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Charcot Arthropathy of the Foot and Ankle

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Level of Evidence: Level V, expert opinion.

Keywords: diabetes, neuropathy

Introduction

Charcot foot arthropathy is a progressive, noninfectious, destructive inflammatory process of the foot and ankle. Traditionally described as a sequela of tertiary syphilis, in the vast majority of current patients it is secondary to long-standing diabetes.[67] Today, there are more than 29 million adults in the United States living with diabetes, and this number is expected to increase.[6] As modern medical treatments continue to improve the management and life span of these patients, the prevalence of diabetes-associated complications will rise. Diabetes-associated Charcot foot arthropathy creates a severe negative impact on health-related quality of life for affected individuals, leading to both substantial disability and a financial burden on the health care system. The aim of this current concepts review update is to summarize our current understanding of this systemic disease with a focus on its pathophysiology in the foot and ankle, as well as to provide an analysis of the latest evidence for preventative therapies, nonoperative management strategies, and evidence-based options for operative intervention.

Background

Impact on Quality of Life

It is well established that Charcot arthropathy secondary to diabetes mellitus severely reduces overall quality of life and dramatically increases the morbidity and mortality of patients. During the validation of the American Orthopaedic Foot & Ankle Society Diabetic Foot Questionnaire, more than 100 patients with Charcot foot arthropathy were followed over a 3-year period. The patient information gathered during this period revealed a significant negative effect on the health-related quality of life in these patients, which was sustained even following successful treatment of the Charcot event.[18] Similar findings were observed in a small cohort of patients being treated in a specialty diabetic foot clinic.[55] Despite the perception among medical and orthopaedic specialists that Charcot neuroarthropathy has a severe detrimental effect on the quality of life for diabetic patients, only a small fraction of clinical research on diabetes-related issues has investigated the morbidity in feet.[15] Therefore, there is a need for further examination of the clinical and scientific evidence available to guide the management of this destructive and potentially devastating disorder of the foot and ankle.

Pathophysiology

There is no single cause for the development of Charcot neuropathy. Two well-accepted explanations of the pathogenesis of Charcot arthropathy are the neurotraumatic and neurovascular theories. The neurotraumatic theory hypothesizes trauma (acute, subacute, or cumulative-repetitive) as the causative factor in the setting of absent protective sensation. Under these circumstances, the initial traumatic incident activates the process. The bone and soft tissues respond with an acute-phase release of proinflammatory cytokines, tumor necrosis factor-α (TNFα), interleukin-1β, and interleukin-6. TNFα upregulates the receptor activator of nuclear factor-κB (RANK) ligand (RANKL) system, which is responsible for abnormally intense osteoclastogenesis and excessive bone turnover. Meanwhile, there is a decrease in anti-inflammatory cytokines, interleukin-4 and interleukin-10, and the antagonist to RANKL activity, osteoprotegerin.[5,37,48]

The neurovascular theory, first described by Charcot, predicates a state of hyperemia generated from overactive vaso-autonomic neuropathy.[34] The increased blood flow

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increases venous pressure and enhances fluid filtration through capillary leakage. This in turn leads to increased compartmental pressure and deep tissue ischemia. The increased pressure and ischemia compromises tendons and ligaments in the foot and ankle leading to joint instability.[68] Additionally, the increased blood flow may directly cause increased bone resorption by increasing the delivery of osteoclasts and monocytes resulting in greater osteoclastic activity in this area.[14] This is consistent with the finding that patients with a Charcot foot show increased blood flow to the area whereas patients with peripheral arterial disease and diabetes are relatively protected from developing the arthropathy.[59,72]

