

Recent Modalities in Management of Charcot Joint in Diabetic Foot

Walid Atef Alian, Mostafa Omar Abdelaziz and Alaaeldin Abdallah Ali Gomah Elghannam

Department of General and Oncology Surgery, Faculty of Medicine – Ain Shams University
alaa.ghannam545@gmail.com

Abstract: Background: Charcot neuroarthropathy is a non-infective, destructive process occurring in patients rendered insensate peripheral neuropathy which is caused mainly by diabetes. Repetitive trauma from standing and walking provides a neuro-traumatic stimulus that leads to dislocation, peri-articular fracture, or both within the ankle. **Objective:** The objective of our systematic review is to outline the current and recent clinical approach to this disabling medical condition. The purpose of the present study is to provide a systematic review of studies published from 2000 to 2017 and to review the indications for surgery. **Patients and Methods:** In our review, 405 patients underwent different treatment modalities of which: 110 underwent non-surgical treatment with variable conservative modalities. While the remaining 295 underwent surgical treatment with different fixation modalities and operative techniques. **Results:** Four papers are included in the group of Non-surgical management, one of them are prospective study level of evidence IV, one is double-blinded randomized controlled trial level of evidence I and two are retrospective study level of evidence III. Sixteen papers are included in the group of surgical management of Charcot Arthropathy, ten of them are prospective study level of evidence IV, one is cohort study level of evidence III and five are retrospective case series level of evidence IV.

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1. Introduction

Neuropathic arthropathy, also referred as Charcot arthropathy which was named after French neurologist Jean-Martin Charcot (1825-1893), is a progressive, denervation-induced degeneration of the foot and ankle joints. Considering devastating outcomes, such as eventual deformity which is almost always inevitable when untreated, the etiology and pathophysiology of this insidious disorder is vigorously studied in the literature as one of the core topics. A significant amount of content is amassing in the literature about this topic and this may be a sign of unclarity about the pathophysiology of Charcot arthropathy. Although numerous factors have been attributed as a contributor, the big picture is still not fully revealed (**Kaynak et al., 2013**).

Charcot neuroarthropathy (CN) is a process marked by bony destruction, bone resorption, and eventual deformity that can be limb-threatening. Historically, syphilis and leprosy were the most common causes of CN; however, diabetes mellitus (DM) has emerged as the most common cause of CN over the past several decades (**Shen and Wukich, 2013**).

With the increased number of diabetics worldwide and the increased incidence of morbid obesity in more prosperous cultures, there has become an increased awareness of Charcot arthropathy of the foot and ankle. Outcome studies would suggest that patients with deformity associated with Charcot Foot

arthropathy have impaired health related quality of life. This awareness has led reconstructive-minded foot and ankle surgeons to develop surgical strategies to treat these acquired deformities (**Shen and Wukich, 2013**).

Diabetes Association estimates that 25 million people in the United States, or 7.8% of the population, have diabetes mellitus. The incidence of Charcot arthropathy appears to be relatively common, perhaps affecting some 8.5 per 1000 people with diabetes per year (**Lowery et al., 2012**).

It affects both type 1 and type 2 diabetes. Recently, a relative preponderance of type 1 diabetes has been noted, and the odds ratio for a patient with type 1 diabetes to develop CN is 3.9 times greater than that of the odds ratio for a patient with type 2 diabetes. It is associated with significant morbidity, and patients often report a reduced quality of life (**Balducci et al., 2014**).

Primary risk factors for this potentially limb-threatening deformity are the presence of dense peripheral sensory neuropathy, normal circulation, and history of preceding trauma (often minor in nature). Trauma is not limited to injuries such as sprains or contusions. Foot deformities, prior amputations, joint infections, or surgical trauma may result in sufficient stress that can lead to Charcot joint disease (**Frykberg et al., 2006**).

Charcot neuroarthropathy has been recognized for more than 130 years, and remains a major cause of

morbidity in diabetic patients. It is a progressive condition of the musculoskeletal system, characterized by joint dislocations, pathological fractures, and debilitating deformities commonly affecting the neuropathic lower extremity. In the United States, many surgical limb salvage procedures for the Charcot foot deformity are performed annually. These procedures range from simple exostectomy to full reconstructions with metatarsal and tarsal osteotomy, arthrodesis, internal and external fixation, free flaps, and, finally, amputation (Pinzur and Schiff, 2017).

Aim of the Work

The objective of our systematic review is to outlines the current and recent clinical approach to this disabling medical condition. The purpose of the present study is to provide a systematic review of studies published from 2000 to 2017 and to review the indications for surgery.

And to correlate patient satisfaction with the outcome of different limb salvage procedures, and make a systemic review on results of methods of treatment of Charcot joint.

