR Test Improves Detection of Web Space Skin Infections

Based on years of research and experience in podiatric pathology, Bako Diagnostics has developed a "BakoDx Web Space" PCR test to identify the infectious agents involved in web space dermatitis. This highly sensitive and highly specific test provides podiatric clinicians with ease of use, rapid results and the most accurate diagnostic method available – allowing for the best patient care.

The test utilizes real-time polymerase chain reaction (RT-PCR) technology to detect the causative agent within the web space keratin when present, resulting in the clinically identified dermatitis. The BakoDx Web Space panel tests for:

- Pan-Dermatophytes
- Candida spp

- Pan gram-negative bacteria
- Staphylococcus aureus*

• Corynebacterium minutissimum

*If positive, reflex test is performed for the mecA gene of methicillin-resistant Staphylococcus aureus (MRSA)

Interdigital infectious dermatitis may be due to a variety of organisms that may look similar, but their treatment differs. Differential diagnosis may include: *Corynebacterium minutissimum* in erythrasma, tinea pedis, candidal intertrigo and/or primary or secondary bacterial infections. There is also a growing awareness of gram-negative bacterial web space infections. The differential diagnosis of web space dermatitis would also include non-infectious etiologies including web space eczema or psoriasis.^{1,2}

"This test is designed for those patients with web space dermatitis, where an infectious etiology may be included in the differential diagnosis," said Dr. Wayne L. Bakotic, Chief Medical Officer at BakoDx. "PCR analysis allows us to identify the infectious agent in the most accurate, efficient and rapid manner."

The BakoDx Web Space panel identifies the causative agent of interdigital skin infections with the highest sensitivity and specificity available, compared to conventional diagnostic methods. Results are available within 1-2 days, giving clinicians the advantage of rapid, targeted patient treatment plans.

Current diagnostic methods including culture, histopathology and KOH have a lower sensitivity and specificity, as compared to the BakoDx Web Space panel. In addition, the limitations of time may make KOH an impractical option. The BakoDx Web Space PCR panel provides the most rapid results with the highest specificity and sensitivity with a simple collection method to give you the time to spend with your patient. In addition, BakoDx's comprehensive, molecular test report provides a clear and detailed explanation of the test results and therapeutic options, with literary references.

	Culture	Histopathology	KOH (fungal)	Web Space PCR Test
Turnaround Time	2-28 days	2-3 days	Same day	1-2 days
Sensitivity	50-75%	85-90% ³	73-91%4	92-100% ⁵
Specificity	100%	72% ³	42-91% ⁴	97-100% ⁵

Comparison of Tests

"The rapid and accurate identification of pathogens present in web space infections is critically important for prompt and effective therapy," said Dr. William P. Scherer, Senior Podiatric Medical Advisor for BakoDx. "Providing the appropriate therapy reduces treatment failures and repeat patient visits. In addition, early and accurate diagnosis may also prevent secondary infections compounding the clinical presentation and adding complexity to the treatment regimen."

EASE OF SAMPLE COLLECTION

The collection method for a patient's specimen is a simple, superficial skin scraping performed in-office with the debris collected in a Dermapak.

When it comes to proper web space specimen collection technique and obtaining adequate tissue, Dr. Scherer states, "the best method is to scrape exfoliated debris directly into the Dermapak followed by wiping the instrument on the inner surface of the collection pack to ensure optimal acquisition. If visible tissue is procured from the scraping then you likely have adequate sample for testing."

This simple collection process is time saving and by far the least invasive sampling method with little to no post procedure wound care. By utilizing the BakoDx Web Space infection test, clinicians also eliminate other time consuming in-office procedures allowing more time to be spent with the patient and increasing patient satisfaction.

"With this rapid and definitive diagnosis in hand through PCR testing, clinicians can feel confident that the first therapy is the appropriate therapy and their patient is well on the way to a resolution," said Dr. Bakotic.

As the leader in lower extremity pathology diagnostics, BakoDx enables clinicians to practice evidence-based medicine and provide their patients with most effective and economic therapeutic options. To get started with BakoDx's Web Space PCR test, call 855-422-5628 or visit bakodx.com/webspace to learn more.

¹ Hainer BL. Dermatophyte infections. Am Fam Physician. 2003; 67(1):101-8.

² Bristow I. Non-ulcerative skin pathologies of the diabetic foot. Diabetes Metab Res Rev. 2008;24(Suppl1):S84-89.

³ J Am Acad DDermatol. 2003 Aug;49(2):193-7.

⁴ Jacob Oren Levitt, Barrie H. Levitt, Arash Akhavan, and Howard Yanofsky, "The Sensitivity and Specificity of Potassium Hydroxide Smear and Fungal Culture Relative to Clinical Assessment in the Evaluation

of Tinea Pedis: A Pooled Analysis," Dermatology Research and Practice, vol. 2010, Article ID 764843, 8 pages, 2010; Journal of Basic & Clinical Medicine 2016; 5(2):4-6

⁵ Internal validation study compared to NYS Dermatophyte, NYS Candida, and Sanger PCR sequencing.





WHY ABPM CERTIFICATION...

Board Certified Right Out of Residency No Case Submission Process Streamlined Maintenance of Certification



WHY WAIT? APPLY NOW!

Application Deadline is July 31, 2022

Certification Exam is October 1, 2022

PodiatryBoard.org



ONE

Student Opportunities & Resources

- ACPM Student Clubs -

- ACPM Expert Lecture Series -

- ACPM Mini-Conferences: Practical Pearls -

- ABPM Young Member Newsletter/Updates -





Podiatric Medicine Road to Success

TWO

Resident Opportunities & Resources - ABPM In-Training Exam -- ACPM Expert Lecture Series -

- ACPM Mini-Conferences: Practical Pearls -

THREE ABPM Diplomate

- ABPM Certification Exam -- Maintenance of Certification -(MOC) Program

FOUR ACPM Fellow

- ACPM e-Learning POD -

- ACPM Mini-Conferences -Practical Pearls

 Review Text in Podiatric -Orthopedics & Medicine

> Annual Billing - & Coding Manual

Visit www.ACPMed.org to Apply for FREE ACPM Student Membership

Dispense & Prosper

Are you meeting your dispensing goals?

Join the thousands of Podiatrists who are meeting their dispensing goals with the help of Blaine Labs' top-performing products.







Call us today & boost your practice's financial health! (800) 307-8818 • BlaineLabs.com



"Doctors Dedicated to Keeping California on Their FEET!"

THE CALIFORNIA PODIATRIC MEDICAL ASSOCIATION IS EVER VIGILANT IN PROTECTING PODIATRIC PHYSICIANS, THEIR PATIENTS, THE PUBLIC HEALTH, AND THE SPECIALTY OF PODIATRIC MEDICINE.



PODIATRIC MEDICINE IS A HEALING ART

7311 Greenhaven Drive, Suite 208 • Sacramento, CA 95831 P: 916-448-0248 • P: 800-794-8988 • F: 916-448-0258 • E: cpma@calpma.org • W: CalPMA.org





twitter.com/CPMATWEETS