Under both of these theories, continued weight-bearing without the use of defensive strategies (ie, guarding, offloading, or activity limitation) propels the course of repetitive microtrauma. This further increases the delivery of proinflammatory cytokines, magnifies the intensity of the Charcot event, and prevents proper bone remodeling in the affected area. Eventually, the structural integrity of the local bones and joints is breached, leading to fracture, subluxation, or dislocation. The competing processes of destruction and repair favors bone resorption, resulting in radiographs that resemble a hypertrophic nonunion.[38] More recent molecular studies continue to support an early inflammatory process in Charcot arthropathy, but do not show a uniform decline in described markers even after treatment.[52] While an initial surge in proinflammatory cytokines and bone turnover markers may be critical to the beginning stage of the disease, the research is not uniform in its conclusions in having this be the sole systemic process in these patients. As established, a better understanding of the interplay between these complex pathways and common genetic polymorphisms among those affected by Charcot arthropathy is required to fully understand its pathogenesis.[25,26,40,58]

Clinical Presentation and Evaluation

History and Physical Examination

Patients typically present between their fourth and sixth decade of life and note acute onset of lower extremity redness, warmth, and swelling. They frequently report a gradual history of sensation loss in the lower extremity, altered gait pattern, and/or no longer fitting into their normal footwear. The Charcot event may or may not be associated with pain in the lower extremity. If present, it may be reported as discomfort and seem less severe compared to patients without neuropathy who have a similar degree of local inflammation.[28,62] The majority of patients will not recall any specific antecedent trauma.[27] However, exploring sources of seemingly minor trauma, such as prolonged walking, is important in this patient population because of their compromised sensation. Typically, patients will not have constitutional signs or symptoms of infection at presentation. However, the clinician must determine if there has ever been existing ulcers or drainage.

Significant past medical history includes any disease associated with neuropathic complications; most commonly, diabetes mellitus. However, far less common etiologies resulting in distal neuropathy should be considered, including leprosy, diseases of the spinal cord and nerve roots, Parkinson disease, HIV, sarcoidosis, rheumatoid disease, and exposure to toxins. Additionally, it should be noted that in one study nearly 40% of Charcot patients have idiopathic neuropathy.[2] Finally, given the abnormal bone resorption in Charcot patients, it is important for the physician to ask questions regarding osteopenia or fragility fractures, as these patients are at high risk.

Physical examination reveals relatively painless erythema, warmth, and inflammation around the involved joints. Using a skin thermometer or thermogram, foot temperature may measure a difference of 10°F or more.[1] A comprehensive vascular examination often shows exaggerated blood flow and palpable pulses. This differentiates a Charcot foot from a diabetic foot with peripheral arterial disease. Skin examination of the foot and ankle may or may not reveal concurrent findings of ulceration, abscess, purulent drainage, and cellulitis. Signs of streaking erythema tracking proximally is not a typical finding and should raise concern for local or hematogenous infection. Stability of the foot and ankle complex needs to be assessed to help determine disease stage. Patients with a more advanced or chronic Charcot foot have greater instability or possible fixed deformity in a midfoot break with collapsed arch and rocker bottom deformity.

Imaging

The diagnosis of Charcot arthropathy is primarily clinical, but imaging plays an important role in definitive diagnosis and the initiation of appropriate treatment. Plain radiographs are the initial imaging modality of choice and may show subtle demineralization and polyarticular changes in the midfoot and flattening of the first metatarsal head.[44] Although plain radiographs have low sensitivity and specificity (<50%) during the early stages of Charcot arthropathy,[13] they are useful in ruling out other pathology. Furthermore, serial imaging allows for longitudinal monitoring of the patient's bone structure and alignment. A recent prospective study examined the radiographic progression of unilateral Charcot arthropathy on 3 weight bearing views taken at sequential time points over a course of 2 years. In this time period, the diseased foot showed greater deformation than the contralateral foot or the diabetic control feet. Radiographs showed that the medial column deformed first over the initial 6 months of the disease process and the cuboid height continued to deform over the following 18 months.[32]

Compared with plain films, computed tomography (CT) is more sensitive for identifying bony abnormalities and early intra-articular fractures. CT may be used with contrast to detect abscess formation. However, CT lacks the ability to detect early bone marrow edema and microfractures seen in the initial acute phase of the disease and is therefore not recommended for diagnosis.[69]

