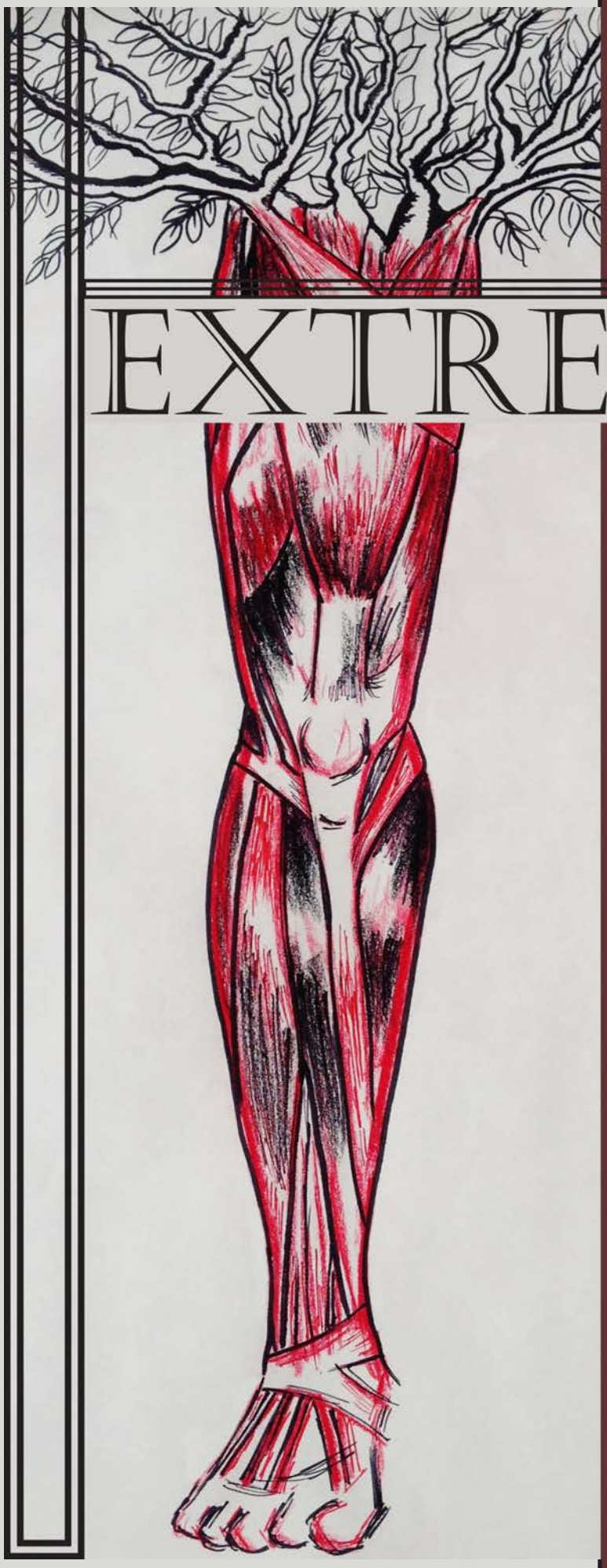

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EXTREMITAS

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It is with great privilege that we present to you the very first issue of "Extremitas: The Journal of Lower Limb Medicine". Our publication that we would like to fondly call "Extremitas" was the brainchild of WesternU's College of Podiatric Medicine faculty and one of the most exciting endeavors we, the student body, have taken on. As a new student ran journal, we have aimed to bring to you various topics that center on the lower extremity as we have sought submissions from all disciplines. It was our goal to bring to you an inter-disciplinary eye into the world of the lower limb. From a look into lower extremity neuropathies and ulcers to surgeries and to many other disease considerations, we bring it all to you. And this of course would not be possible without the support of our many sponsors, faculty and staff, WesternU student body, family and friends -- you all have been there in various stages of our publication and have been our source of needed support and encouragement. It is our hope that you all enjoy this year's selection of articles and further encourage scientific research for a better tomorrow.

Sincerely,
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THANK YOU

Dr. Philip Pumerantz founded the College of Osteopathic Medicine of the Pacific in 1977 and has since helped revolutionize medicine. One name change and 8 additional colleges later, Western University of Health Sciences has become a model for inter-professional education. As the university's sole acting president, Dr. Pumerantz has inspired the College of Podiatric Medicine to expand on his philosophy by starting this journal in which life-long learners of multiple disciplines contribute their medical research.

Holding true to university tradition, Extremitas's purpose is to act as a benchmark for interprofessional teamwork in all things considering the Lower Extremity, and reach healthcare professionals and students from all schools of thought.

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Case Study: Short Leg Syndrome & Associated Somatic Dysfunction

Nicole Furr, B.S. - 3rd year Osteopathic Medical Student at Western University of Health Sciences

Background

J.S. is a 68 year-old Caucasian female who presents to the osteopathic clinic with complaints of chronic thoracic and low back pain bilaterally for almost 50 years. The pain is constant, throbbing, and rated as a +4/10 in terms of pain intensity. Standing or sitting for long periods of time make it worse. Being active (within reason) and Ibuprofen make the pain better. She first noticed the pain after she was involved in a motor vehicle accident in 1966, and it has continued to bother her since then. The MVA caused fractures of her left tibia and fibula bones. Her lower extremity injuries required multiple surgeries and skin grafts, ultimately leaving J.S. with a shortened left lower extremity. This was confirmed through radiographic evaluation. The patient has also suffered from peripheral neuropathy in her left limb since the accident, as well as occasional left ankle and knee pain.

Physical Exam

While observing the patient entering the room, a prominent left-sided antalgic gait and mildly humped posture was observed. There was a scar located on the left medial calf from prior surgeries and mild non-pitting edema of the left foot with prominent varicose veins around the left ankle. There was no tenderness to palpation of the left foot or lower leg and no change in skin temperature of the left foot. However, trophic changes including decreased hair growth and skin thinning were observed on the left lower extremity. Anterior and posterior drawer tests of the knees and ankles bilaterally were found to be negative, but the patient reported a point of tenderness along the lateral aspect of the left knee.

The Adams Forward Bend Test revealed a thoracic levoscoliosis with apex location at the T7 vertebrae. This finding was associated with decreased rib expansion on the right with inhalation and palpable muscle tightness in the psoas and quadratus muscles in the right lumbar region with limited lumbar flexion. Following a hip flop, the right medial malleolus was found to be inferior in relation to the left by ~3cm, confirming the diagnosis of a left-sided short leg previously made by x-ray.

Diagnosis

Based on the history and physical exam findings for J.S., the most plausible diagnosis is anatomical left-sided short leg syndrome secondary to trauma from the motor vehicle accident, leading to a functional thoracic levoscoliosis and the associated findings of somatic dysfunction and pain in the ribs, thoracic spine, lumbar spine, and lower extremity regions.[5]

Osteopathic Manipulative Treatment

In this case, high-velocity low amplitude treatment would be relatively contraindicated due to the age and questionable fragility of J.S. Keeping this in mind, a more indirect approach was employed. Soft tissue massage of the thoracic and lumbar regions helped relax the musculature and improve range of motion of the spine and ribs. In soft tissue massage, the muscles are gently bow-stringed to relax any tension and break up fibrous adhesions. Rib raising articulatory technique was also employed as a means of improving rib-cage motion and correcting the respiratory somatic dysfunction induced by the thoracic levoscoliosis. This was done by having the patient lie supine, with a rocking superior force applied at the rib angles to free up the range of motion. Additionally, the use of counter-strain technique to relax the muscle spasm of the quadratus and psoas muscles on the left helped to relieve some of the patient's lower back pain. This was achieved by placing the muscles into a position of ease to decrease pain fiber output, and then holding that position of ease for at least 90 seconds to reset the nociceptive fibers and decrease pain output. Counter-strain to the left lateral meniscus was also utilized to reset the nociceptive fibers in the knee to decrease pain. The treatment session

was concluded with several cranial techniques, which increase CSF flow and decrease tension in the skull, to relax the patient and aid the body in self-healing.

Following the manipulative treatment, the patient was advised to increase her water intake and refrain from any heavy lifting for several days while her body adjusted to the changes. She was also advised that soreness is to be expected with correction of chronic somatic dysfunction, and that NSAIDs may be taken to ease the discomfort. A brochure was given on various stretching techniques that could be completed at home to increase her spinal range of motion and decrease muscle tension.

Other Treatment Modalities

J.S. was also advised that she should be fitted for a heel lift to help correct her leg-length discrepancy and take some of the strain off of her back, knee, and ankle. The lift height should ultimately be ½ to ¾ of the total measured discrepancy, as any more can cause increased pain by over-aggressively changing the compensation pattern that is already in place. Therefore, because this was a chronic problem, the lift height should be slowly increased to the desired level.[7]

Response to Treatment

Following her first treatment session, J.S. experienced immediate relief of her knee pain, as well as decreased lower back pain and improved respiratory motion. She did admit to soreness for several days following treatment, but her discomfort was relieved with Ibuprofen. She made an appointment with a podiatrist to get a heel lift fitted and returned for follow-up OMM treatments weekly with slow improvement of her symptoms and decreased scoliotic curvature of her thoracic spine, as measured through osteopathic exam findings and radiography.

Short Leg Syndrome Pathophysiology

Short Leg Syndrome is defined as any condition in which an anatomical or functional leg length discrepancy results in sacral base unleveling, vertebral side-bending and rotation, and innominate rotation.[6] It is a very common problem, with 23% of the population having a discrepancy of at least 1 cm. Discrepancies of < 2 cm rarely cause any symptoms, but differences in length of > 2 cm can manifest as back, hip, knee, and ankle pain.[1]

There are two different categories of short leg syndrome: anatomical and functional. An anatomical short leg is when one leg is actually shorter than the other, as in our patient. This can be caused by trauma, polio, or birth defects, among other causes, and is diagnosed through radiographic imaging. The main treatment for this is the use of a heel lift. If not used or properly fitted, however, the short extremity will cause further problems for the spine and lower extremities, ultimately leading to chronic pain and muscular spasm.[2][3]

Functional short leg is when one leg simply appears to be shorter than the other due to pelvic dysfunction or postural irregularities. The treatment of choice in this case is osteopathic manipulative treatment. A heel lift should only be employed for a functional problem if osteopathic manipulation cannot correct the deficit or if irreversible fibrous change has occurred due to the chronicity of the dysfunction. [2]

Case Discussion

In the case of J.S., all of her structural problems began following the trauma to her left leg, resulting in a shortened left lower extremity. This leg length inequality led to an unleveling of the sacral base which the body automatically tries to compensate for in order to keep the eyes level. This compensation is achieved through contraction of the lumbar musculature (psoas and quadratus muscles) contralateral to the short leg side in an effort to decrease the length discrepancy. This contracture or muscular spasm in the lumbar region was the cause of the lower back pain experienced by our patient. The contracture also pulls on the thoracic spine, leading initially to a C-shaped curve concave away from the short leg, which can induce thoracic spine pain as well as respiratory dysfunction. Over time, this curve can evolve to an S-shaped curve with a thoracic concavity towards the short leg, and a lumbar concavity away from the short leg, as seen in the image on the left from Foundations of Osteopathic Medicine. [1][4]

Luckily for J.S., her functional scoliosis had not progressed to the S-shaped curve. However, the stress and tightness of her lumbar region indicated that transformation would have occurred had she not sought treatment for her dysfunction. [4]

Conclusion

The case of J.S. is a prime example of how the structural dysfunction of a single area in the body can affect the function of the whole. If her dysfunction had been managed appropriately with a heel lift and OMT from the beginning, perhaps J.S. would not have suffered from chronic pain for so many years. In cases like this, both allopathic and osteopathic physicians must work together to support the patient medically, emotionally, and structurally, as uncorrected somatic dysfunction can lead to worsening of the initial problem, extension into initially uninvolved areas, and often chronic pain.

Osteopathic manipulative treatment can offer relief for patients suffering from pain due to somatic dysfunction both acutely after a trauma and years later, but the effectiveness and speed of recovery decreases with prolonged structural dysfunction. Recognizing the need for OMT and understanding the usefulness of manipulation in the management of various medical conditions is something that the medical community today is lacking. Lower back pain is a very common complaint that many patients have today and medical management is often used to mask symptoms of pain without addressing the underlying problem, as in the case of J.S. However, in many cases the need for pain medication can be decreased or eliminated through spinal manipulation and reinstitution of structure into a dysfunctional spine. Increasing the awareness of osteopathic medicine and educating allopathic physicians in its usefulness could lead to a vast reduction in the number of chronic pain syndromes and significant improvement in patient outcome

References

(1) Chila, Antony G. Foundations of Osteopathic Medicine. Lippincott Williams & Wilkins, 2010.
(2) Dalton, Eric. "Short Leg Syndrome: Part 2." Dalton Myoskeletal. Freedom from Pain Institute, 2011. http://erikdalton.com/media/published-articles/short-leg-syndrome-part-2/
(3) Landauer, Franz. "Diagnosis and Treatment of Leg Length Discrepancy in Adults." SOSORT 2013. http://www.scoliosisjournal.com/content/pdf/1748-7161-8-S2-O41.pdf
(4) Ohio University College of Osteopathic Medicine: Centers for Osteopathic Research and Education. "Lumbar Dysfunction in Short Leg Syndrome." 2006. http://www.ohiocore.org/gfx/media/contribute/1LumbarDysfShrLgSyndv2.pdf
(5) Raczkowski, J.W., Daniszewska, B., Zolynski, K. Functional Scoliosis Caused By Leg Length Discrepancy. Archive of Medical Science, 2010. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3282518/
(6) Savarese, Robert G. OMT Review, 3rd Edition. Jacksonville Orthopaedic Institute, 2009.
(7) Vogel, F. "Short-leg Syndrome." Clinical Podiatry.

Hydroxyurea-Associated Lower Extremity Ulcers

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Introduction

Hydroxyurea is a hydroxylated derivative of a urea drug first synthesized in 1869. This drug has been recognized since 1960 to be an effective anti-neoplastic drug. [1] It specifically inhibits DNA synthesis by blocking diphosphate reductase, a ribonucleotide, causing the reduction of ribonucleotides to deoxyribonucleotides in treatment of various hematologic and oncologic disorders. Due to the mechanism of action, it functions as a potent chemotherapy agent in treatment of chronic myeloproliferative disorders including polycythemia vera, essential thrombocythemia, and acute myelogenous leukemia. Other indications include treatment of psoriasis vulgaris, sickle cell anemia, and inhibition of viral replication in HIV.

Hydroxyurea is effective against blocking the production of proliferative neoplastic bone marrow cells. At lower doses, hydroxyurea has been used instead of methotrexate to treat severe psoriasis vulgaris. In polycythemia vera, the medication is used to lower red blood cells, leukocytes and platelet counts. Hydroxyurea is also used in the treatment of sickle cell disease due to its mild side effects, ability to work fast, and quick patient recovery when cell counts drop too low. [2] The exact mechanism of action of hydroxyurea in sickle cell disease is not entirely clear, but it is believed that the drug works by increasing the production of fetal hemoglobin (HbF), normally found infants, and blocks polymerization of sickled hemoglobin (HbS) thereby reducing painful crisis.

The side effect of this medication is varied but in this article, we highlight the rare complication of painful lower extremity ulcers associated with use of hydroxyurea.

Hydroxyurea-Associated Leg Ulcers

Dermatologic reactions to hydroxyurea include alopecia, diffuse hyperpigmentation, scaling, poikiloderma, atrophy of the skin and subcutaneous tissues, or nail changes. [3] A case study by Sierieix found that use of hydroxyurea for myeloproliferative disease can result in the patient's first incidence of ulcer formation and exhibit delayed healing of lower extremity ulcers. [4]

The disruptive effect of hydroxyurea on DNA synthesis in the cell cycle causes damage to the basal keratinocytes and hindrance of collagen production. This cumulative toxicity to the basal layer can lead to epidermal skin breakdown. Additionally, hydroxyurea results in the formation of megaloblastic erythrocytes, which are vulnerable to microvascular destruction. An exacerbation of tissue anoxia is created in the microcirculation leading to impaired wound healing. [5] The most common area where hydroxyurea-associated ulcers arise in the lower extremity is the ankle malleolus. [6] Other locations in the lower extremity include the tibia, dorsal aspect of the feet, and calf. The bony prominence and potential exposure to trauma leads to a preponderance for these ulcers to develop around the ankle region. Hydroxyurea associated ulcers can also develop spontaneously without inciting trauma.

Clinical findings

The wound base typically has an ischemic appearance with pale, yellow or fibrotic tissues that may not bleed when debrided (Figure 1). The shape of the ulcer is variable and can be round, punched out, patchy or have irregular borders. Patients often experience pain with these ulcers. These characteristics are also seen in other ulcers in the lower extremity such as pressure, arterial, and venous ulcers. When the ulcers heal, it leaves a

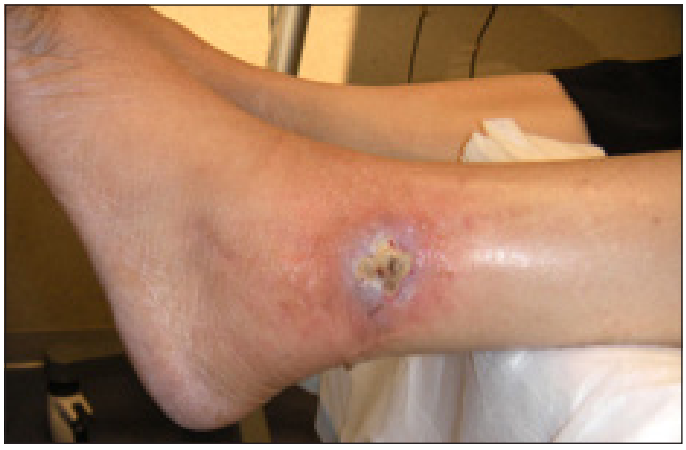

Figure 1: Hydroxyurea associated ulcer over the lateral malleolus with entirely fibrotic wound base.

patch of skin that is hypopigmented, similar to atrophy blanche. Other differential diagnoses include but are not limited to autoimmune or vasculitic ulcers and pyoderma gangrenosum.