Magnetic resonance imaging (MRI) has become more common in the initial evaluation of Charcot arthropathy given its ability to effectively detect soft tissue edema, joint effusion, and bone marrow changes early in the disease process. MRI findings on T2-weighted images can show high intensity signal at the Lisfranc ligament—representing early collapse of the longitudinal arc—and/or abnormalities in the subchondral bone of the subtalar joint or cuboid, indicating early malalignment due to joint subluxation.[77] MRI is a useful tool to help rule out abscess, fistulas, sinus tracts, and osteomyelitis (eg, focal involvement of the forefoot or calcaneus).[76]

Nuclear imaging techniques targeting biologic level of activity during the process of bone turnover has been examined in efforts to delineate a Charcot process from osteomyelitis. Technetium99 methylene diphosphonate labels hydroxyapatite. This marker is useful in identifying areas of bone repair but cannot differentiate between infection or trauma as the etiology. Indium-111 marks leukocytes, which associate with neutrophil-mediated inflammatory processes observed in bacterial infections of bone marrow. When combining technetium99 methylene diphosphonate and indium-111 white blood cell imaging, there were little differences in the sensitivity and specificity values for patients with osteomyelitis and those with Charcot osteoarthropathy.[70] Meanwhile, Technetium 99m sulfur colloid identifies areas of reticuloendothelial cells commonly found in the liver, spleen, and bone marrow. Bacterial seeding causes bone marrow edema, necrosis, and abscess formation. Infarction within the bone marrow leads to decreased amounts of the sulfur colloid uptake. Thus, if there is an infectious process, the scan with the technetium 99m sulfur colloid will have low uptake, while the indium-111 white blood cell image will have high uptake. Conversely, if there is a presence of both sulfur colloid as well as labeled leukocytes, the likelihood of osteomyelitis is reduced.[50,51] Technetium-99m sulfur colloid bone marrow imaging rather than technetium99 methylene diphosphonate in conjunction with indium-111 labeled leukocyte scans may thus improve the ability to distinguish osteomyelitis and inflammation in the Charcot patient.

Another imaging option is fluorodeoxyglucose proton emission topography-CT (FDG PET-CT). Shagos et al recently compared the efficacy of this technique to 3-phase bone scan (TPBS). The authors concluded that although TPBS had an 81% sensitivity for detecting Charcot neuroarthropathy, it was limited by a low specificity (28%). However, FDG PET-CT was more sensitive than TBPS and had a stronger negative predictive value for diagnosing pedal osteomyelitis.[71] Likewise, Basu et al showed in a prospective study that FDG PET-CT was effective at diagnosing osteomyelitis and differentiating it from neuroarthropathy.[3] Current economic and logistical considerations prevent FDG PET-CT from being a common screening test, but this imaging modality should be considered when the diagnosis remains unclear.

Aside from imaging for diagnostic purposes, dual energy x-ray absorptiometry to evaluated bone density should be considered in the initial work-up of Charcot patients. Joint dislocation and fracture risk is elevated in these patients if mineralization levels are normal or low, respectively.[33,62] Knowing a patient's baseline bone mineral density level helps determine the need to start a systemic treatment (eg, bisphonsonates) and allows for more specific prognostic counseling.

In conclusion, several imaging modalities are used in the evaluation of patients with Charcot neuroarthropathy. Early evidence suggests that FDG PET-CT may be useful in distinguishing Charcot neuroarthropathy from osteomyelitis; however, further research into this promising yet costly technology is necessary, supporting a grade I recommendation (Table 1).

Table 1. Level of Evidence and Grade of Recommendation.

Level of Evidence
Level I: High-quality prospective randomized clinical trial
Level II: Prospective comparative study
Level III: Retrospective case-control study
Level IV: Case series
Level V: Expert opinion
Grades of Recommendation
Grade A: Treatment options are supported by strong evidence (consistent with Level I or II studies)
Grade B: Treatment options are supported by fair evidence (consistent with Level III or IV studies)
Grade C: Treatment options are supported by either conflicting or poor-quality evidence (Level IV studies)
Grade I: There is insufficient evidence to make a recommendation

Classification

The original classification schemes for Charcot arthropathy relied on either the anatomic distribution of the pathologic changes or the radiographic appearance of the bones regardless of location. Recent classification systems attempt to incorporate prognosis and advanced imaging into their staging.