Diagnosing Hydroxyurea-Associated Leg Ulcers

A thorough examination of the patient's medical history, medication list, and careful evaluation of the lower extremity ulcer must be performed to rule out other ulcer etiologies. Hydroxyurea is known by its brand name Droxia or Hydrea and dosing ranges from daily to every three days depending on the indication. The duration of hydroxyurea use before appearance of ulcers in one study of patients being treated for various hematologic disorders was 1 to 10 years (mean 3 years). [7] Despite documented case reports of hydroxyurea associated lower extremity ulcers, there is no consistent correlation between dose and duration of drug therapy with regards to ulcer occurrence. [8] Nor is there a relationship between the size and depth of the ulcers with drug dosage. There is however, an increase incidence of developing ulcer recurrence once hydroxyurea therapy is resumed after a previous history of ulceration.

A biopsy of the ulcer may be helpful in supporting the diagnosis but findings still need to be correlated with the medical history. Examination of histologic findings in hydroxyurea associated ulcer reveals endothelial cell edema, thickening or hyalinization of the blood vessel wall in the dermis, and perivascular lymphocytic inflammation. [8]

Etiologies, such as peripheral arterial disease (PAD) and pressure ulcers should be ruled out. A laser Doppler device (Sensilase PAD-IQ, by Vasamed) is helpful in measuring skin perfusion pressure (SPP) to determine ulcer healing potential. SPP values below 30mmHg indicates PAD and necessitates referral to a vascular specialist. Similarly, pressure ulcers over ankle malleolus may resemble hydroxyurea ulcers in some patients. For this reason, evaluation of frailty and mobility of each individual patient should be performed.

Wound care strategies that include regular debridement, control of inflammation, and reduction in bacterial bioburden are essential for wound bed preparation. Treatment including topical and systemic antibiotics, wound dressings, compression therapy, and steroids are often implemented to promote wound healing. However, wound healing may be stalled even with these treatment modalities so long as patients remain on hydroxyurea.

Treatment of Hydroxyurea-Associated Leg Ulcers

After diagnosing an ulcer associated with the use of hydroxyurea, the first step of treatment is to contact the prescribing physician, often times the hematologist or oncologist, to determine if the medication can be safely discontinued. In some rare cases, such as polycythemia vera, the medication may be the only and life-saving treatment for this disease. Once hydroxyurea is discontinued, spontaneous resolution of these leg ulcers is often seen. [8]

Good local wound care is the mainstay for ulcer healing. It is generally advised against aggressive surgical debridement of these ulcers as it may result in enlarged ulcer size. At our institution, we have successfully treated many of these ulcers by utilizing low-frequency ultrasound debridement device (Quostic device, by Arobella Medical) as well as topical debridement agents, such as medical honey gel (Therahoney, Medline) or Collagenase ointment (Santyl, Smith & Nephew) to achieve a clean granular wound base (Figure 2A, 2B). The ulcers should be covered with non-adherent dressings to minimize pain during dressing changes. Leg edema may be treated with gentle compression therapy using multi-layer compression bandages, such as Comprifore bandages (BSN Medical).

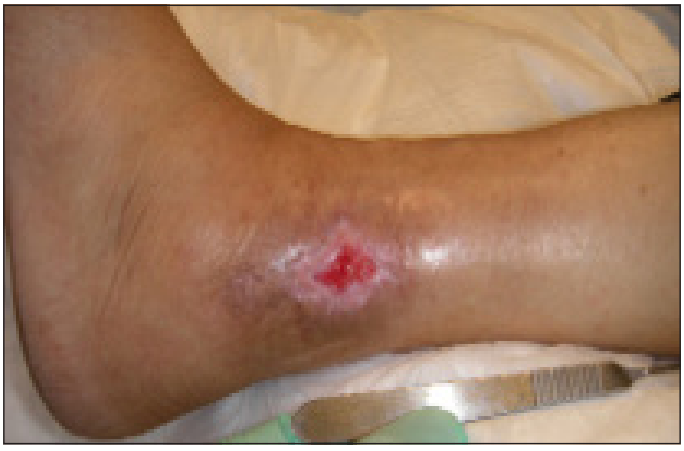

Figure 2A: Hydroxyurea was discontinued by the prescribing physician. The ulcer was debrided with Quostic ultrasound by Arobella and a healthy granular wound base was observed.

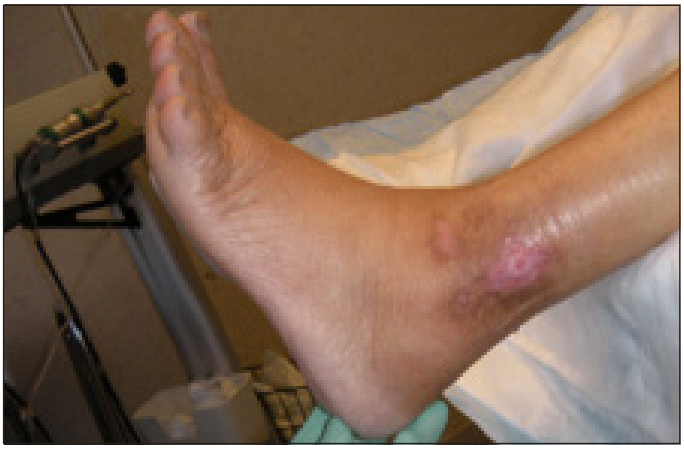

Figure 2B: Healed ulcer seen after 4 months of local wound care. Regular debridement was performed and a non-adherent dressing and compressive wrap was utilized. Note the hypo-pigmented skin after ulcer heals mimicking presentation of other ulcers.

Case report

A 35 year old African American female with history of sickle cell anemia, DVT, aseptic necrosis of bilateral humeral and femoral heads, MRSA bacteremia, and numerous hospital admissions for vaso occlusive crisis developed an ulcer on the dorsum of her right foot. The patient notes that her dog caused a traumatic injury by stepping on the dorsal aspect of her foot. She subsequently developed a blister with an underlying ulcer. There was significant pain and swelling. Her ulcer had been present for 2 months and was refractory to treatment with standard wound care. No major vascular disease had been found. Reassessment of the treatment approach was indicated and it was determined that hydroxyurea should be discontinued in order to optimize her wound healing potential.

Upon review of her medical records, she had been placed 1500 mg/day of hydroxyurea for 2.5 years. In Figure 3A, a full thickness ulcer on the dorsal medial aspect of the right foot is seen with a 100% fibrotic wound base. Hydroxyurea was discontinued after contacting the patient's hematologist. The ulcer was sharply debrided with a scalpel and Santyl (Smith and Nephew) was used for topical debridement (Figure 3B). Once the wound was devoid of fibrotic tissue, negative pressure wound therapy was initiated. Shortly after discontinuation of hydroxyurea and implementation of comprehensive wound care, improved granulation tissue and wound contracture was seen within 3 weeks of treatment (Figure 3C).

Conclusion

Hydroxyurea is a chemotherapeutic agent widely used in many hematologic disorders. There is an association between hydroxyurea therapy and lower extremity ulcers with some documented case reports. These ulcers are rare and often mimic other ulcers seen in the lower extremity. Therefore high clinical suspicion is necessary to obtain an accurate diagnosis in order to employ the proper treatment approach. Noticeable signs of wound healing may not occur until a concerted effort is made to discontinue hydroxyurea therapy.

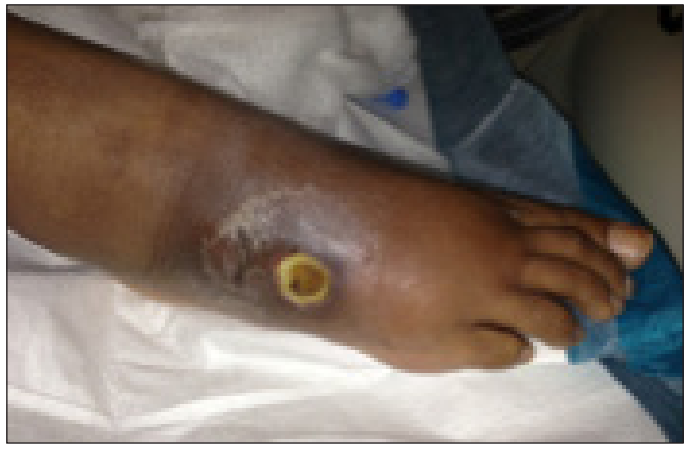

Figure 3A: 35 year old African American female with sickle cell anemia on hydroxyurea for 2.5 months with 2 month long history of right dorsum foot ulcer secondary to traumatic injury by her dog. The ulcer base is entirely fibrotic.

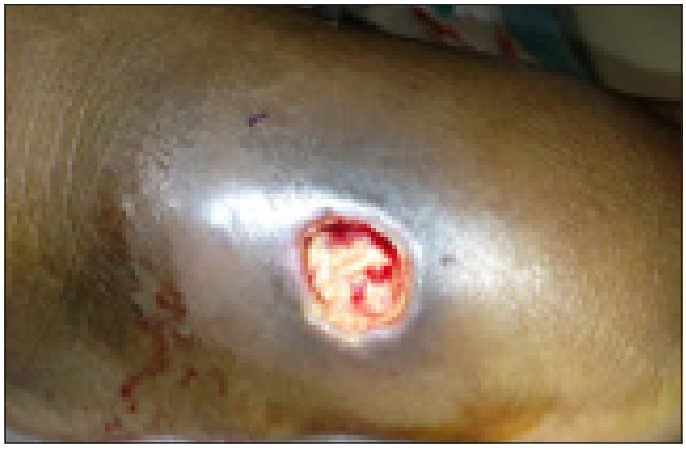

Figure 3B: Mild bleeding seen with sharp debridement. Santyl was also used as a topical agent for about a week.

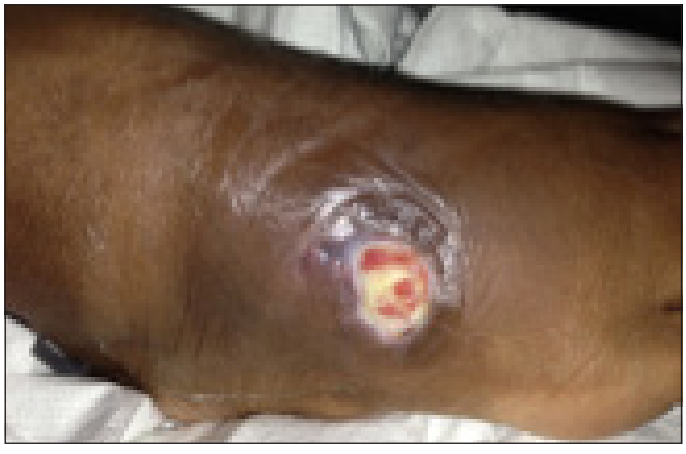

Figure 3C: Hydroxyurea had been discontinued and negative pressure wound therapy had been initiated for 3 weeks. Improved granulation tissue within ulcer base is evident.

References

(1) Stock CC, Clarke DA, Phillips FS, Barclay RK. Sarcoma 180 screening data. Cancer Research. 1960; 20(2): 193-381.

(2) Reichard KK, Larson RS, Rabinowitz I. Chronic myeloid leukemia. In Greer JP, Foerster J, Rodgers GM, Paraskevas F, Glader B, Arber DA, Means RT, eds., Wintrobe's Clinical Hematology, Philadelphia: Lippincott Williams and Wilkins; 2009; 12 (2); 2006-2030.

(3) Kennedy BJ, Smith LR, Goltz RW. Skin changes secondary to hydroxyurea therapy. Arch Dermatol 1975; 111:183-7.

(4) Sirieix ME, Debure C, Baudot N, et al. Leg ulcers and hydroxyurea: forty-one cases. Arch Dermatol 1999; 135: 818-20.

(5) Kersgard C, Osswald MB. Hydroxyurea and Sickle Cell Leg Ulcers. American Journal of Hematology. 2001; 68: 215-217.

(6) Weinlich G, Schular G, Greil R, Kofler H, Fritsch P. Leg ulcers associated with long-term hyrdroxyurea therapy. J Am Acad Dermatol. 1998 Aug; 39(2 Pt 2):372-4.

(7) Dissemond J, et al. Leg ulcer in a patient associated with hydroxyurea therapy. International Journal of Dermatology 2006; 45: 158-160.

(8) Best PJ, Daoud MS, Pittelkow MR, Petitt RM. Hydroxyurea-induced leg ulceration in 14 patients. Ann Intern Med. 1998 Jan 1; 128(1):29-32.

Hallux Interphalangeal Joint Arthroplasty for Non-Healing Neuropathic Ulcerations

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Abstract

A plethora of treatment options exist, both conservative and non-conservative, that attempts to rectify the diabetic foot ulcer. Much research has been performed on various surgical procedures. However, little has been published concerning the hallux interphalangeal joint arthroplasty for diabetic neuropathic ulcerations. Here, a discussion about the hallux interphalangeal joint arthroplasty - its uses, technique, and outcomes - will be considered.

Historical Perspective

Approximately 15% of all diabetics are affected by diabetic foot ulcers leading to more than 80,000 amputations performed within the United States yearly.[1] The plantar interphalangeal joint (IPJ) is a common site for foot ulcers in diabetics due to reduced mobility at the first metatarsophalangeal joint (MPJ) and the resultant increased pressure that is transferred to the IPJ.[2]

Only two sources in the literature have described hallux IPJ arthroplasty as a method to correct this frequent diabetic complication. Rosenblum and colleagues first described their experience with the hallux IPJ arthroplasty in a 1994 study.[3] They demonstrated a success rate of 91% for healing of the ulcerations in their cohort of 45 arthroplasty procedures with a follow-up of 23.6 months. In 1997, Martin and Blitch followed suit to discuss their success with the procedure.[4] Of the 25 procedures they performed, 23 cases healed uneventfully in less than four weeks. Overall, both have shown the hallux IPJ arthroplasty to be a valuable procedure in helping to eliminate recurrent diabetic ulcers at the hallux IPJ.

Biomechanics

The progression of neuropathy coupled with structural foot deformities involving limited joint mobility can greatly affect the lower extremity.[5] Ulcerations develop after loss of protective sensation and repetitive injury at high pressure areas of the plantar aspect of the foot.5 Corrective measures, such as debridement and pressure reduction, can be ineffective in treating ulcers due to their rate of recurrence, as high as 60%.[6] The high rate of recurrence leads to an increased risk of infections and other complications, which factors into more than 80% of lower extremity amputations in the diabetic population.5

The hallux in particular is a site susceptible to ulceration because of its central role in toe off during the gait cycle. When hallux limitus or hallux rigidus is present, functionality of the hallux is reduced due to the decreased motion at the MPJ.[4] A compensatory dorsiflexion at the IPJ may be noted in some instances and can result in additional pressure at that joint, ultimately leading to ulceration in that area (Fig. 1). In such cases, hallux IPJ arthroplasty can be a viable method to help prevent the recurrence of diabetic foot ulcers.[4]

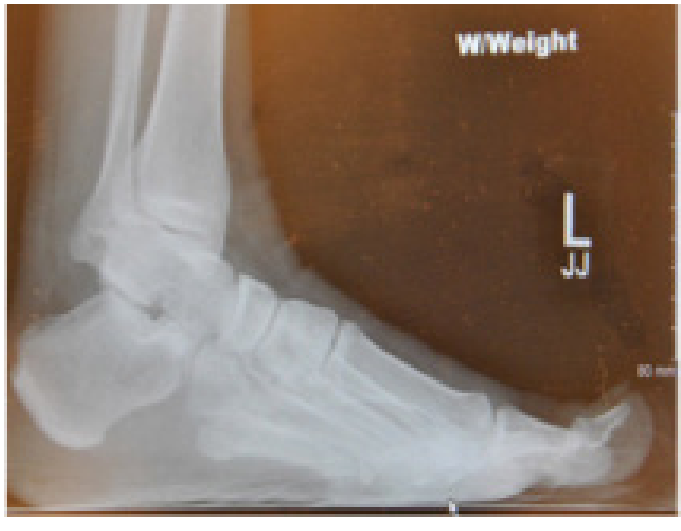

Fig. 1 Radiograph demonstrating compensatory dorsiflexion at the hallux IPJ causing increased plantar pressure at that joint. Courtesy of Jarrod Shapiro, DPM.

Indications

Rosenblum and colleagues identified the indication for this procedure as a chronic diabetic neuropathic ulcer with failed extensive conservative treatment (Fig. 2).[3]

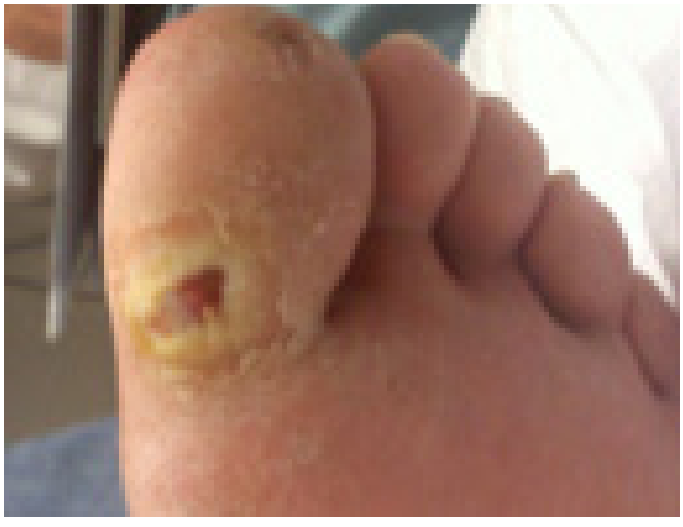

Fig. 2 Chronic diabetic ulcer on plantar medial IPJ. Courtesy of Jarrod Shapiro, DPM.

Technique

Local anesthesia with proper use of sterilization is administered in any case where sensation is still present.[3] Depending on the surgeon's choice, a dorsolinear L-shaped, transverse elliptical, or lazy "S," incision may be used (Fig. 3).[3] The layers of the dorsal surface of the hallux IPJ are dissected until the dorsal capsule and extensor hallucis longus tendon are visible. The blended capsule and extensor hallucis longus tendon are transected to expose the joint. The proximal phalanx head is then removed using a sagittal saw (Fig. 4). Proper culturing and biopsies can be taken at this time in cases where osteomyelitis or other infections may be suspected. A sesamoidectomy can be performed through the same incision if an interphalangeal sesamoid bone is present. Sterile saline is used to irrigate the area. A pin can serve as a viable option to stabilize the site during the post-operative period but is not strictly necessary. Nondegradable sutures are placed according to the surgeon's preference.

Postoperative Care

The hallux IPJ arthroplasty allows for immediate weight

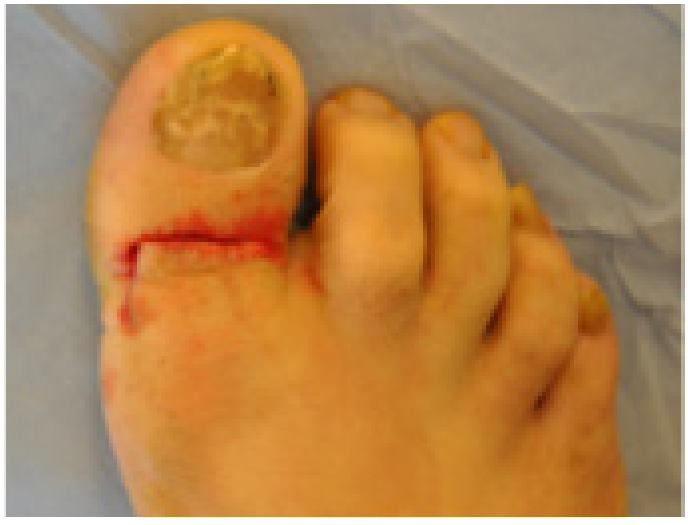

Fig. 3 Dorsolinear L-shaped incision made on the IPJ. Courtesy of Jarrod Shapiro, DPM.

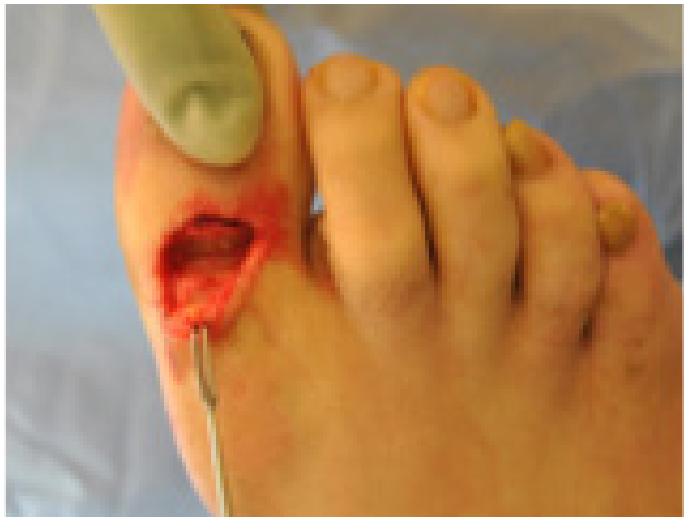

Fig. 4 Surgical site appearance after excision of the proximal phalangeal head. Courtesy of Jarrod Shapiro, DPM.

Fig. 5 Surgical site completely healed after 6 weeks post-operative. Courtesy of Jarrod Shapiro, DPM.

bearing in a post-op shoe. The minimal period for healing time contributes to its numerous advantages and reduces morbidity (Fig. 5).[4]

Results

The present literature has shown the hallux IPJ arthroplasty to be a safe and successful alternative procedure for diabetic patients with nonhealing recurrent ulcers who may have predisposing factors, such as hallux rigidus and hallux limitus.[4] Although limited, its presence within the literature has shown its efficacy and proven it to be an optimal procedure for ulcerations at the hallux IPJ with limited complications including infection, dehiscence, fixation failure, digital malalignment, and more importantly, recurrence.[4]

Conclusion

While the hallux IPJ arthroplasty has been documented to be of value, future studies need to be performed to demonstrate a more quantitative significance for its use.

Acknowledgments

Dr. Jarrod Shapiro, DPM and Dr. David Shofler, DPM for their assistance.

References

(1) Dinh, T., Tecilazich, F., Kafanas, A., Doupis, J., Gnardellis, C., Leal, E., Tellechea, A., Pradhan, L., Lyons, T., Giurini, J., & Veves, A. (2012). Mechanisms involved in the development and healing of diabetic foot ulceration. Diabetes Journal, 61, 2937-2947. Retrieved from http://diabetes.diabetesjournals.org/content/61/11/2937.full.pdf html

(2) Lin, S., Bono, C., & Lee, T. (2000). Total Contact Casting and Keller Arthoplasty for Diabetic Great Toe Ulceration under the Interphalangeal Joint. Foot Ankle International, 21(7), 588-593. Retrieved from http://fai.sagepub.com/content/21/7/588

(3) Rosenblum, B., Giurini, J., Chrzan, J., & Habershaw, G. (1994). Preventing loss of the great toe with the hallux interphalagneal joint arthroplasty. The Journal of Foot and Ankle Surgery, 33(6), 557-560.

(4) Martin, D., & Blitch, E. (1997). Hallux interphalagneal joint ulceration: A surgical correction. Retrieved from http://www.podiatryinstitute.com/pdfs/Update_1997/1997_49.pdf

(5) Lavery, L. (2012). Effectiveness and safety of elective surgical procedures to improve wound healing and reduce re-ulceration in diabetic patients with foot ulcers. Diabetes/Metabolism Research and Reviews, 28, 60-63.

(6) Peters, E., Armstrong, D., & Lavery, L. (2007). Risk factors for recurrent diabetic foot ulcers. Diabetes Care, 30(8), 2077-2079. Retrieved from http://care.diabetesjournals.org/content/30/8/2077.full.pdf html

Equinus – Fact or Fiction?

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The Big Question

Ever since the establishment of the Silfverskiold test in 1924, podiatrists and other physicians have been diagnosing ankle equinus in a number of patients, attributing it as the cause of a wide variety of lower extremity deformities, such as plantar fasciitis, Achilles tendinitis, metatarsalgia, Morton's neuroma, and hallux abductovalgus.[1] While numerous research studies have been conducted on the role of equinus in pathological conditions, including cerebral palsy or forefoot ulcers in neuropathic patients, only minimal effort has been put into the exploration of the presence and prevalence of equinus in asymptomatic patients. According to the few studies that have been done, it appears that a significant number of asymptomatic subjects possess ankle equinus.[2],[3] If this is the case and people diagnosed with the condition have otherwise normal functioning of their foot, we are left to wonder - can we always label equinus as a "pathological deformity"? If we cannot, how then do we explain the presence of equinus in healthy, asymptomatic people?

Background

Ankle equinus is a common condition that is currently understood to be a pathological deformity resulting in limited dorsiflexion at the ankle joint.[4] The Silfverskiold test was a method published in 1924, but it has continued to be the accepted standard for diagnosing equinus in patients today. Normal dorsiflexion of the ankle when the knee is extended is defined as ten degrees past neutral, which is a ninety degree foot to leg angle.[5] Dorsiflexion below this value indicates that the subject has a form of equinus. There are various forms of equinus, one of which is gastrocnemius or gastrocnemius-soleus equinus. This type is thought to be due to a pathological contracture and shortening of the muscle fibers of the gastrocnemius and/or gastrocnemius soleus complex.5 This shortening of muscle fibers can then create or worsen other problems of the lower extremity.[4] Using

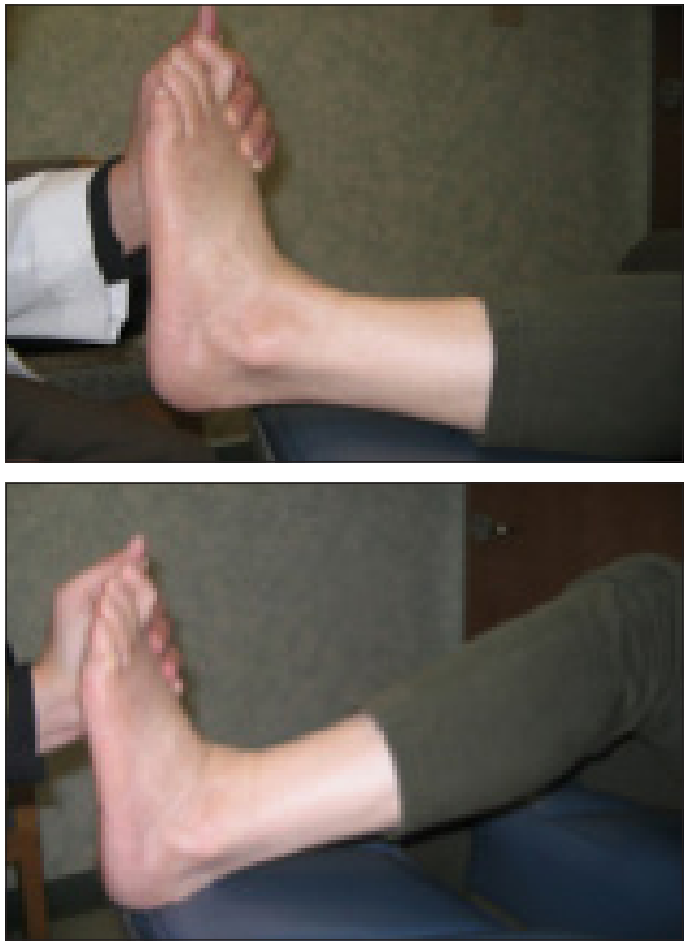

Figure 1: Silfverskiold maneuver testing for ankle joint equinus. Notice the improved dorsiflexion of the ankle in the right image, indicating a gastrocnemius equinus.

the Silfverskiold test, gastrocnemius equinus presents as improved dorsiflexion of the ankle with the knee flexed, compared to dorsiflexion of the ankle with the knee extended (Figure 1).

It is important to note, however, that the Silfverskiold maneuver was originally published as a test specific for patients with spastic conditions. Their spastic condition caused them to have increased, involuntary muscle contractures in the gastrocnemius, leading to the diagnosis

of gastrocnemius equinus.[5] This is often overlooked, and thus, this technique has been adopted for patients who do not possess spastic contractures of the posterior calf. Consequently, information was extrapolated from the spastic patients used in the original literature and applied to the non-spastic population seen in clinics today. This may have led to the inappropriate conclusion that tightness of the gastrocnemius-soleus complex is always "pathological", when in reality, that assumption should have never been generalized to non-spastic individuals.

Anatomical Considerations

Though much attention has been given to Silfverskiold for his maneuver that tests for equinus, he also described another concept called the "transmission effect" that could potentially explain the presence of decreased ankle dorsiflexion in the asymptomatic population. Under this concept, anatomists state that if a muscle crosses two or more joints, then movement in one joint will be transmitted to the other.[5] In other words, if a muscle traverses two joints, motion at the proximal joint will affect motion of the distal joint. One example that Silfverskiold provides is that of the long hamstring muscle, which traverses the hip and knee joints. He states that in a healthy man, "when the hip is strongly flexed, the knee can not be stretched owing to the insufficiency of the long hamstring muscles."[5] This does not mean that the knee is "pathological" because it cannot be fully extended, but rather, tension of the muscle at the hip joint impedes the full range of motion at the knee simply as a normal consequence of structure and attachment. Silfverskiold termed this overstretching of the muscle "passive insufficiency." There are numerous examples of this type of insufficiency found throughout the body, most of which anatomists simply consider as normal physiological consequences. The concept has even been applied to self-defense techniques, where in order to disarm an opponent who is holding a weapon, such as a knife, one should bend his or her adversary's wrist sharply because it will lead to a subsequent stretching of the fingers, thus loosening the grip of the opponent's power.[5]

Interestingly, Silfverskiold specifically included the gastrocnemius as one of the muscles that manifests this type of insufficiency. This muscle crosses not only two, but three joints – the knee, ankle, and subtalar joints. He clearly mentions that "the foot can not be dorsally flexed to a maximum with the knee stretched (passive insufficiency of the gastrocnemius)."[5] Additionally, he states that the "bending of the knee relaxes the gastrocnemius and facilitates so far a dorsal flexion of the foot".[5] This helps explain why many people have limited dorsiflexion of the ankle when the knee is extended, but then greater range of motion when the knee is flexed. Thus, there is no apparent "abnormality" in the muscle itself. Rather, extension of the knee allows the muscle to reach its maximal stretch, resulting in an apparent lack of dorsiflexion. And then by bending the knee, the muscle is loosened, allowing for greater range of motion at the distal joint. Silfverskiold also makes it a point to mention that this physiological phenomenon is seen in the healthy patient, and only becomes problematic when the muscles are spastic, leading to ill-timed or increased contraction.[5]

Review of the Research

Thus, if what we know as gastrocnemius equinus can be explained as the passive insufficiency of the muscle crossing multiple joints, then, hypothetically, many healthy people without major deformities should exhibit a decreased range of dorsiflexion when the knee is extended. Unfortunately, very little has been studied regarding the presence and prevalence of equinus in the asymptomatic population. One study that did explore this topic was conducted by Amol Saxena and Will Kim in 2003.[2] Their study examined forty high school athletes without a history of ankle injury, measured their ankle dorsiflexion, and compared those values with previously defined values found in the literature. Potential subjects were screened and exclusion criteria included a history of ankle injury, sprain, tendonitis, surgery, and a neurologic condition affecting the lower extremity. Ankle dorsiflexion was then recorded for each subject's right and left foot using a goniometer, following Silfverskiold's maneuver technique. The results indicated that the average ankle dorsiflexion in asymptomatic adolescent athletes was approximately zero degrees with the knees extended and five degrees with the knees flexed. This led to the conclusion that some degree of equinus could be considered "normal" for this population.

Another study conducted by DiGiovanni et al in 2002 examined the existence of isolated gastrocnemius contracture in normal patients without neurological conditions.[3] They looked at two different populations. The first "patient population" was comprised of patients diagnosed with metatarsalgia or related midfoot and/or forefoot symptoms, and the second population was the

"control group" comprised of subjects without foot or ankle symptoms. They measured ankle dorsiflexion in both groups with the knee fully extended and with the knee flexed. It was identified that gastrocnemius contracture was present in 65% of the patient population, compared with 24% of the control. Although there was a higher prevalence of gastrocnemius contracture in the symptomatic population, it should be noted that having 24% of healthy, asymptomatic patients diagnosed with equinus should still be considered a significant number and could potentially be explained by the passive insufficiency of the muscle traversing multiple joints.

Looking forward

Further research still needs to be done in this area to either support or refute the notion that gastrocnemius equinus in the asymptomatic population is not necessarily caused by a pathological contraction of muscle fibers, but is instead the result of normal passive insufficiency of the muscle. If this hypothesis is proven to be true and we are left to alter our entire paradigm of muscular equinus, it can lead to profound consequences in the field of medicine, ultimately altering how doctors approach treatment in both surgical and non-surgical care of the lower extremity.

References

(1) Frykberg, Robert G., DPM, MPH, Joel Bowen, DPM, Jared Hall, DPM, Arthur Tallis, DPM, Edward Tierney, DPM, and Denise Freeman, DPM, MSE. "Prevalence of Equinus in Diabetic versus Nondiabetic Patients." Journal of the American Podiatric Medical Association 102.2 (2012): 84-88.

(2) Saxena, Amol, DPM, Will Kim, DPM. "Ankle Dorsiflexion in Adolescent Athletes." Journal of the American Podiatric Medical Association 93.4 (2003): 312-314.

(3) DiGiovanni CW, Kuo R, Tejwani N, et al: "Isolated gastrocnemius tightness." J Bone Joint Surg Am. 84 (2002). 962.

(4) Hill, Russell S., DPM. "Ankle Equinus - Prevalence and Linkage to Common Foot Pathology." Journal of the American Podiatric Medical Association 85.6 (1995): 295-300.

(5) Silfverskiold N: Reduction of the uncrossed two-joint muscles of the leg to one-joint muscles in spastic conditions. Acta Chir Scand 56: 315, 1924.