In 1996, Eichenholtz initially classified Charcot neuroarthropathy according to clinical, radiographic, and pathologic findings collected from a series of patients.[20] Based on

these data, which included all joints of the appendicular skeleton, Eichenholtz believed Charcot arthropathy followed a predictable temporal series of events and used these findings to determine the disease stage. Stage I (development and fragmentation) is characterized by articular debris, subchondral and cartilaginous fragmentation, and joint capsule distention with subsequent subluxation and dislocation. Stage II (coalescence) is defined by fine debris absorption, new bone formation, fusion of the larger fragments, and sclerosis of the bone ends. Finally, Stage III (reconstruction and reconstitution) occurs when there is less sclerosis, rounding of the major fragments, and reformation of the joint architecture, leading to a fixed and stable deformity. Eichenholtz noted that some patients repeated the stages multiple times, while others never progressed through all 3 stages. The major critique of this classification was the lack of inclusion of the early stage of disease, when clinical symptoms are evident but radiographs are normal. Hence in 1990, Shibata et al added a Stage 0 to account for this period of early inflammatory changes.[73]

Brodsky[7] introduced an anatomic classification to describe the Charcot process. Type 1, the most common, affects the tarsometatarsal and naviculocuneiform joints. Type 2 involves any distribution of the talonavicular, calcaneocuboid, or subtalar joints. Type 3A involves the ankle joint. Type 3B, the least common, is defined by compromise of the calcaneal tuberosity and associated Achilles tendon avulsion. Type 4 has any combination of the above, and Type 5 solely affects the forefoot. The Sanders and Frykberg classification similarly uses an anatomic-based scheme: Pattern I, forefoot; II, Lisfranc; III, Chopart; IV, ankle and subtalar; and V, calcaneal tuberosity.[66] The Rogers classification combines the anatomic location (hindfoot, midfoot, forefoot) with clinical characteristics (deformity, ulceration, osteomyelitis) to predict the risk of amputation.[61] The utility of the Rogers classification requires further validation.

Recently, Chantelau proposed a new classification of Charcot arthropathy based on MRI findings.[12] Stage A represents active or acute arthropathy and Stage B is inactive or "becalmed" arthropathy. These stages are differentiated based on bone marrow edema on MRI. Each stage is then numerically graded with either 0, representing low severity (no cortical fracture or deformity), or 1, to represent high severity (with cortical fracture, skeletal deformity). The stage affects treatment decisions, while the grade affects foot function, shoewear, and prognosis. Each of the 4 possible scenarios have unique clinical, MRI, and histopathologic features. Although not widely used at this time, it offers a different framework to consider the disease. The Chantelau classification scheme uniquely highlights the critical Stage 0 of arthropathy, which when treated appropriately, can prevent major foot deformity and progression through the original Eichenholtz stages.

Treatment

Nonoperative

The goals of nonoperative treatment of Charcot feet are resolution of the inflammatory process and prevention of foot deformity. Immobilization remains the initial management of early Charcot neuroarthropathy (Eichenholtz Stage 0, 1). This traditionally used nonweightbearing in a total-contact cast until the warmth and edema of the area subsides, heralding the dissipation of the inflammatory event. Studies now show patients may be allowed to weight bear during their cast treatment without an increase in deleterious effects.[16,57] The reported time necessary to achieve the target endpoint from casting varies widely between 9 weeks and 11 months.[4,57] Two Level IV case series support total-contact cast with weight bearing and its efficacy in preventing collapse and deformity of the foot.[11,64] There are, however, risks associated with this form of nonoperative treatment. One study looking at 70 patients who underwent serial casting reported ulceration rates as high as 30%.[30] Thus, frequent cast removal (3-4 weeks) and skin examination should be considered during treatment. Patients may be transitioned to appropriate diabetic footwear or orthotics after the casting period to prevent recurrence or ulceration.

Other studies have investigated weight bearing in a prefabricated removable walking boot to allow patients to perform daily skin examinations during treatment. Biomechanically, these boots are able to offload the forefoot/midfoot at the expense of the hindfoot.[31] This treatment modality can result in high patient satisfaction and prevention of deformity.[78] One nonrandomized study found a longer time to symptom resolution with removable boots versus total contact casts.[27] In summary, a grade B recommendation is given to total contact casting for all cases of acute Charcot arthropathy, with a grade B recommendation for prefabricated removable boots in only those cases of arthropathy isolated to the midfoot.

The efficacy of adjuvant therapy with bisphosphonates to offset increased osteoclastic activity has been investigated. In a double-blind randomized controlled trial (RCT), pamidronate administration, in addition to immobilization and restricted weight bearing over 12 months, resulted in decreased serum and urinary markers of bone turnover and reduced pain in the foot compared to the saline group.[39] Another RCT noted similar beneficial effects of the bisphosphonate alendronate.[58] However, the immobilization time was shown to be longer with use of bisphosphonates,[49] and no follow-up studies have been published to examine the long-term effects or risk of recurrence following bisphosphonate therapy. As such, a grade I recommendation is given to bisphosphonate therapy.

In patients with obvious progressive arthropathy, there are still treatment options to prevent limb-threatening complications. Generally, these seek to prevent plantar

ulceration that result from increased shear and compressive forces on the skin beneath bony prominences at the apex of deformity.[24] In rockerbottom deformity, these most commonly occur laterally beneath the cuboid and medially beneath the medial cuneiform as the medial longitudinal arch collapses and the forefoot adducts and dorsiflexes. Accommodative orthosis can be molded to match the uneven plantar surface to dissipate pressure in less severe deformity, whereas rockerbottom shoes combined with an ankle foot orthosis (AFO) or Charcot restraint orthotic walker (CROW) can be used to manage more severe deformity. Numerous retrospective studies demonstrate prevention of ulceration and preservation of the limb using these shoewear modifications[45,46,53]; however, follow-up was generally limited and thus only support a grade B recommendation for the longitudinal management of severe Charcot arthropathy. In addition, patient satisfaction with the daily use of cumbersome shoewear perceived to limit mobility can lead to poor compliance with therapy and limit its effectiveness.

Operative

The goals of operative intervention in the treatment of Charcot arthropathy include prevention or correction foot and ankle deformity with the hopes of providing a plantigrade and functional foot, treatment or prevention of ulceration, eradication of concurrent osteomyelitis, and limb salvage.

Operative management of early-stage Charcot arthropathy includes Achilles tendon lengthening, arthrodesis in situ, or realignment procedures that seek to prevent collapse into the rockerbottom deformity and preserve weight bearing with decreased risk of plantar ulceration. Achilles tendon lengthening alone in diabetics with plantar ulcers demonstrated healing rates between 91% and 100% with decreased recurrence when compared to casting alone.[36,47] A retrospective study (Level IV evidence) of 14 Eichenholtz stage I Charcot patients undergoing debridement and ORIF with autologous bone grafting of the midfoot demonstrated that in all patients the reconstruction had healed without complications and they returned to full weight bearing 15 weeks following surgery and wearing regular shoes 27 weeks postoperatively.[75] None of these patients developed a plantar ulcer at mean follow-up of 41 months. However, no studies directly compare immobilization therapy to early operative intervention, making the indication for the procedure unclear. There is also a lack of published results on the reconstruction of early hindfoot or ankle arthropathy. Thus, a grade I recommendation is given to operative intervention prior to developing deformity or ulceration.

Operative management of more severe deformity ranges from exostectomy of bony prominences to more extensive realignment and arthrodesis of the foot or ankle via internal or external fixation. This is often combined with debridement of coexistent osteomyelitis and Achilles tendon lengthening. Indications for concurrent soft tissue and bony procedures include persistent or recurrent limb-threatening ulceration(s) despite the use of accommodative shoewear. Diabetic neuropathic patients at this stage of disease usually have multiple medical comorbidities (especially cardiovascular, renal), are obese, and present with severe localized osteopenia. Given the extensive dissection required for reconstruction, these patients are at high risk for wound complications, delayed fusion, loss of fixation, and recurrence of deformity.