(6) Gastrocnemius.http://www.cea1.com/anatomy-sistems/gastrocnemius-muscle/

Recognizing and Treating Early Stages of Charcot Neuroarthropathy

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The Charcot Foot and Ankle

The Charcot foot was first described as a complication of diabetes mellitus by William Reilly Jordan in 1936. Since then, diabetes has become the most common cause of Charcot Neuroarthropathy (CN) and the incidence of the disease has increased [1]. Individuals with longstanding diabetes and uncontrolled blood glucose are at risk for developing peripheral neuropathy that manifests in either a sensory, motor, or autonomic fashion. Charcot Neuroarthropathy is classically thought to occur due to a combination of peripheral neuropathy, repetitive trauma, and an underlying bone weakness [2]. The pathological process is characterized by osseous changes in the foot and ankle, which leads to instability and subsequent loss of limb function. Oftentimes, an injury occurs to the affected limb which triggers a bony destructive process that is accompanied by warmth and swelling. Only 22% of patients recall a specific traumatic event that preceded the onset of their condition, however, supporting the thought that repetitive trauma to the insensate foot contributes to the acute form of disease [3]. Patients with concomitant diabetic neuropathy may continue to ambulate on this injured limb, which can progressively lead to collapse of the foot arch, forming what is characteristically known as the "rocker-bottom" foot type.

Epidemiology

Population-wide studies to determine the incidence of CN in diabetics with peripheral neuropathy are difficult to perform due to missed or unreported diagnosis of the condition. The literature estimates that CN affects 0.08% of diabetics. However, the prevalence can be as high as 13% in high-risk diabetic patients [4]. Patients with type 1 diabetes present during their 5th decade, while those with type 2 diabetes present during their 6th decade. Patients with type 2 diabetes typically present with CN after 5-9 years of being diagnosed with diabetes [5]. In a study of the physical health of Charcot foot patients, those with the disease had a significantly lower Physical Health Component Score than the general population. Also, patients who were unemployed and retired had a lower score than those who were employed. This not only suggests that Charcot patients have a debilitating condition, but that there is a possible link between a patient's physical health, as determined by the Physical Health Component Summary Score, and access to health care [6]. It has also been demonstrated that patients with diabetes and CN have lower Foot and Ankle Ability Measurement (FAAM) scores than those who solely have diabetes. Patients with CN were also reported to have a lower Activities of Daily Living (ADL) score, which is a self-reported scale that asks patients to grade a set of activities from no difficulty to unable to perform, than those with just diabetes [7]. It is important to take into account that patients with diabetic CN often have other comorbidities associated with advanced diabetes, such as retinopathy or nephropathy, which can contribute to the lower quality of life scores.

Natural History of Diabetic neuropathy and CN

The complexity of CN makes it essential for practicing physicians to be aware of the potential for limb loss and mortality in patients whose course of disease is not interrupted with adequate treatment and care. The presence of bony fragmentation with subsequent foot deformity and instability may cause the patient to develop further complications, such as ulcerations and infection.

Flattening of the foot's plantar arch with a pronatory tendency is commonly seen in diabetic neuropathic patients. Garcia et al. studied the presence of limited joint mobility in diabetics and non-diabetics and found the most significant differences to occur between inversion of the STJ, dorsiflexion of the 1st MTPJ when unloaded, and degrees of valgus in neutral calcaneal stance [8]. Limitation of dorsiflexion of the 1st MTPJ requires there to be a compensatory longitudinal arch collapse and hyperextension of the IPJ in order to achieve toe off during gait, further increasing plantar medial pressures. Increased

plantar medial pressures with the pronated foot predisposes the neuropathic foot to ulceration and diabetic CN [9]. Furthermore, diabetic neuropathy has been shown to be associated with alterations in the Achilles tendon, which contributes to increased forefoot loading [10].

CN itself has been associated with limitations in ankle joint and subtalar joint range of motion. Sinacore et al. found there to be an increasing talar declination angle and decreasing calcaneal inclination angle, thereby decreasing ankle joint plantarflexion. This limits the ability of the foot to effectively counter ground force while ambulating and can contribute to excess stress being placed on the plantar aspect of the foot during gait, resulting in plantar ulceration [2].

Other variables, such as obesity, may also play a role in flattening of the arch and can be detrimental, especially in the wake of a neuropathic process. Stuck et al. studied 561,597 diabetic patients of the VA and had their height and weight measured in 2003. They found that incidence of Charcot increased by 59% in patients solely with obesity, increased by 14 times in those solely with neuropathy, and increased 21-fold in patients with both conditions. The authors also showed that an elevated HbA1c is associated with greater than a 30% increase in risk for developing CN [11].

The importance of preventing ulceration of the Charcot foot is accentuated by a retrospective study conducted by Gazis et al. in which they studied the difference in survival and incidence of amputation between patients with a Charcot foot and those with diabetic neuropathic ulcerations. They found no difference in mortality between the two groups, suggesting that neuropathy could be the independent factor involved in mortality rates [12]. Sohn et al. further stratified their subjects into Charcot patients, patients with foot ulcers, and patients with both Charcot and foot ulcers. The study compared the risk of amputation between the three groups. The authors found that those with an ulcer alone had a 7 times higher risk of amputation than those with Charcot alone, while those with both Charcot and an ulcer had a 12 times higher risk, ultimately concluding that CN does not pose a more significant risk for amputation than ulceration unless the Charcot foot is complicated by an ulcer [13]. Even a digital amputation can increase the risk of ulcer development. In a study of great toe amputations, there were increased postoperative peak plantar pressures in the foot [9]. This increases the risk of developing ulcers and has a higher mortality rate.

Symptoms of Charcot

When a diabetic patient with neuropathy presents with foot complaints, conducting a thorough history and physical to confidently reach a diagnosis can prove to be a daunting task for the physician. Knowing what to look for will help eliminate possible differentials for which Charcot may be commonly mistaken. Early presentation of CN includes erythema, edema, and warmth. These findings may appear to be nonspecific to the untrained eye and are often misdiagnosed as cellulitis or infection of the lower extremity. Other misdiagnoses include deep vein thrombosis, gout, or traumatic ankle sprain. In their series of case studies, Gill et al. state that a safe clinical policy to follow would be to assume that diabetic patients with acute foot or ankle swelling have a neuroarthropic condition until proven otherwise [14]. Other clinical findings of acute CN include mild to moderate pain or discomfort despite the presence of neuropathy. A temperature difference of several degrees between the two limbs may also be noted. This finding can be explained by the increased arterial blood flow to the affected limb, characterized by bounding pulses if edema does not obscure it [15].

The Eichenholtz classification scheme is commonly used to stage Charcot symptoms. Later stages of the disease show a decrease in warmth and erythema, coalescence, and bone remodeling. No foot temperature difference is noted in these patients. The presence of bone destruction, fragmentation, and disorganized joint architecture are visible on plain radiographs at this stage [16]. Acute Charcot is often missed because fractures may not be visible on plain radiographs early in the course of the disease. However, MRI is more diagnostically useful in earlier stages of CN and will show increased bone marrow edema [17]. Chantelau et al. conducted a study using 24 patients that had a red, hot, swollen, and relatively painful foot. In all 24 patients, plain film radiographs were taken within 2 weeks and were deemed to be normal. All patients continued ambulation until referral to a foot and ankle specialist and two patients were instructed to increase walking in order to improve circulation to their limbs. Despite the difficulties of identifying early CN,

early diagnosis should be achieved so that an appropriate treatment regimen can be established before complete fracture and permanent deformity develops [18].

Osteomyelitis

The presence of an open wound in conjunction with a red, hot, and swollen foot should introduce osteomyelitis to the list of differential diagnoses. This infectious process can occur with concomitant neuroarthropathy [4]. If there is a high index of suspicion for osteomyelitis based on the incidence of the condition in a given population, a probe to bone test can be useful in diagnosis. The gold standard for diagnosis, however, is a bone biopsy, which provides information about the invading pathogen and provides direction for treatment regimen. Since osteomyelitis is inherently an infectious process, one may expect elevated C-reactive protein (CRP) and leukocytes in acute infections, though they are nonspecific findings. Acute infectious markers are expected to be normal in CN, although this finding is expected in chronic osteomyelitis as well [19]. An elevated ESR is suggestive of osteomyelitis if combined with positive clinical findings for the condition. A retrospective study conducted by Fleischer et al. found that both CRP (> 3.2 mg/dL) and ESR (> 80 mm/h) yielded more sensitive results for osteomyelitis when combined with clinical presence of ulcer depth > 3 mm, with CRP being the most accurate laboratory marker for osteomyelitis [20]. Because of the morbidity of this condition, osteomyelitis must be included as a differential diagnosis for a patient presenting with diabetic neuropathy and an ulcer.

Pathophysiology of CN

Despite increasing awareness of this debilitating disease, the initiating factor for the development of CN has not been thoroughly established. Multiple theories that explain the pathogenesis of the disease exist. What is clear, however, is the fact that repeated trauma to the insensate foot of a neuropathic patient plays an important role, as per the neurotraumatic theory. Recent studies have set out to find the link between the visualized bone destruction and a possible alteration in inflammatory mediators that contribute to the disease.

With regard to diabetic neuropathy, factors such as hyperglycemia-induced production of acetylated glycation end products (AGE) and microvascular complications have been associated with peripheral neuropathy [21]. Endothelial nitric oxide synthase (eNOS) plays an important role in mediating microvascular permeability and blood flow [22]. Previous studies have shown there to be reduced expression of eNOS in diabetic neuropathic patients with and without vascular disease compared to those with uncomplicated diabetes, revealing the role of microvascular complications in the development of neuropathy [23]. La Fontaine, Harkless et al. conducted a pilot study which compared the expression of eNOS between Charcot patients in stages 2 or 3 and diabetic patients with and without neuropathy. Bone samples were collected from consenting patients of each of the three aforementioned groups undergoing corrective procedures and were sent for immunehistochemical analysis. Patients with a history of neuropathic ulceration were excluded from the study in order to eliminate the possibility of underlying osteomyelitis in bone specimens. The authors found a significant decrease in eNOS expression between the samples from patients with Charcot stage 2 or 3, and those with diabetes with and without neuropathy. The authors note that reduction of eNOS contributes to a decrease in NO, which increases osteoclastogenesis in the Charcot foot [24].

Advanced glycation end products (AGEs) are formed during hyperglycemic states and are implicated with cross-linking of extracellular matrices and cellular dysfunction when accumulated intracellularly. Its effects are mediated by the actions of its receptor, RAGE [21]. Witzke et al. found that patients with CN have a decreased level of RAGE, thereby limiting the ability of these patients to combat oxidative stress [25].

The osseous changes observed in the Charcot foot have also been linked to increased resorption facilitated by an increased level of osteoclastic precursors. Using Type I collagen serum carboxyterminal telopeptide (1CTP) as a marker of osteoclastic bone resorption, Gough et al. found that 1CTP was raised in the dorsal venous arch region in those with acute CN compared to those with chronic CN, diabetic, and non-diabetic controls. The authors concluded that the acute Charcot foot has increased expression of osteoclastic activity without an increase in osteoblastic activity [16]. Furthermore, bone mineral density has been found to be decreased in the Charcot foot compared to the non-Charcot foot at clinical presentation

[5]. Supplementing this finding is the fact that the affected Charcot foot has been found to have a lower bone mineral density than the unaffected foot [26].

TNF-alpha is another inflammatory cytokine that has been implicated in pathogenesis of the disease. Mabilleau et al. found there to be a 1.7 fold increase in TNF-alpha compared to diabetics (p=0.014) and a 2.2 fold increase compared to healthy controls (p=0.009), suggesting that excess bone resorption in CN is linked with increased levels of TNF-alpha and osteoclast precursors [27]. In addition, genetic factors have also been implicated. Through genotyping, Burakowska et al. found two polymorphisms for OPG at the 245 and 1217 residues. An increased risk of developing CN occurred when the TT genotype was present at these locations as opposed to the TC or CC genotype [28].

The aforementioned studies can be helpful in the discovery of novel screening procedures or pharmacotherapies that exploit these changes in inflammatory molecules and presence of gene polymorphisms.

Acute Charcot Foot Treatment - The Gold Standard

The aim of therapy for CN is to maintain a plantigrade foot in order to arrest the development of osteoarthropathy. The eventual goal is to allow the patient to bear weight in a shoe or brace [29]. Immobilization and offloading are recommended for the initial management of the acute Charcot foot [30]. Offloading helps to reduce inflammation and fracture formation in CN. Other beneficial effects of this modality are reduction of RANKL and NF-kb and protection of the bones and joints that are vulnerable to fractures, dislocations, and resultant deformities [31].

Many research studies have advocated the use of total contact casts (TCC) in offloading. A total contact cast is a non-removable, below-knee plaster cast with minimal to no padding that fits the lower leg like a glove. It increases the surface area of the plantar foot in order to distribute the forces and eliminates the vertical forces of gait by locking the ankle [32]. The use of a total contact cast is contraindicated in the presence of an infected ulceration, excessive edema, peripheral vascular disease, dermatitis, or claustrophobia. It has found use in treating uninfected plantar foot ulceration, acute Charcot, and postoperative procedures where weight bearing needs to be decreased. Because there are several steps involved in making a total contact cast, it is recommended that a highly trained casting technician or podiatric surgeon attempt the application [32]. The total contact cast should be initially changed every 4-5 days, then every 1 to 2 weeks as needed. The average total duration of immobilization and casting is 4-6 months. However, this number varies according to the location of the CN. Patients with an affected ankle, hindfoot, or midfoot will generally have longer healing times than those affected in the forefoot [33].

The duration of casting depends on the resolution of the inflammation and bone destruction phase of CN. Studies have reported casting durations anywhere from 10 weeks to one and a half years, including casting time for recurrences [34]. A recent review on the management of the Charcot foot has stated that the general evaluation of the resolution of the acute phase is determined clinically by the reduction in redness, swelling, and temperature as measured by an infrared thermometer. The temperature difference between the affected Charcot foot and the unaffected contralateral foot should be less than 2 degrees. When this point has been reached, the total contact cast should be removed and the patient should be transitioned into another form of support.

The complications that may result from a total contact cast are as follows: [34]

- Risk of ulceration and risk of amputation
- Loss of muscle tone and body fitness
- Poor glycemic control
- Increase in BMI
- Risk of falling
- Negative impact on quality of life
- Inappropriate duration of therapy

Casting therapy that is too short may result in an increased risk of deformity or deterioration of an existing foot deformity. If the casting therapy is too long, there is a risk of reduced bone mineral density, which increases the risk for further fractures [34]. The rehabilitation from casts to footwear must be gradual because rapid mobilization may reactivate bony destruction and joint damage.

Though the TCC is the gold standard of treatment, there are alternative non-removable cast options that may be

offered to patients. The fiberglass cast is made of woven fiberglass coated with polyurethane resin. One advantage of plaster over fiberglass casting is that plaster is more pliable and has a slower setting time than fiberglass, allowing more application and molding time before setting [35]. Slower setting times produce less heat, which decreases the risk of burns and discomfort. Contrastingly, an advantage of using a fiberglass cast is that it is lighter for the patient and produces less of a mess in application. It also requires changing every 1 to 2 weeks.

For patients who do not want a non-removable cast, there are removable offloading options. However, these alternatives do not offer as much support and will be removed often, causing longer healing times [31]. There are pre-fabricated removable walking cast options such as the instant total contact cast (iTCC), which is a hybrid between a total contact cast and a removable walking cast. The iTCC is a modification of a removable cast, making it less easy to take off by the patient, thereby improving patient compliance and healing. For patients who would like more freedom than a removable cast walker can offer, the removable Aircast may be a feasible option. This type of offloading allows indoor walking with crutches and may be removed at night unless there is ankle CN or gross instability. Patients can even use this device to exercise on a bicycle [34]. A research study on the removable Aircast showed that the less restrictive offloading with early and gradually augmented re-load on the foot obtained clinical healing in less than 6 months, which is comparable to the average healing time with the TCC. What is important to consider when offering these options to patients is the level of compliance that is expected. A research study on the recurrence of acute Charcot after conservative treatment showed that a high predictor of recurrence was non-compliance [36]. Thus, it may be beneficial to use the total contact cast in order to ensure proper offloading.

Much controversy exists as to whether or not the patient should be weight-bearing with the total contact cast. An analysis of weight-bearing vs. non-weight-bearing for total contact casts showed that there is no clear evidence to suggest that one way is more superior than the other [29]. A recent study of 27 patients with CN allowed weight-bearing as tolerated and resulted in no deleterious effects. However, 40% patients that were non-weight-bearing reported a development of CN in the contralateral foot [29]. This may suggest that non-weight-bearing increases the mechanical forces on the contralateral foot, thereby increasing the risk of developing CN. The physician may want to advise the patient to use crutches or a wheelchair to reduce contralateral foot pressure if they are non-weight-bearing [29]. Some clinicians may advocate initial non-weight-bearing in the TCC and gradually allow weight-bearing. Others prefer non-weight-bearing throughout the use of a TCC. Thus, duration and aggressiveness of offloading and removability of the cast should be guided by the clinical assessment of healing in the acute Charcot foot. The clinical assessment is based on the same criteria used to evaluate the progression of the inflammatory stage. Evidence of healing on an x-ray or MRI can also help to strengthen the clinical decision [30]. Use of bone scanning has also shown correlation to the clinical assessment of Charcot and may help determine further therapy [37].

Transition Footwear

If the total contact cast is chosen for treatment and the inflammation phase has resolved, the patient should be transitioned from the cast to a removable total-contact bivalve cast walker or Charcot Restraint Orthotic Walker (CROW). This device externally fixates the ankle, provides padding to the medial malleoli region, and accommodates deformities in order to prevent further ulcerations [29]. The patient must assess for swelling, redness, and warmth of the foot each day to monitor any possible return of inflammation. If these symptoms are absent, the patient may proceed with a few more steps the next day. The patient can then transition from a CROW to ankle-foot orthosis (AFO) with bespoke footwear (custom-made shoes) [38].