The most commonly performed operative procedures for Charcot arthropathy involve the midfoot. Ostectomy without reconstruction has been successful in treating nonhealing ulcers of the medial column. One study found a healing rate of 94% (17/18) of medial column ulcers, but 66% of lateral column ulcers failed to heal.[10] Similarly, a study of surgically treated lateral column ulceration noted that 11 of 32 feet experienced dehiscence, infection or recurrence. However, after revision surgery (4 with rotational flaps), only 3 of 32 were deemed unsalvagable.[63] Finally, in a study of 20 feet treated with exostectomy, 18/20 initially healed, but there were 9 recurrent ulcerations, 66% under the lateral column.[42] These Level IV studies support a grade B recommendation for the use of exostectomy of medial column ulcers but grade C for lateral column ulcers.

A variety of operative options exist to achieve arthrodesis of the involved joints and realign the rockerbottom deformity to recreate a plantigrade foot. Given the poor wound healing potential of these patients, success has been obtained with external fixation,[23] which allows limited incisions, weight bearing, and can be prolonged until fusion occurs. A study of obese Charcot patients treated with a 3-level ring external fixator achieved ulcer- and infection-free feet able to ambulate in commercial shoes and orthoses in 24 of 26 patients.[54] Recently, a study of 11 Charcot feet introduced a more limited external fixation system, the multiaxial correction (MAC) fixator that is placed on the dorsum of the foot. All patients went on to union and were able to ambulate. The fixator was removed after an average of 8.7 weeks, and no pin tract infections were encountered.[43]

Due in part to the risk of recurrence of the rockerbottom deformity after initial treatment with external fixation, multiple authors have recently reported on the use of intramedullary axial screws or solid-core bolts to support the medial and lateral columns of the midfoot. In one study, intramedullary screws resulted in a stable foot with significantly improved foot angle measurements in 21 of 22 patients and all patients were ambulatory; however, screw complications were common (12 of 22 patients).[65] Substantial deformity correction was also obtained in other studies using a medial midfoot fusion bolt, but the risk of bolt migration was reported to range from 37.5% to 60%.[8,79] Another study reported that the medial midfoot fusion bolt, when used in isolation, failed in 6 of 7 feet.[22] Given these construct

failures, use of a single medial midfoot fusion bolt alone is not recommended. However, other literature supports that the use of 2 or more fusion bolts to support the medial and lateral columns of the foot or combining the bolts with external fixation yields high fusion rates (98%-100%) and lower rates (6%-18%) of fixation failure.[29,41,60] With regard to plate fixation, there are no recent publications on outcomes with this construct.

Combined, these studies support a grade B recommendation for the use of external fixation and/or medial and lateral column support using more than 1 solid bolt in the treatment of midfoot Charcot arthropathy.

Charcot of the ankle is often managed with early surgery to fuse the joint and permit ongoing weight bearing, as attempts to treat with constant use of an AFO or CROW alone puts the patient at high risk for dissociation of the malleoli from the distal tibia and subsequent amputation. Retrograde tibiotalocalcaneal nails, which also can address subtalar deformity, have demonstrated fusion rates of 70% to 100% and limb salvage rates of 75% to 100%.[9,17,56,74] Drawbacks of the procedure include the medial talar translation required for proper nail positioning, which creates hindfoot varus and a locked transverse tarsal joint resulting in a rigid foot. Tibial diaphyseal stress fractures have also occurred at the tip of the nail. External fixation can also be considered for the ankle. El-Gafary et al reported a 100% fusion rate and a mean time to regular shoewear at an average of 26.5 weeks after use of an Ilizarov frame for an average span of 18 weeks.[21] Electric current bone growth stimulators have also been used to improve fusion of the ankle arthrodesis. While the rate of fusion may be as high as 90%,[35] it has not been directly compared to arthrodesis alone. In summary, hindfoot fusion nails and external fixation receive a grade B recommendation for the treatment of hindfoot Charcot arthropathy, and electric current bone growth stimulators receive a grade I recommendation.