Pharmacological therapy

The goal of pharmacological management in acute CN is to correct the imbalance between bone resorption and formation. The main drugs that have been proposed for use in acute CN management are bisphosphonates, calcitonin, and human parathyroid hormone.

Currently, bisphosphonates are not FDA approved for use in the management of acute CN. Recent studies on bisphosphonates such as Pamidronate, Zoledronate, and Alendronate have shown a reduction in bone turnover

through inhibition of osteoclast bone resorption and possibly direct anti-inflammatory action [39]. The reduction was shown to last 6 months after administration. The effect on pain symptoms has varied between studies with some showing improvement while others show no difference. However, there are no long term studies that have demonstrated the effects of bisphosphonates in fracture healing and resolution of the acute stage of CN. The goal of CN management is to prevent foot deformities, ulceration, and amputation, but the current studies have not provided information regarding these outcomes [38]. A pilot study of Zoledronic acid has shown a longer immobilization time compared to a control group in which only casting therapy was initiated [40]. However, it is possible that bisphosphonates may be useful during a certain time frame in which extensive bone fragmentation and fractures have not yet developed, but further studies need to be done. The contraindications against the use of bisphosphonates include chronic kidney disease, a complication that is often seen in diabetic patients with CN [39].

Intranasal calcitonin has shown to decrease excessive bone turnover in Charcot patients and is considered an alternative to bisphosphonates. This can be used in patients with renal insufficiency [39]. Its mechanism of action is to reduce the expression of RANKL [31]. It is most effective when supplemented with calcium.

Human parathyroid hormone is a new interest in research for the treatment of acute Charcot foot. Currently, only a pilot study has been completed and a double-blinded randomized controlled trial is currently underway [41]. TNF-alpha and RANKL antagonists may also show promising results and should be future topics of research for the treatment of acute Charcot. In summary, there is little evidence for the use of bisphosphonates as routine management for diabetic with CN. It is still recommended that the mainstay of treatment be offloading and immobilization of the affected limb.

Recurrence & Prevention

A research study with 52 patients showed that high predictors of recurrence after conservative treatment is insufficient offloading due to obesity and unattainable immobilization due to non-compliance [36]. Patients with less time between onset of symptoms and start of treatment are found to have less recurrence rates of CN. In addition, those with shorter casting duration had more favorable results than those with longer casting therapy. However, patients with longer casting therapy may have been identified at a later stage of Charcot, which may have predisposed them to an increased risk of recurrence [34]. Thus, it is favorable to identify patients at an early stage of CN and be aware of the risk factors which increase the chances of recurrence. On the patient's end, blood glucose levels should be monitored. Body temperature, cast stains, cracks, cast rubs, ulcers, and infections should also be inspected daily in order to prevent recurrence and further complications of CN [29].

References

(1) Sanders LJ. The Charcot foot: historical perspective 1827-2003. Diabetes Metab Res Rev. 2004 May-Jun;20 Suppl 1:S4-8.

(2) Sinacore, Gutekunst DJ, Hastings MK, Bohnert KL, Prior FW, Johnson JE. Neuropathic midfoot deformity: associations with ankle and subtalar joint motion. J Foot Ankle Res. 2013 Mar 25;6(1):11. doi: 10.1186/1757-1146-6-11.

(3) Armstrong DG, Todd WF, Lavery LA, Harkless LB, Bushman TR. The natural history of acute Charcot's arthropathy in a diabetic foot specialty clinic. Diabetic Med. 1997;14(5):357-363.

(4) Donegan R, Sumpio B, Blume PA. Charcot foot and ankle with osteomyelitis. Diabet Foot Ankle. 2013 Oct 1;4. doi: 10.3402/dfa.v4i0.21361. eCollection 2013.

(5) Petrova NL, Foster AV, Edmonds ME. Difference in presentation of charcot osteoarthropathy in type 1 compared with type 2 diabetes. Diabetes Care. 2004 May;27(5):1235-6.

(6) Sochocki MP, Verity S, Atherton PJ, Huntington JL, Sloan JA, Embil JM, Trepman E. Health related quality of life in patients with Charcot arthropathy of the foot and ankle. Foot Ankle Surg. 2008;14(1):11-5. doi: 10.1016/j.fas.2007.07.003. Epub 2007 Oct 22.

(7) Raspovic KM, Wukich DK. Self-Reported Quality of Life in Patients With Diabetes: A Comparison of Patients With and Without Charcot Neuroarthropathy. Foot Ankle Int. 2013 Dec 18.

(8) García-Álvarez Y, Lázaro-Martínez JL, García-Morales E, Cecilia-Matilla A, Aragón-Sánchez J, Carabantes-Alarcón D. Morphofunctional characteristics of the foot in patients with diabetes mellitusand diabetic neuropathy. Diabetes Metab Syndr. 2013 Apr-Jun;7(2):78-82. doi: 10.1016/j.dsx.2013.02.029. Epub 2013 Mar 15.

(9) Lavery LA, Lavery DC, Quebedeax-Farnham TL. Increased foot pressures after great toe amputation in diabetes.Diabetes Care. 1995 Nov;18(11):1460-2.

(10) Batista F, Nery C, Pinzur M, Monteiro AC, de Souza EF, Felippe FH, Alcântara MC, Campos RS. Achilles tendinopathy in diabetes mellitus. Foot Ankle Int. 2008 May;29(5):498-501.

(11) Stuck RM, Sohn MW, Budiman-Mak E, Lee TA, Weiss KB. Charcot arthropathy risk elevation in the obese diabetic population.Am J Med. 2008 Nov;121(11):1008-14. doi: 10.1016/j.amjmed.2008.06.038.

(12) Gazis A, Pound N, Macfarlane R, Treece K, Game F, Jeffcoate W. Mortality in patients with diabetic neuropathic osteoarthropathy (Charcot foot). Diabet Med. 2004 Nov;21(11):1243-6.

(13) Sohn MW1, Stuck RM, Pinzur M, Lee TA, Budiman-Mak E.Lower-extremity amputation risk after charcot arthropathy and diabetic foot ulcer. Diabetes Care. 2010 Jan;33(1):98-100. doi: 10.2337/dc09-1497. Epub 2009 Oct 13.

(14) Gill GV, Hayat, Majid. Diagnostic delays in diabetic Charcot arthropathy. 2004. Pract Diab Int

(15) Rogers LC, Frykberg RG.The Charcot foot. Med Clin North Am. 2013 Sep;97(5):847-56. doi: 10.1016/j.mcna.2013.04.003
(16) Gough A, Abraha H, Li F, Purewal TS, Foster AV, Watkins PJ, Moniz C, Edmonds ME. Measurement of markers of osteoclast and osteoblast activity in patients with acute and chronic diabetic Charcot neuroarthropathy.Diabet Med. 1997 Jul;14(7):527-31.
(17) Chantelau EA, Richter A. The acute diabetic Charcot foot managed on the basis of magnetic resonance imaging--a review of 71 cases.Swiss Med Wkly. 2013 Jul 29;143:w13831.
(18) Chantelau E. The perils of procrastination: effects of early vs. delayed detection and treatment of incipient Charcot fracture. Diabet Med. 2005 Dec;22(12):1707-12.
(19) Ertugrul BM, Lipsky BA, Savk O. Osteomyelitis or Charcot neuro-osteoarthropathy? Differentiating these disorders in diabetic patients with a foot problem. Diabet Foot Ankle. 2013 Nov 5;4.
(20) Fleischer AE, Didyk AA, Woods JB, Burns SE, Wrobel JS, Armstrong DG. Combined clinical and laboratory testing improves diagnostic accuracy for osteomyelitis in the diabetic foot. J Foot Ankle Surg. 2009 Jan-Feb;48(1):39-46.
(21) Tan AL, Forbes JM, Cooper ME. AGE, RAGE, and ROS in diabetic nephropathy. Semin Nephrol. 2007 Mar;27(2):130-43.
(22) Durán WN, Breslin JW, Sánchez FA. The NO cascade, eNOS location, and microvascular permeability. Cardiovasc Res. 2010 Jul 15;87(2):254-61.
(23) Veves A, Akbari CM, Primavera J, Donaghue VM, Zacharoulis D, Chrzan JS, DeGirolami U, LoGerfo FW,Freeman R. Endothelial dysfunction and the expression of endothelial nitric oxide synthetase in diabetic neuropathy, vascular disease, and foot ulceration. Diabetes. 1998 Mar;47(3):457-63.
(24) La Fontaine J, Harkless LB, Sylvia VL, Carnes D, Heim-Hall J, Jude E. Levels of endothelial nitric oxide synthase and calcitonin gene-related peptide in the Charcot foot: a pilot study. J Foot Ankle Surg. 2008 Sep-Oct;47(5):424-9.
(25) Witzke KA, Vinik AI, Grant LM, Grant WP, Parson HK, Pittenger GL, Burcus N. Loss of RAGE defense: a cause of Charcot neuroarthropathy? Diabetes Care. 2011 Jul;34(7):1617-21.
(26) Gutekunst DJ, Smith KE, Commean PK, Bohnert KL, Prior FW, Sinacore DR. Impact of Charcot neuroarthropathy on metatarsal bone mineral density and geometric strength indices. Bone. 2013 Jan;52(1):407-13.
(27) Mabilleau G, Petrova N, Edmonds ME, Sabokbar A. Number of circulating CD14-positive cells and the serum levels of TNF-α are raised in acute charcot foot. Diabetes Care. 2011 Mar;34(3):e33.
(28) Korzon-Burakowska A1, Jakóbkiewicz-Banecka J, Fiedosiuk A, Petrova N, Koblik T, Gabig-Cimińska M, Edmonds M, M ałecki MT, Węgrzyn G. Osteoprotegerin gene polymorphism in diabetic Charcot neuroarthropathy.Diabet Med. 2012 Jun;29(6):771-5.
(29) Petrova NL, Edmonds ME. Medical management of Charcot arthropathy. Diabetes Obes Metab. 2013 Mar;15(3):193-7.
(30) Rogers LC, Frykberg RG, Armstrong DG, Boulton AJ, Edmonds M, Van GH, Hartemann A, Game F, Jeffcoate W, Jirkovska A, Jude E, Morbach S, Morrison WB,Pinzur M, Pitocco D, Sanders L, Wukich DK, Uccioli L. The Charcot Foot in Diabetes. Diabetes Care. 2011 34:2123–2129
(31) Game F, Jeffcoate W. The charcot foot: neuropathic osteoarthropathy. Adv Skin Wound Care. 2013 Sep;26(9):421-8.
(32) Malhotra S, Bello E, Kominsky S.Diabetic foot ulcerations: biomechanics, charcot foot, and total contact cast.. Semin Vasc Surg. 2012 Jun;25(2):66-9.
(33) Blume PA, Sumpio B, Schmidt B, Donegan R. Charcot Neuroarthropathy of the Foot and Ankle: Diagnosis and Management Strategies. Clin Podiatr Med Surg. 2014 Jan;31(1):151-72.
(34) Christensen TM, Gade-Rasmussen B, Pedersen LW, Hommel E, Holstein PE, Svendsen OL. Duration of off-loading and recurrence rate in Charcot osteo-arthropathy treated with less restrictive regimen with removable walker. J Diabetes Complications. 2012 Sep-Oct;26(5):430-4.
(35) Boyd AS, Benjamin HJ, Asplund C. Principles of casting and splinting. Am Fam Physician. 2009 Jan 1;79(1):16-22.
(36) Osterhoff G, Böni T, Berli M. Recurrence of acute Charcot neuropathic osteoarthropathy after conservative treatment. Foot Ankle Int. 2013 Mar;34(3):359-64.
(37) M.McGill, L.Molyneaux, T. Bolton, K. Ioannou, R.Uren, D.K.Yue. Response of Charcot's arthropathy to contact casting: assessment by quantitative techniques. Diabetologia. 2000 Apr;43(4):481-4.
(38) N. L. Petrova, M. E. Edmonds. Charcot neuro-osteoarthropathy – current standards. Diabetes Metab Res Rev. 2008 May-Jun;24 Suppl 1:S58-61.
(39) Richard JL, Almasri M, Schuldiner S.Treatment of acute Charcot foot with bisphosphonates: a systematic review of the literature. Diabetologia. 2012 May;55(5):1258-64.
(40) Pakarinen TK, Laine HJ, Mäenpää H, Mattila P, Lahtela J. The effect of zoledronic acid on the clinical resolution of Charcot neuroarthropathy: a pilot randomized controlled trial. Diabetes Care. 2011 Jul;34(7):1514-6.
(41) EU Clinical Trials Register. Available from URL: http://www.clinicaltrialsregister.eu/ctr-search?query=2009-016873-13+.

Total Knee Arthroplasty and Ambulation: Adductor Canal Block vs. Femoral Nerve Block

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Introduction

A recent topic of interest in the field of anesthesia is total knee arthroplasty (TKA), the different approaches currently available to achieve anesthesia and their effects on ambulation. The two main techniques that have been studied extensively are the adductor canal block (ACB) and the femoral nerve block (FNB). This article will review current anesthesia research regarding the management of TKA and compare the two techniques to each other, as well as analyze them individually in terms of their relation to ambulation. Aspects of ambulation that were studied include: strength of quadriceps1,[2] range of motion in knee flexion[3], distance ambulated[4], and time taken to ambulate a fixed distance[2],[6]. Correlations between strength, range of motion, distance walked, timed-up-and-go test and practical ambulation are not directly established. However, these studies are a step towards optimizing recovery time through choice of anesthesia delivery and minimizing immobility, which prevents risks for the patient.

Time of Follow-up	ACB N = 46	FNB N = 47	Difference: ACB-FNB (95% CI)	Test of Equal Medians: *P* Value (Holm-Bonferroni)*
Operative leg				
Preoperative, kgf	15.6±8.5 12.3 [9.6, 20.2]	14.8±8.2 11.6 [8.3, 20.1]	0.8 (−2.7 to 4.2)	0.9999
Postanesthesia 6—8h, kgf	7.3±5.4 6.1 [3.5, 10.9]	2.2±3.8 0.0 [0.0, 3.9]	5.2 (3.1–7.2)	<0.0001
Postanesthesia 24h, kgf	3.9±4.2 3.5 [1.1, 4.4]	4.0±4.0 2.8 [1.1, 6.8]	−0.1 (−1.9 to 1.6)	0.9999
Postanesthesia 48h, kgf	2.2±2.9 1.8 [0.0, 3.3]	2.8±3.2 1.7 [0.0, 4.1]	−0.6 (−1.9 to 0.7)	0.9999
Nonoperative leg				
Preoperative, kgf	18.5±9.1 16.7 [11.6, 24.4]	18.3±9.2 16.9 [10.7, 27.4]	0.2 (−3.6 to 4.0)	0.9999
Postanesthesia 6−8h, kgf	15.8±7.6 14.4 [9.9, 21.3]	16.2±10.3 13.9 [8.1, 25.4]	−0.4 (−4.4 to 3.6)	0.9999
Postanesthesia 24h, kgf	16.7±7.4 15.7 [10.2, 22.6]	17.8±9.0 16.9 [10.1, 25.4]	−1.1 (−4.6 to 2.5)	0.9999
Postanesthesia 48h, kgf	16.7±7.8 15.1 [12.0, 22.0]	18.5±11.8 16.4 [9.2, 26.3]	−1.8 (−6.2 to 2.6)	0.9999

Results presented as mean ± SD, median [first, third quartiles].
* Holm-Bonferroni adjusted *P* <0.05 is considered statisttically significant.
ACB − adductor canal block; FNB − femoral nerve block; kgf − kilogram-force unit.

Table 1. Strength of Quadriceps with ACB vs. FNB 1

Strength

The first aspect of ambulation analyzed was strength. In a study published January 2014 in Anesthesiology[1], the strength of patients' quadriceps was measured by dynamometer in kilograms-force (kgf) units. This study compared 93 patients who received TKA, with 46 receiving ACB using 15ml Bupivacaine 0.5% and 5 µg/ml Epinephrine versus 47 receiving FNB using 30ml Bupivacaine 0.25% and 5 µg/ml Epinephrine. Six to eight hours after the surgery, the mean quadriceps strength in patients who received the ACB was 6.1 kgf, compared to patients who received the FNB who had a mean of 0 kgf (p value <0.0001, Table 1). However, a note of interest was that 24 hours post-op, the ACB patients went on to have a decrease in mean strength from 6.1 to 3.5 kgf, while the FNB patients had an increase in mean strength from 0 to 2.8 kgf. Although the group with the ACB eventually had decreased mean strength relative to 6 to 8 hours post-op, they still had greater strength than the group with the FNB.

Another study done in November 2013 in Regional Anesthesia and Pain Medicine2 also compared the quadriceps strength in those who received ACBs and FNBs. The study was double-blind, randomized and controlled, measuring percentage of muscle contraction in 48 participants: 22 in the adductor group and 26 in the femoral group. Both groups were given a bolus of 30ml Ropivacaine 0.5% then 8ml/hour Ropivacaine 0.2% for 24 hours. Patients who received the ACB had 25% of the baseline maximum voluntary isometric contraction 24 hours after surgery, compared to only 18% in those who received FNB (p value < 0.004, Figure 1).

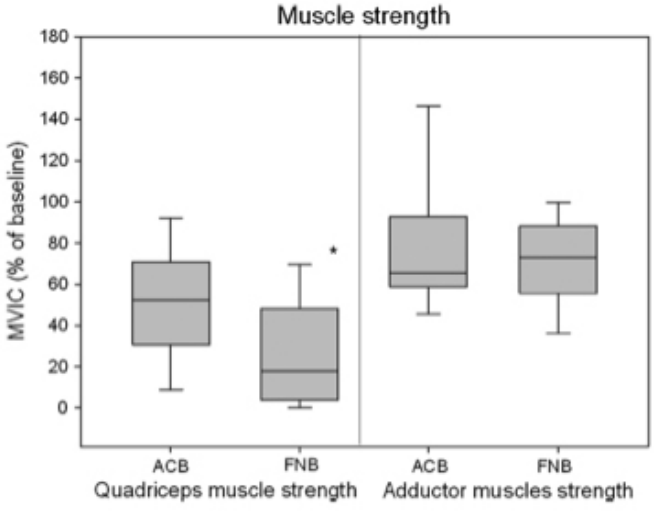

Figure 1. Strength in Quadriceps and Adductor with ACB vs. FNB measured in % of baseline Maximum Voluntary Isometric Contraction (MVIC)2

Both of these studies indicate that there is a significant gain of quadriceps muscle strength postoperatively in patients who received ACBs relative to those who received FNBs. However, it is uncertain whether that benefit is transient, as demonstrated in the 2014 study[1], or lasting at least 24 hours, as was shown by the 2013 study[2]. In order to address this, a study conducted with a longer time frame post-op to measure outcomes is needed to determine if any longer-term (48 hours to 7 days) benefit is gained by one block over the other. Another topic of consideration that arose in the 2014 study[1] was that the FNB group had 3 patients who "buckled" (near fall) while ambulating, which was attributed to quadriceps weakness. Although not an objective strength measurement, there were no patients in the ACB group who "buckled." A further study with a larger sample size is needed to assess whether this "buckling" is a legitimate fall risk with a demonstrably significant difference in the groups.

Range of Motion

Another aspect of ambulation is range of motion (ROM) of the joints involved, particularly the lower extremity, in this case focusing on the knee status post TKA. A prospective, randomized and controlled study conducted at the Osaka University, Graduate School of Medicine in Japan, May 2013 in The Journal of Arthroplasty[3] assessed ROM in 60 patients, 30 who received continuous femoral nerve block (CFNB) with an additional single injection tibial nerve block versus 30 who received a continuous epidural anesthesia (CEA), all of whom used Ropivacaine 0.3%.

Patients who received a CFNB could passively flex their knee to 120^{o} at a mean of 8 days postoperatively, as opposed to patients who only received a CEA who needed an average of 15 days to achieve the same ROM. The difference in time to full 120^{o} was about 6.5 days, with a 95% confidence interval and p-value <0.001. Even prior to attaining the full passive ROM, on Post-Op Day (POD) 4, patients in the CFNB arm had achieved a mean of

100^0 ROM, compared to patients in the CEA arm, who had only achieved 90^0. Even at this point, the difference between these groups was statistically significant, with the p-value <0.001. Therefore there was a significant gain in degrees in ROM in patients who received the CFNB, even relatively early (POD 4) in the post-operative course.

Unfortunately, the study is not purely in support of CFNB because the arm of the study that received CFNB also received a tibial nerve block, thus confounding the comparison. Additionally, a unique aspect about this study was that the ROM parameters were set to 120^0 rather than the typical 90^0 that many other studies use. The researchers explained that in Asian and Middle Eastern cultures, squatting, kneeling and sitting with one's legs crossed were far more common activities, compared to Western cultures, where patients are more commonly sitting in chairs; therefore, the norm of 90^0 would not be sufficient to evaluate their population. Finally, due to the institution's policies concerning patient safety, the study was not double-blinded and did not contain a placebo group.

Distance & Time

Further studies have examined ACBs and FNBs, focusing instead on the distance or time. One method involved measuring the distance ambulated by patients after receiving the different blocks. The first study, published July of 2013 in Regional Anesthesia & Pain Medicine[4], examined the distance that patients could ambulate post-operatively status-post TKA. Nearly 300 patients were included over an 8 month period and were divided into three groups exploring three different modalities of anesthesia: local infiltration analgesia (LIA), LIA plus adductor canal block (LIA plus ACB), and continuous femoral nerve block (CFNB). The LIA was accomplished with 150ml Ropivacaine 0.2%, 30mg Ketorolac, and 0.6mg Epinephrine. The LIA plus ACB used 20ml Ropivacaine 0.5% and the CFNB used 30ml Ropivacaine 0.2% then 5ml/hour Ropivacaine 0.2%. The average distance that patients were able to ambulate on POD 1 that received LIA plus ACB was 30 meters. Those who only received LIA could only walk an average of 20 meters while those that received CFNB averaged 0 meters. While the results displayed a statistically significant difference in these modalities of anesthesia delivery, with a p-value <0.001, the inclusion of LIA presented a confounding variable in a straight comparison between adductor and femoral nerve blocks. The study was also a retrospective, non-randomized and observational cohort study and thus did not provide Grade A evidence.

Another method examined the time it took for patients to ambulate a fixed distance using the Timed-Up-and-Go (TUG) test. The TUG test was first developed and described in a study in February 19915 with a cohort of 60. To conduct the TUG test, the patient starts seated in a chair, with an observer who has a stopwatch. The observer starts the time when the patient gets up out of the chair. Once the patient has risen from the chair, they are to walk 3 meters, turn around, return to the chair and sit down, at which time the stopwatch is stopped and the time measured.

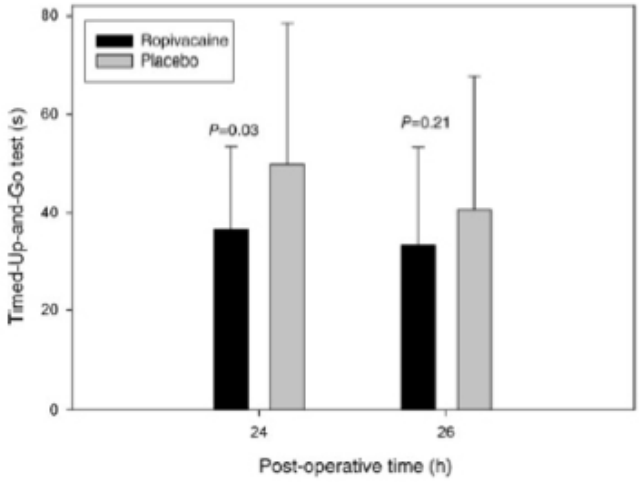

Figure 2. Mean times of completion of the TUG test in patient's receiving ACB with 30ml Ropivacaine 0.75% vs. Placebo (isotonic saline) at 24 hours Post-Op as well as at 26 hours after both receiving a bolus of Ropivacaine 0.75% following the 24 hour measurement6.

A double-blinded, randomized study conducted March 2012 in Acta Anaesthesiologica Scandinavica[6] used the TUG test to compare 71 patients who received either ACB using 30ml Ropivacaine 0.75% or an ACB placebo using isotonic saline. Patients receiving the true ACB took an average of 36 seconds to complete the TUG test 24hr post-operatively, compared to the placebo group who took 50 seconds, with a p-value 0.03. After the TUG test was completed, both groups received a bolus of 15ml Ropivacaine 0.75% and two hours later—at 26 hours post-operatively—the groups completed another TUG

test (Figure 2). The ACB group took 33 seconds and the placebo group took 41 seconds to complete, with p-value 0.21, demonstrating a less significant difference between the groups than at 24 hours.

Another study published November 20132, which was referenced earlier in the discussion about quadriceps strength, also utilized the TUG test in comparing the ACB and FNB. 22 patients in the ACB arm had an average TUG test of 37 seconds 24 hours post-operatively, while 26 patients who received the FNB had an average of 39 seconds. With a p-value 0.59, the study did not demonstrate a significant difference between the two groups in terms of TUG performance.

Conclusion

In compiling the recent research comparing different anesthesia modalities and ambulation of patients status-post TKA, there is support that ACBs result in greater quadriceps strength post-operatively[1],[2]. ACBs also result in faster walking times for fixed distances, evaluated using the TUG test, compared to a placebo[6]. However, there is no significant difference between the ACB and the FNB in the TUG test 24 hours post-operatively[2]. Still, patients who received the ACB walked considerable longer distance on POD 1 than those with CFNB, although this study was complicated by the fact that the patients in the ACB arm also received LIA[4]. Additionally, the CFNB resulted in greater ROM compared to no regional block[3].

An interesting point of consideration remains after discussion of the current literature. Even though these studies all examine objective measures such as strength[1],[2], ROM[3], distance traveled[4], time to travel a fixed distance[2],[6], it has yet to be established how these measurements correlate to patient outcomes in terms of health and safety. In a clinical setting, significant concerns include deterring the consequences of immobility, such as prophylaxis and prevention of deep vein thrombosis (DVT) and pulmonary embolism (PE) formation, as well as ensuring safe ambulation, assessing fall-risk and employing proper fall precautions. Further research will need to be done before it can be determined how these results can be applied to actual anesthesia practice.

References

(1) Kim DH, Lin Y, Goytizolo EA, Kahn RL, Maalouf DB, Manohar A, Patt ML, Goon AK, Lee YY, Ma Y, Yadeau JT. Adductor Canal Block versus Femoral Nerve Block for Total Knee Arthroplasty: A Prospective, Randomized, Controlled Trial. Anesthesiology 2014; 120:XX-XX

(2) Jæger P, Zaric D, Fomsgaard JS, Hilsted KL, Bjerregaard J, Gyrn J, Mathiesen O, Larsen TK, Dahl JB. Adductor canal block versus femoral nerve block for analgesia after total knee arthroplasty: a randomized, double-blind study. Regional Anesthesia and Pain Medicine 2013; 38:526–532

(3) Sakai N, Inoue T, Kunugiza Y, Tomita T, Mashimo T. Continuous femoral versus epidural block for attainment of 120° knee flexion after total knee arthroplasty: a randomized controlled trial. The The Journal of Arthroplasty 2013; 28:807-814

(4) Perlas A, Kirkham KR, Billing R, Tse C, Brull R, Gandhi R, Chan VW. The impact of analgesic modality on early ambulation following total knee arthroplasty. Regional Anesthesia & Pain Medicine 2013; 38:334–339

(5) Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. Journal of the American Geriatrics Society. 1991; 39:142-148

(6) Jenstrup MT, Jæger P, Lund J, Fomsgaard JS, Bache S, Mathiesen O, Larsen TK, Dahl JB. Effects of adductor-canal-blockade on pain and ambulation after total knee arthroplasty: a randomized study. Acta Anaesthesiologica Scandinavica. 2012; 56:357-64

Lower Limb Disease: Considerations in Psychiatric Patients

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Diagnosing and treating lower limb disease can be particularly challenging in patients with mental illness, especially for providers who lack familiarity with this patient population. Nonetheless, psychiatric patients may suffer from a host of problems affecting the lower extremity. Besides lower limb disease that affects the population at large, there are particular manifestations that are more common in psychiatric patients. These manifestations can be related to the effects of psychotropic medications, or may be secondary to the mental disorder itself.

As medical providers caring for psychiatric patients, it is important to be both vigilant and empathetic when assessing for lower limb disease. Non-compliance with both treatment and follow-up is a major hurdle when attempting to treat psychiatric patients and is not limited to treatment of mental illness. Such patients are often also non-compliant with medications for their medical illnesses, such as that for diabetes and hypertension. They may refrain from seeing primary care physicians on a regular basis and from engaging in preventative care. They may also neglect their physical symptoms, including those stemming from podiatric illness. Therefore, a patient may not present for medical care until late in the disease process, when the severity of their illness can no longer be ignored. An example is a patient suffering from severe depression and uncontrolled diabetes, whose profound fatigue and avolition prevents them from seeking medical attention, or even getting out of bed, when they develop a lower extremity ulcer.

Communication of one's symptoms can also prove to be an arduous task for a patient suffering from mental illness, limiting their ability to provide meaningful history or advocate for themselves. Depending on the level of thought organization, the patient may not be able to articulate their symptoms. Patients with psychosis may have disorganized and fragmented thoughts, as well as impoverished speech. Additionally, a patient who suffers from delusions may complain of improbable symptoms, which are overlooked by providers as delusional content, when really they may be a distortion of a true underlying illness. When a provider is faced with managing lower leg illness in a patient who is a poor historian, seeking out collateral information (i.e. from a patient's spouse, family, healthcare proxy, case manager, psychiatrist, therapist, social worker, etc.) is paramount.

The following are examples of lower limb pathology that may be encountered when treating patients with mental illness. This list is by no means exhaustive:

1. *Neuropathy:* Second generation antipsychotic medications carry an increased risk of impaired glucose tolerance, predisposing patients to developing diabetes, thus placing them at increased risk for developing complications including diabetic neuropathy. Alcoholic neuropathy is also a consideration as alcohol dependence commonly co-occurs with mental illness.

2. *Infection:* Psychiatric illness and chemical dependency are often interrelated. A myriad of comorbid illness affects patients struggling with chemical dependency. A common complication is infection associated with drug use. A chronic intravenous drug user will often inject their drug of choice into sites all over the body, including the lower limbs, which can lead to cellulitis, abscess formation, osteomyelitis and septicemia. Cocaine and opiate users can also engage in "popping" which involves administering the drug under the skin, either subcutaneously or intradermally. Cases of botulism and tetanus have been reported with this mode of drug use[1].

3. *Thromboembolic disease:* Catatonia has traditionally been viewed as a feature of schizophrenia; however, catatonic features can be encountered in patients with a variety of psychiatric disorders, including depression and bipolar disorder. Catatonic patients who demonstrate significant immobility and negativism are at an increased risk of developing deep vein thrombosis and pulmonary embolism. Additionally, if they are experiencing thought impoverishment or mutism, they are

less likely to verbalize their symptoms associated with thromboembolic disease, including leg pain.

4. *Skin reactions:* When presented with patients who complain of rashes of the lower extremities, drug-rash is an important consideration. The patient's medication list should be reviewed thoroughly, including psychotropic medications. Lamotrigine and carbamazepine, both anticonvulsant medications that are also used as mood-stabilizing agents, have been known to cause Stevens-Johnson Syndrome, a life-threatening skin rash[2].

Another type of skin lesion that has become increasingly problematic recently is the necrotizing lesions associated with the street drug "krokodil", which is an injectable opioid analogue that is often mixed with red phosphorous, lighter fluid, paint thinner and even gasoline. Users inject the drug into the skin, which can lead to necrosis, thrombophlebitis and gangrene[3]. Though still fairly rare in the United States, providers should keep this drug in mind if a patient with suspected substance history presents with these unusual lesions in the lower extremities or other areas of the body.

5. *Edema:* Several psychotropic medications can lead to the development of edema, including lithium and valproic acid, which are commonly used in the treatment of Bipolar Disorder. Cases of edema have also been linked to venlafaxine (an SNRI anti-depressant), as well as trazodone and mirtazapine, agents used for treating both depression and insomnia. Gabapentin, used to treat seizures, neuropathic pain, and anxiety, can also cause peripheral edema.

6. *Self-Injury:* Patients with borderline personality disorder may present with self-inflicted wounds. These wounds often manifest as multiple superficial lacerations on the upper extremities; however, it is not uncommon for such patients to cut themselves on the lower extremity, especially the anterior thighs. In severe cases of psychosis (including substance-induced psychosis), serious self-injury, even self-amputation has occurred. Also, factitious disorder with physical symptoms (formerly Munchausen Syndrome) must be considered if a patient presents with unusual patterns of injury with inconsistent history.

Extrapyramidal symptoms: When a patient presents with new onset gait disturbance, restlessness or abnormal involuntary movements of the lower extremities, it is important to review their medications, as they may be suffering from Extrapyramidal Symptoms (EPS). EPS is a group of drug-induced side effects, affecting gait, movement, and posture that are most commonly caused by anti-psychotic medications, but can also be seen in treatment with some antidepressants[4]. These symptoms can be very distressing and disabling to patients, and in some cases, can become permanent if swift action is not taken. When EPS is suspected, it is important to reach out to their mental health provider to determine whether the psychotropic agent should be decreased in dosage, changed to another agent or discontinued altogether. When presented with patients with a history of mental illness complaining of symptoms related to the lower limb, providers may make the mistake of overlooking a patient's symptoms as disingenuous or not real, especially if the patient is inaccurately assessed as being delusional, somatizing, or feigning their symptoms. It is important to treat these patients diligently to exclude the possibility of true illness before jumping to such conclusions. Providers should not hesitate to consult their colleagues in mental health when confronted with such situations.

References

(1) Necrosing Narcotic 'Krokodil' Makes its Way to US Streets. Deborah Brauser. Medscape Medical News. Sept 27, 2013. www.medscape.com/viewarticle/811802

(2) Toxic epidermal necrolysis and Stevens-Johnson Syndrome. Thomas Harr & Lars E, French. Orphanet Journal of Rare Diseases. 2010, 5:39. http://www.ojrd.com/content/pdf/1750-1172-5-39.pdf

(3) Wound botulism from heroin skin popping. Larry E. Davis & Molly K. King. Current Neurology and Neuroscience Reports. November 2008, Volume 8, Issue 6, pp 462-468.