When patients present with recurrent or persistent ulcers, osteomyelitis, or abscesses of the foot (with or without prior attempted limb salvage), amputation should be considered. In patients who primarily have a foot infection, the Syme amputation is an alternative to typical below knee amputation and preserves the tibial metaphysis for weight bearing. In a series of 8 patients (9 feet) who underwent Syme amputation for the above indications, after 4 to 6 weeks all the patients were able to weight bear through the limb in a prosthesis without supportive devices and did not require further surgery.[19] Despite intensive disease-specific treatment, the overall risk of amputation in Charcot arthropathy remains high, especially in those with ulceration. One study with a 3.8-year median follow-up demonstrated a 2.7% annual rate of amputation, and a cumulative risk of 7% for those presenting without ulceration and 28% cumulative risk for patients presenting with ulceration.[64]

Conclusions

1. Understanding the pathophysiology, determining the presence or absence of commonly associated risk factors, performing a comprehensive clinical examination with a complete review of systems, and ruling out an open soft tissue injury or vascular compromise is essential to arriving at a diagnosis and initiating early treatment.
2. Plain films and MRI are the initial imaging modalities of choice in the workup and longitudinal care of patients with Charcot neuroarthropathy. MRI best depicts bone marrow and soft tissue edema, as well as fistulas and sinus tracts. TPBS and FDG-PET are emerging imaging modalities that have been shown to be effective at differentiating the Charcot process from infection but whose cost benefit ratio has yet to be fully determined (grade I recommendation).
3. Adjuvant therapy with bisphosphonates to offset the increased osteoclastic activity shows promise at the molecular level. However, there are no long-term studies that demonstrate clinical benefit (grade I recommendation).
4. Total contact casting is an effective treatment to prevent collapse and deformity of the foot in early-stage arthropathy (grade B recommendation). The patient may be weight bearing or non-weight bearing. This decision should be based on patient-specific factors. All patients should undergo frequent cast removal (3-4 weeks) and skin examination given the high complication rate related to ulceration.
5. Weight bearing in a prefabricated removable walking boot is also an effective treatment in the early stages of Charcot arthropathy and allows patients to independently perform frequent skin examinations and reduces the complication of ulceration (grade B recommendation).
6. Late stage arthropathy may still be treated nonoperatively in accommodative orthosis, rockerbottom shoes combined with an AFO, or CROW. These have been shown to be effective in preventing ulceration and limb preservation (grade B recommendation).
7. Operative treatment with ostectomy without reconstruction has been more successful in treating nonhealing ulcers of the medial column than the lateral column. Studies support a grade B recommendation for the use of exostectomy of medial column ulcers and a grade C for the use of ostectomy lateral column ulcers.
8. Midfoot arthropathy is the most common form of Charcot foot and has been successfully treated with external fixation and/or internal medial and lateral column support using bolts or screws (grade B recommendation) (Table 2).

Table 2. Summary of Grades of Recommendation.

Diagnostic Imaging modality with FDG PET-CT	Grade I
Adjuvant therapy with bisphosphonates	Grade I
Nonoperative treatment with total-contact casting in early-stage arthropathy	Grade B
Nonoperative treatment with a prefabricated removable walking boot and weight bearing as tolerated in early-stage arthropathy	Grade B
Nonoperative treatment in accommodative orthosis, rockerbottom shoes combined with an ankle foot orthosis (AFO), or Charcot restraint orthotic walker (CROW) in late-stage arthropathy	Grade B
Operative treatment with ostectomy without reconstruction for treatment of nonhealing ulcers of the medial column	Grade B
Operative treatment with ostectomy without reconstruction for treatment of nonhealing ulcers of the lateral column	Grade C
Operative treatment of midfoot arthropathy with external fixation and/or internal medial and lateral column support using bolts or screws	Grade B

Declaration of Conflicting Interests

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