(4) Extrapyramidal symptoms associated with antidepressant. Subramoniam Madhusoodanan MD, et al. Annals of Clinical Psychiatry.2010; 22(3):148-156. https://www.aacp.com/pdf%2F0810%2F0810ACP_Madhusoodanan.pdf

A Review of Opioid Induced Hyperalgesia (OIH) for Podiatric Physicians

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Introduction

Opioids have long been used to treat acute pain. For the podiatric surgeon desiring to manage postoperative pain, opioids can be tremendously effective. Nonetheless, it is important for the podiatric physician to understand the various outcomes that may result from their use [39]. There are four outcomes that may result from the use of opioids: tolerance, addiction, withdrawal, and opioid induced hyperalgesia (OIH). Though these outcomes are all interrelated, the ability to distinguish the difference between each will lead to better outcomes for patients and will also decrease the overall pain that patients experience. This paper will focus on existing literature that discusses the different outcomes of opioids, the mechanism and treatment of OIH, and finally will introduce future areas of research on the mechanism of OIH.

Signs of Tolerance

Opioid tolerance develops when increased amounts of opioid are required to produce an equivalent level of efficacy [1]. Tolerance and physical dependence often occur after just one to two weeks of daily use [1]. An appropriate medical practitioner can often identify signs of tolerance. Some important questions to include while eliciting the history should include the amount of drug used recently, time of last use, previous attempts at drug treatment, and problems resulting from drug use. A positive family history can also be predictive of opioid tolerance [2]. The clinician should also try to determine if the patient has been using incrementally larger amounts of opioid to get the same pain relief.

Signs of Addiction

Opioid addiction can be defined as a form of psychological dependence. Extreme behavior patterns are often associated with both procuring and consuming narcotics [3]. A suspicious behavior to look for is an early patient request for refills. A classic example would be a patient presenting for an urgent unscheduled visit with a list of excuses for running out of the medicine early. Multisourcing is another example of addictive behavior. Patients will visit multiple physicians, recruit surrogates to obtain the medicine for them, or even purchase drugs illegally over the internet. Addicted patients may also beg, plead, or pressure in order to obtain their medication [4].

Again, careful patient evaluation can help increase the awareness of addiction. A major risk factor for opioid addiction is prior substance abuse or addiction. Physical complaints suggestive of chronic use of opioids include constipation, drowsiness, excess sweating, and peripheral edema [5]. Opioid addiction can also result in hyperalgesia, which can develop within a month of initiating opioid therapy [6]. Narcotic bowel syndrome has also been associated with long term opioid use. This is characterized by chronic, recurrent abdominal pain, often relieved with cessation of the opioid [7]. Urine drug screening can also help identify opioid addiction. The metabolites of opioid can be detected up to three to four days after last use and even longer in chronic users [8].

Signs of Withdrawal

Opioid withdrawal, though often confused with drug seeking behavior, is a separate entity. Generally, it refers to a set of symptoms that presents with opioid cessation, or after receiving an opioid antagonist. A major difference between withdrawal and addiction is that in withdrawal, there is no craving for the opioid. Distinguishing between the two can be critical, as withdrawal may be life threatening. Opioid withdrawal is typically divided

into two types: normal withdrawal (cessation of opioid) and ultra-rapid withdrawal (antagonist used).

The amount of time that it takes for symptoms to develop typically varies based on the medication and whether or not an antagonist was used. Short-acting opioids may present with withdrawal signs and symptoms, as early as 6-12 hours after the last dose. However, a longer-acting opioid, such as methadone, may take 24-48 hours for signs of withdrawal to appear and the symptoms of withdrawal may present immediately when using antagonists [10]. In general, the symptoms of opioid withdrawal (normal and ultra-rapid) are broken into early and late symptoms. Early symptoms include: agitation, anxiety, muscle aches, increased tearing, insomnia, runny nose, sweating, and yawning. Late symptoms include abdominal cramping, diarrhea, dilated pupils, goose bumps, nausea, and vomiting [11].

Ultra-rapid opioid detoxification may present with additional symptoms. After giving a μ-opioid receptor antagonist for reversal of the opioid, there are elevations of adrenocorticotropic hormone (ACTH) and cortisol. Within 240 minutes of administration of the μ-opioid receptor antagonists, elevations in systolic blood pressure, heart rate, and respiratory rate can occur. In the weeks following administration of the antagonist, patients may report increased gastrointestinal distress, insomnia, irritability, and fatigue [9]. However, symptoms of anxiety or depression experienced at baseline may improve and there may also be an improvement of sleep and appetite.

Opioid-Induced Hyperalgesia Versus Addiction

Opioid-induced hyperalgesia (OIH) is a common occurrence among patients requiring long-term opioid pain management, but many practitioners are unfamiliar with the condition. Simply put, it refers to an increased sensitivity to pain as a result of opioid exposure [16]. Difficulty arises in the diagnosis of OIH due to a frequent association with opioid addiction.

While the earliest studies on OIH reported on the condition occurring among patients addicted to opioids, OIH often occurs without the concurrence of addiction [15, 17]. Evidence shows that OIH can also occur among patients on long-standing opioid maintenance or even in those receiving short courses of opioids in the perioperative period [13]. It can be induced in healthy non-addicted adults, as well as in patients with a past history of opioid abuse [14, 15].

Patients with OIH can be found in a vicious pain cycle, where OIH eventually leads to addiction. The hypersensitivity to pain caused by OIH leads to an increase in drug-seeking behavior, which incidentally increases depression and anxiety. With the increase in opioid use, the effects of OIH also become enhanced, perpetuating the cycle [16]. Breaking the cycle of hyperalgesia and addiction requires addressing the underlying causes [18].

Cause and Mechanism of OIH

Again, OIH in simplest terms is an adverse effect causing increased sensitivity to pain with the use of opioids. When prescribing opioids, it is important to keep in mind that doing so can lead to OIH with certain prescribing habits. It is also important to be aware of the signs that may present. The first method of administering opioids that has been documented as leading to OIH is found in maintenance dosing. Doverty et al. gave maintenance doses of methadone and then measured the pain threshold and tolerance to pain by electrical stimulation and cold pressor test, showing that the patients on methadone maintenance dosing had a smaller threshold and less tolerance [27].

Withdrawal from opioids can also lead to OIH. Peggy et al. showed that individuals who had no addiction to opioids with a single dose of opioids could develop hyperalgesia upon withdrawal [26]. OIH is also found to occur with very high or escalating doses [24]. It is possible to mitigate those effects by dropping the dose to 25% of the peak without causing a withdrawal [23]. Finally, OIH is found to occur with very low doses. As demonstrated by Kayser et al., low dose morphine heightened the nociception in rats [25].

There are several theories as to the mechanism of OIH. A popular theory is that OIH is caused by a sensitization of the pronociceptive pathway, such that an increase in opioid will only lead to an increase in hyperalgesia [22]. Drdla et al. proposed that this was due to the same synaptic pathway that is responsible for injury-induced hyperalgesia: long-term potentiation at synapses between nociceptive C fibers and neurons in the superficial spinal dorsal horn [21]

Treatment options for OIH prevention and management

Treatment of OIH often revolves around the use of opioid rotation/switching route of administration and coanalgesics to mitigate the effects of OIH rather than removal of the opioids. This is because removal of the opioids may lead to increases in pain as well as severe side effects [40].

DRUG ROTATION/ SWITCHING ROUTE

Rotation involves the use of equianalgesic dose tables and dose adjustments to switch from one opioid to another or from one route of administration of a particular opioid to another. Fine et al. came up with a guideline for opioid rotation. When rotating a new opioid using equianalgesic dose tables, a dose 25-50% lower than what was calculated should be given. 50% less is given if the patient is currently receiving a high dose of analgesic. The dose should only be reduced by 25% if the patient is switching routes of administration or if the patient is currently on a low dose analgesic.

However, these conversions should not be used if switching to methadone or fentanyl. Methadone should be given at only 75-90% of the calculated equianalgesic dose and transdermal fentanyl doses should be calculated using equianalgesic dose ratios, included in the package insert. Finally, a second assessment of pain and side effects should be performed to determine if the dose should be decreased or increased between 15-30% [41]. A final point to be made about equianalgesic dose tables is that the guidelines presented by these tables are meant to be looked at with clinical judgment for each individual patient, as each patient will have different effects. Knotkova et al. presented this idea by showing that people of Asian heritage will receive a greater effect by the same dose of opioid when compared to a Caucasian [42].

COANALGESICS

Drugs that are used for the management of OIH are often also used in the prevention of OIH. These drugs work by different mechanisms and their effectiveness is determined by how they are administered.

NMDA blockers

Prevention

Blockage of NMDA for treatment of OIH was first accomplished by Jolly et al. through the use of ketamine, during and after surgery accompanying the use of high dose remifentanil [32]. The results of the study, though successful, did not show that ketamine with high dose remifentanil was more effective at reducing pain than just low dose remifentanil [33]. This was accomplished by Yalcin et al., who showed that it would be more effective if the first bolus dose of ketamine was used prior to the opioid implementation. This experiment administered IV bolus ketamine 5 mg/kg prior to induction of anesthesia and also maintained 5 μg/kg/min ketamine intraoperatively until skin closure [32].

Another method of blocking NMDA has been accomplished through methadone. Salpeter et al. did a retrospective observational study looking at the use of methadone and haloperidol in hospice care to reduce OIH. They showed that the use of 5 mg of methadone per day, along with 3 mg of haloperidol per day, could successfully block NMDA and prevent opioid induced hyperalgesia [30].

Management

Methadone can also be used as a treatment for someone who is currently experiencing OIH. Axelrod et al. showed that simply rotating into methadone after OIH has developed could greatly reduce the hyperalgesia for effective treatment of the patient's pain [29]. Though the use of these two drugs has shown positive results, dextromethorphan, another NMDA antagonist, has been shown to have no effect on OIH [28].

Prostaglandin E2 inhibitors

Yalcin et al. provided us with the use of NSAIDS as a potential inhibitor of hyperalgesia through the inhibition of spinal prostaglandin E2 (PGE2). They concluded that 1000 mg of paracetamol IV, before induction of anesthesia, was as effective as ketamine in preventing opioid induced hyperalgesia [32].

Kappa receptor antagonists

Buprenorphine is a kappa receptor antagonist, and though the exact role of the kappa receptor in OIH is unknown, it has been shown to have some effect in decreasing OIH. Koppert et al. showed that 0.15 mg buprenor-

phine IV or 0.2 mg buprenorphine sublingual had both analgesic and anti-hyperalgesic effects [43].

Hypnotic/amnestic

Propofol is often implicated in treating OIH, however there are no human studies illustrating its effectiveness. Singler et al. showed that though propofol could decrease OIH, the effect was only temporary and would only last as long as propofol was being transfused [44].

Clonidine

Clonidine can successfully be used in the prevention of OIH if administered properly. Kock et al. showed that administration of 300 μg of clonidine prior to general anesthesia was effective in decreasing postoperative secondary hyperalgesia. However, it also had the added benefit of increasing immediate postoperative analgesia [31].

Further Studies for OIH

There are many areas of ongoing research for the topic of OIH. The first major area of current research deals with finding the best management for OIH. A study in April of 2013 documents the efficacy of dexmedetomidine, an alpha 2 agonist, for the alleviation of OIH. Further research studies investigating the use of dexmedetomidine as part of a multimodal approach for OIH are yet to be explored [36]. In addition to alpha 2 agonists, studies have demonstrated use of calcium channel blockers like pregabalin to manage OIH [37]. These drugs block the alpha 2 delta subunit of calcium channels to inhibit the release of neurotransmitters causing pain.

The other major area of ongoing research involves identifying the precise molecular mechanism of OIH beyond the NMDA receptor system, which is yet to be understood. Much of it focuses on the role of toll-like receptor 4 (TLR4) antagonists [35]. It is believed that selectively antagonizing TLR4 receptors would be a clinical approach for separating the analgesia and the unwanted actions of opioids, such as hyperalgesia. Recently posed hypotheses suggest the homeostatic up-regulation of non-opioid-mediated ascending nociceptive pathways such as the thalamocortical, ventral spinothalamic, and midline dorsal column tract [38]. If proven true, treatment with opioid agents combined with adjuvant agents would have the best patient outcome for intractable pain. The focus of treatment would transition on inhibiting non-opioid ascending dependent tracts as well as opioid-dependent tracts.

References

(1) Effective Medical Treatment of Opiate Addiction. JAMA. 1998; 280:1936-1943

(2) Gelemter J, Panhuysen C, Wilcox M. Genomewide linkage scan for opioid dependence and related traits. American Journal of Human Genetics. 2006; 78:759-69

(3) Zacny J, Bigelow G, Compton P, Foley K, Iguchi M, Sannerud C. College on Problems of Drug Dependence taskforce on prescription opioid non-medical use and abuse: position statement. Drug and Alcohol Dependence. 2003; 69:215-232

(4) Chou R, Fanciullo GJ, Fine PG, Miaskowski C, Passik SD, Portenoy RK. Opioids for Chronic Noncancer Pain: Prediction and Identification of Aberrant Drug-Related Behaviors: A Review of the Evidence for an American Pain Society and American Academy of Pain Medicine Clinical Practice Guideline. The Journal of Pain. 2009; 10:131-146.e5

(5) O'Conor LM, Woody G, Yeh HS, Manny I, Dhopesh V. Methadone and edema. Journal of Substance Abuse Treatment. 1991; 8:153-155.

(6) Pud D, Cohen D, Lawental E, Eisenberg E. Opioids and abnormal pain perception: New evidence from a study of chronic opioid addicts and healthy subjects. Drug Alcohol Dependance. 2006; 82:218-223

(7) Grunkemeier DM, Cassara JE, Dalton CB, Drossman DA. The narcotic bowel syndrome: clinical features, pathoyphysiology, and management. Clinical Gastroenterol Hepatology. 2007; 5:1126-39.

(8) Humeniuk R, Ali R, Babor TF. Validation of the Alcohol, Smoking And Substance Involvement Screening Test (ASSIST). Addiction. 2008; 103:1039-47.

(9) Brieter Hans, D' Ambra Michael, Elman Igor, Gastfriend David, Kane Martha, Krause Sara, Morris Robert, Tuffy Liam, Ultrarapid Opioid Detoxification: effects on cardiopulmonary Physiology, stress, hormones, and clinical outcomes. Drug and Alcohol Dependence. 2001;61(2):163-172 http://dx.doi.org/10.1016/S0376-8716(00)00139-3

(10) Donaher, Paul Managing Opioid Addiction with Buprenorphine, Am Fam Physician. 2006 May 1;73(9):1573-1578, Accessed 4/25/2013

(11) Perez, Eric Opiate Withdrawal Department of Emergency Medicine, St. Luke's-Roosevelt Hospital Center http://stlukesemergency.adam.com/content. aspx?productId=117&pid=1&gid=000949 Published 6/17/2011 Accessed 4/25/2013

(12) Franck LS, Harris SK, Soetenga DJ, Amling JK, Curley MAQ. The Withdrawal Assessment Tool–1 (WAT–1): an assessment instrument for monitoring opioid and benzodiazepine withdrawal symptoms in pediatric patients. Pediatric Care Med. 2008;9(6):573–580. doi: 10.1097/PCC.0b013e31818c8328.

(13) Vanderah TW, Ossipov MH, Lai J, et al. Mechanisms of opioid-induced pain and antinociceptive tolerance: descending facilitation and spinal dynorphin. Pain 2001; 92:5-9.

(14) Compton P, Athanasos P, Elashoff D, Withdrawal hyperalgesia after acute opioid physical dependence in nonaddicted humans: a preliminary study. The Journal of Pain 2003; 9:511-19

(15). Schall U, Katta T, Pries E, et al. Pain perception of intravenous heroin users on maintenance therapy with levomethadone. Pharmacopsychiatry 1996; 29:176-9.

(16) Ling W, Mooney L, Hillhouse M. Prescription opioid abuse, pain and addiction: Clinical issues and implications. Drug and Alcohol Review 2011; 30:300-305

(17) Fishbain DA, Cole B, Lewis JE, Gao J, Rosomoff RS. Do opioids induce hyperalgesia in humans? An evidence-based structured review. Pain Med 2009;10:829–39.

(18) Silverman S, Opioid induced hyperalgesia: clinical implications for the pain practitioner. Pain Physician 2009; 12:679-684

(19) Effective medical treatment of opiate addiction. National consensus

development panel on effective medical treatment of opiate addiction. JAMA 1998; 280:1936-43
(20) Chen L, Huang LY, Protein kinase C reduces Mg2+ block of NMDA-receptor channels
(21) Angst M, Clark D, Opioid-induced Hyperalgesia, Anesthesiology 2006; 104:570–87 http://www.pain-consultant.co.uk/pdf/Opioidinducedhyperalgesia.pdf Accessed May 8, 2013
(23) Zylicz Z, Twycross R, Opioid-Induced Hyperalgesia May Be More Frequent Than Previously Thought DOI: Journal of Clinical Oncology, 26(9); 1564 10.1200/JCO.2007.15.6919
(24) De Conno F, Caraceni A, Martini C, et al. Hyperalgesia and myoclonus with intrathecal infusion of high-dose morphine. Pain. 1991;47:337–339 accessed May 8, 2013
(25) Kayser V, Besson JM, Guilbaud G. Paradoxical hyperalgesic effect of exceedingly low doses of systemic morphine in an animal model of persistent pain (Freund's adjuvant-induced arthritic rats). Brain Res. 1987;414:155–157, http://www.sciencedirect.com/science/article/pii/00068993879133, accessed May 8, 2013
(26) Compton P, Athanasos P, Elashoff D, Withdrawal hyperalgesia after acute opioid physical dependence in nonaddicted humans: a preliminary study, Pain, 2003; 4 (9); pages 511-519. http://dx.doi.org/10.1016/j.jpain.2003.08.003
(27) Doverty M, White JM, Somogyi AA, Bochner F, Ali R, Ling W, Hyperalgesic responses in methadone maintenance patients, Pain, 2001; 90 (1-2); pages 91-96. http://dx.doi.org/10.1016/S0304-3959(00)00391-2
(28) Compton P; Ling W, Torrington M, CLINICAL STUDY: Lack of effect of chronic dextromethorphan on experimental pain tolerance in methadone-maintained patients, Addiction Biology. 13(3-4); 393-402; 10.1111/j.1369-1600.2008.00112.x
(29) Axelrod DJ, Reville B, Using methadone to treat opioid-induced hyperalgesia and refractory pain, Journal of Opioid Manag. 2007 r;3(2):113-114; accessed June 1, 2013
(30) Salpeter S, Buckley J, Bruera E, The Use of Very-Low-Dose Methadone for Palliative Pain Control and the Prevention of Opioid Hyperalgesia, JOURNAL OF PALLIATIVE MEDICINE 16 (6) DOI: 10.1089/jpm.2012.0612
(31) De Knock M, Lavand'homme P, waterloos H, The Short-Lasting and Long-term antihyperalgesic effect of intrathecal clonidine in patients undergoing colonic surgery 2005; 101(2): 566-572 http://ovidsp.tx.ovid.com/sp-3.9.0b/ovidweb.cgi?T=JS&PAGE=fulltext&D=ovft&AN=00000539-200508000-00045&NEWS=N&CSC=Y&CHANNEL=PubMed accessed July 23 2013.
(32) Yalcin, N, Uzun S, Reisli R, Borazan H, Otelcioglu S, A Comparison of Ketamine and Paracetamol for Preventing Remifentanil Induced Hyperalgesia in Patients Undergoing Total Abdominal Hysterectomy, Int J Med Sci. 2012; 9(5): 327–333. 10.7150/ijms.4222
(33) Jolly V, Richebe P, Guignard B, Fletcher D, Maurette P, Sessler DI, et al. Remifentanil-induced postoperative hyperalgesia and its prevention with small-dose ketamine. Anesthesiology. 2005;103:147–155
(34) Lee M., Silverman S., Hansen H., Patel V, and Manchikanti L, A Comprehensive Review of Opioid-Induced Hyperalgesia, Pain Physician, 2011; 14:145-161.http://www.painphysicianjournal.com/2011/march/2011;14;145-161.pdf accessed June 1, 2013
(35) Li Q. Antagonists of toll like receptor 4 maybe a new strategy to counteract opioid-induced hyperalgesia and opioid tolerance. Medical Hypotheses 2012; 79:754-56
(36) Lee C, Kim YD, Kim JN, Antihyperalgesic effects of dexmedetomidine on high-dose remifentanil-induced hyperalgesia. Korean Journal of Anesthesiology 2013; 64(4): 301-307
(37) Lee C, Kim YD, Kim JN, Effect of oral pregabalin on opioid-induced hyperalgesia in patients undergoing laproendoscopic single-site urologic surgery. Korean Journal of Anesthesiology 2013; 64(1): 19-24
(38) Goldberg JS, Chronic Opioid Therapy and Opioid Tolerance: A New Hypothesis. Pain Research and Treatment 2013; 2013: 407504
(39) Whittle S, Richards B, Buchbinder R, Opioid Analgesics for Rheumatoid Arthritis Pain.The Journal of the american Medical association 2013; 309(5):485-486: doi:10.1001/jama.2012.193412.
(40) Inturissi C, Clinical Pharmacology of Opioids for Pain.Clinical Journal of Pain 2002; 18(4): 3-13: http://journals.lww.com/clinicalpain/Abstract/2002/07001/Clinical_Pharmacology_of_Opioids_for_Pain.2.aspx accessed July, 15 2013
(41) Fine P, Portenoy R, Establishing "Best Practices" for Opioid Rotation: Conclusions of an Expert Panel. Journal of Pain and Symptom Management 2009; 38(3): 418-425. http://www.sciencedirect.com.proxy.westernu.edu/science/article/pii/S0885392409006290?np=y accessed July 15 2013.
(42) Knotkova H, Fine P, Portenoy R, Opioid Rotation: The Science and theLimitations of the Equianalgesic Dose Table Journal of Pain and Symptom Management 2009; 38(3): 426-439. http://ac.els-cdn.com.proxy.westernu.edu/S0885392409006307/1-s2.0-S0885392409006307-main.pdf?_tid=50be2a02-f329-11e2-97ba-00000aab0f02&acdnat=1374537135_a0bd2f3140104e87765e6165f-aede856 accessed July 22, 2013.
(43) Koppert W, Ihmsen H, Korber N, Wehrfritz A, Sittl R, Shuttler J, Schmelz M, Different profiles of buprenorphine-induced analgesia and antihyperalgesia in a human pain model 2005; 118(1): 15-222 http://www.painjournalonline.com/article/S0304-3959(05)00382-9/ accessed July 22, 2013.
(44) Singler B, Troster A, Manering N, Modulation of Remifentanil induced postinfusion, hyperalgesia by propofol. Anasthesia analog 2007; 104-1397-403 http://www.anesthesia-analgesia. org/content/ 104/6/1397.long accessed July 23 2013.

Bosworth Ankle Fracture Dislocation: A Case Report

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Abstract

The Bosworth fracture-dislocation is a rare and potentially problematic ankle injury. On initial clinical exam and radiographs, it appears to be a routine ankle fracture. In a Bosworth fracture, however, the proximal aspect of the distal fibula lodges posteriorly to the tibia, making closed reduction nearly impossible. This potential oversight can lead to improper treatment in the emergency room and a poor outcome for the patient. If recognized, however, these injuries can be successfully treated via early open reduction and internal fixation. This rare injury is presented in the following case of a 35-year-old male who underwent an open reduction and internal fixation after multiple failed closed reduction attempts.

Introduction

Ankle fracture-dislocations are common injuries that have long been noted by the medical community and patients alike. Case reports date back to 1836 in which the fibula was dislocated posteriorly in an ankle fracture.[2] Practitioners have methodically improved treatment protocols for this injury, effectively reducing the risk of complications, which include severe soft tissue swelling, compartment syndrome, skin necrosis, and unsuccessful attempts at closed reduction. Misdiagnosis or mistreatment has historically left patients disabled, in pain, arthritic, unsatisfied, and in need of more drastic surgical options.

Bosworth ankle fracture-dislocation is a rare yet severe injury that was originally described in 1947 by David Bosworth, M.D.[1] This fracture-dislocation was described as an irreducible dislocation of the proximal aspect of the distal fibula posterior to the tibia. Five patients were described in the original paper: two fracture-dislocations were not recognized, leading to malunion and eventually requiring arthrodesis; one fracture-dislocation was recognized late but appropriately treated with satisfactory results; and the remaining two fracture-dislocations were recognized and treated, leading to excellent results.[1]

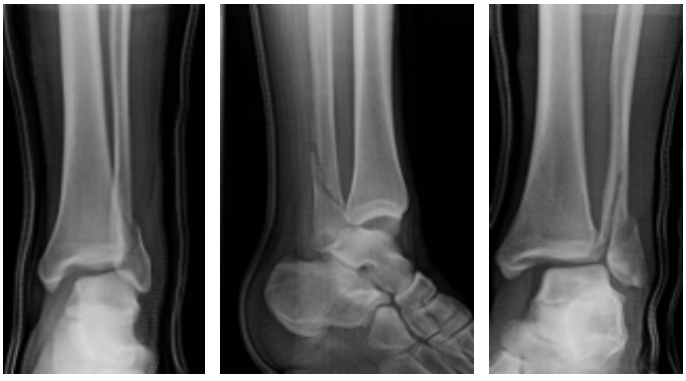
Approximately sixty Bosworth fracture-dislocation cases have been documented since Bosworth's initial description.[2],[3] New information has been presented with several of these publications including age variations, cases with intact fibulas, level of the fracture in relationship to the syndesmosis, mechanism of injury, cases with successful closed reduction, and additional injury.[2],[3] Yet this fracture-dislocation is often misdiagnosed and mistreated, potentially leading to devastating consequences. With the pressure for more middle level practitioners, the possibility for more unrecognized diagnosis is inevitable. A case report is presented below to help accurately diagnose and treat the Bosworth ankle fracture-dislocation.

Case Report

A 35-year-old male was transferred to our facility for higher level of care, complaining of a left ankle fracture sustained while playing soccer the previous day. On the date of injury, the patient was playing soccer at an indoor facility equipped with synthetic turf with typical soccer cleats. The mechanism of injury was a "slide tackle" in which a soccer player extends his leg in an attempt to steal the ball away from an opposing player. Patient claims that his cleats gripped the turf and twisted his ankle in an external rotation fashion.

Closed reduction was attempted at the transferring institute under conscious sedation with minimal improvement of bony alignment. The patient was complaining of 8/10 throbbing pain in his left lower extremity with associated swelling and the inability to bear weight on the extremity.

On examination of the patient's left ankle, there was an equinus and external rotation deformity. There was moderate left ankle swelling with associated medial ecchymosis and a 2 cm medial fracture blister. Pulses were weakly palpable, but the foot was warm and the capillary refill was brisk. Gross motor was intact. There was some decreased sensation in the distribution of the first web space.

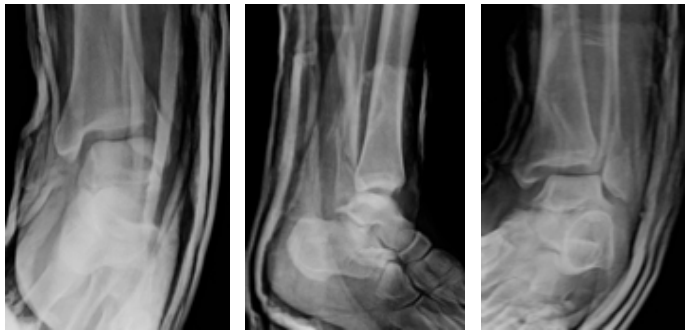


A B C

Figure 1 A, Anteroposterior radiograph showing increased tibiofibular overlap. B, Lateral radiograph showing tibiotalar as well as distal tibiofibular subluxation. C, Mortise radiograph

The initial radiographs showed a tibiotalar dislocation with a bimalleolar equivalent ankle fracture (Fig. 1A-C). The initial radiographs can be scrutinized for what appears to be an overly externally rotated lateral radiograph, an AP radiograph which shows increased tibiofibular overlap, and a nearly normal mortise view. Post-reduction x-rays showed a failed reduction attempt with minimal change in bony alignment (Fig. 2A-C). Given the irreducible nature of the fracture, the patient was admitted and taken to the operating room for open reduction and internal fixation.

During surgery, the distal fibula was approached in a standard posterior lateral incision. Once the fracture site was exposed, it was noted that the proximal aspect of the distal fibula was entrapped behind the posterior lateral edge of the tibia (Fig. 3). The fibula was released and reduced anatomically in relation to the distal tibia and stabilized with a one-third tubular plate. The syndesmosis appeared stable on stress radiographs, and therefore a syndesmotic screw was not inserted (Fig. 4A-C). The patient was placed in a three-sided splint and kept non-weight bearing. At week six, weight bearing in a CAM (controlled ankle motion) walker boot was initiated. Patient currently has full range of motion and is able to weight bear without significant pain.



A B C

Figure 2 A-C, Radiographic ankle series demonstrating failed reduction attempt

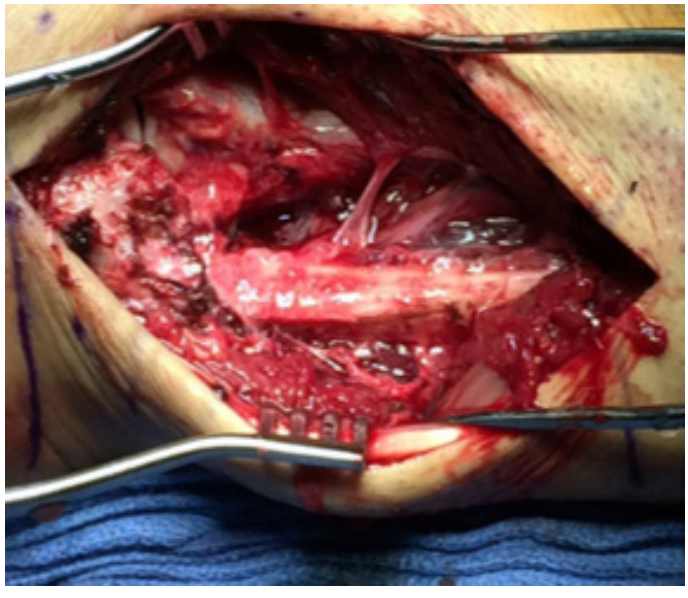
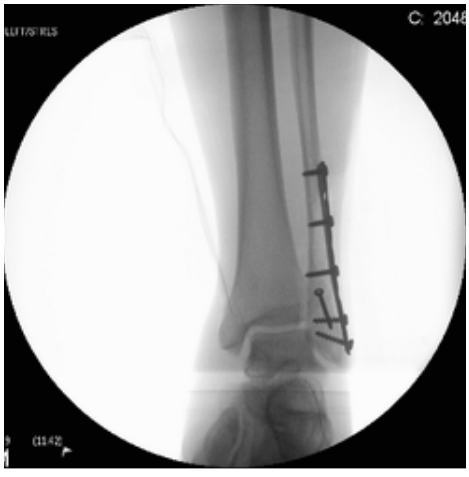


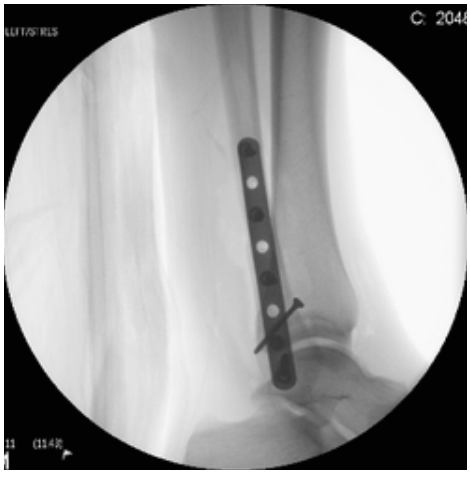
Figure 3, Intraoperative image of entrapped proximal fragment of distal fibula

Discussion

Differentiating a Bosworth ankle fracture-dislocation from a typical ankle fracture is difficult. It is recommended that good quality radiographs be obtained. Given the external rotation position of the ankle, adequate radiographs can be difficult to obtain. Some authors argue that radiographs that include the knee and ankle on one film will allow for a more accurate interpretation of the fracture pattern.[3] It has also been described that computed tomography may play a role in diagnosis.[5] If there is any doubt after good quality radiographs have been obtained, a CT with thin cuts and 3D reconstruction will definitively show if the proximal aspect of the distal fibula is entrapped behind the tibia. A pathognomonic ra-



A



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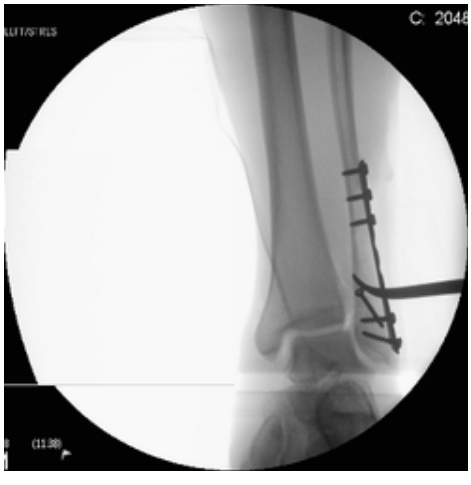

C

Figure 4 A-C, Fluoroscopic images demonstrating open reduction with internal fixation of fibula

diographic sign has also been described in recent literature. "The Axilla sign," a cortical density in the axilla of the medial tibial plafond, was determined to be present exclusively in Bosworth fractures.[4] The presence of this cortical density should alert the practitioner to a potential Bosworth fracture. Once the diagnosis has been made, treatment can proceed in a straightforward manner. After open reduction of the entrapped proximal fibula fracture, fixation via interfragmentary compression and a neutralization plate will provide adequate fixation. The need for syndesmotic reduction and fixation will be determined intraoperatively. During our review of the literature, all Bosworth fractures required syndesmotic fixation; however, in our case, the syndesmosis was appropriately stressed and did not require fixation.

Conclusion

While the diagnosis of a Bosworth fracture can be challenging, having a high index of suspicion will allow for prompt recognition and early open reduction and internal fixation. This will ultimately provide the patient with the best possible outcome.

References

(1) Bosworth DM. Fracture-dislocation of the ankle with fixed displacement of the fibula behind the tibia. J Bone Joint Surg AM 1947; 29:130-5.

(2) Bartonicek, J, Fric, V, Svatos, F, Lunacek, L. Bosworth-type fibular entrapment injuries of the ankle: Bosworth lesion. A report of 6 cases of literature review. J Orthop Trauma 2007;21:710-717

(3) Hoblitzell, RM, Ebraheim, NA, Merritt, T, Jackson, WT. Bosworth fracture-dislocation of the ankle. A case report and review of the literature. Clinical Orthopaedics and Related Research. 1990; 255:257-262.

(4) Khan, F, Borton D. A constant radiological sign in Bosworth's fractures: "the axilla sign". Foot Ankle Int 2008; 29:55-57.

(5) Wright SE, Legg A, Davies MB. A contemporary approach to the management of a Bosworth injury. Injury 2012; 43:252-253.

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