This review will show different literature, research and statistical analysis of results.

2. Materials and Methods

This is a systematic review article on results of different methods of treatment of Charcot arthropathy of ankle joint.

Points of comparison in our research were as follows:

Patient demographics (age, sex). Follow up periods. Type of treatment. Follow up data. Results.

The inclusion criteria for the selected articles were:

Articles from 1995-2018. English literature only. Human studies. Clinical trials.

Exclusion criteria:

In vitro studies. Duplicated articles by the same authors unless with longer follow up studies. Non diabetic causes of Charcot neuroarthropathy (i.e., leprosy, syringomyelia, syphilis, and alcohol). Those describing Charcot neuroarthropathy in areas of the body other than the foot and ankle.

Articles included in this systematic review consisted of the clinical studies concerning with different methods of treatment of Charcot arthropathy of ankle joint. The review includes prospective case series, and nonrandomized prospective comparative studies, retrospective studies and observational studies.

3. Results

Table (1): Non-surgical management of Charcot arthropathy.

A) Medical treatment of Charcot arthropathy

Article	Study design/level of evidence	No of patients	Stage of disease	Non-surgical technique	Follow up data.	Follow up period	Results
1) E.B. Jude et al., (2001)	Double blinded RCT/level I	N=39 Study = 21 Placebo = 18	Stage I	Patients received 90 mg of pamidrotate over 4- 24 hr as a single in fun on dose or placebo (saline)	Ankle temperature, symptoms and markers of bone turnover {bone specific alkaline phosphatase and deoxypyridiолone crosslinks)	12 months	An improvement in symptoms was seen in the active group compared with placebo group. Reduction in bone turnover was greater in the active than in the control group
2) Anderson et al., (2004)	Retrospective study level III	N = 23 Study = 13 Control = 10	Stage I	The 13 study patient administered Pamidronate were compared with 10 control patients who were treated with traditional immobilization methods	Limb temperature and alkaline phosphatase	3 week	After pamidronate infusion limb temperature decreased 7.4 by 2 week. The alkaline phosphatase also decreased an average 53% 2 necks after infusion The control group show no significance reduction on limb temperature or alkaline phosphatase

B) Non-medical treatment of Charcot arthropathy

Article	Study design/level of evidence	No of patients	Stage of disease	Non-surgical technique	Follow up data.	Follow up period	Results
3) Shwan Verity et al (2008)	Retrospective study/level III	N=21	Stage III	Prefabricated pneumatic removable walker brace filled with a custom orthotic insole	Patient interview, examination and radiography	33 months	Patients' subjective impression of removable walker brace: Greatly helpful, 84% Moderate helpful 8% Minimally helpful 0% Not helpful at all 4% Aggravated condiltou:4%
4)leo (2008)	Retrospective study level IV	N=27	Stage I/II	Immobilization in a weight bear total contact east	Patient interview, examination and radiography	5.5 months	No deleterious effect from weight bearing

Table (2): Surgical management of Charcot arthropathy.

Article	Study design/level of evidence	No of patients	Stage of disease	Non-surgical technique	Follow up data.	Follow up period	Results
1) Caravaggi et al., (2006)	Cohort/level III	No = 45	Unspecified	Tibiocalcaneal arthrodesis using retrograde intramedullary nail fixation	Patient interview, examination and radiography	5±2.85 years	4 patients (8.88%): below knee amputation 2 patients (4.44%): fibrous union and required pneumatic casts for ambulation 39 patients (86.67%) solid union and returned to independent ambulation wearing custommade shoes with molded insoles
2) Pawar et al. (2013)	Prospective study/level IV	N = 5	Stage I/III	Retrograde antibiotic-coated locked intramedullary nail	Patient interview, examination and radiography	12-24 months	All achieving infection control and bony union
3) Fabrin et al. (2007)	Prospective study/level IV	N = 11	Unspecified	Arthrodesis with external fixation	Patient interview, examination and radiography	48 months	7 cases tibiotalar arthrodesis was performed: 5 bony union 2 fibrous union 5 cases tibiocalcaneal arthrodesis was performed: arthrodesis was performed: 1 bony union 2 stable fibrous union 1 unstable fibrous union 1 amputation
4) Ayoub (2008)	Prospective study/level IV	N = 17	Stage II/III	Tibiotalar arthrodesis (crossed screw technique)	Patient interview, examination and radiography	26 months	Success rate: 82.4% 9 patients: bony union 5 patients: stiff fibrous union 3 patients: below knee amputation

Article	Study design/level of evidence	No of patients	Stage of disease	Non-surgical technique	Follow up data.	Follow up period	Results
5) El-Gafary et al., (2009)	Prospective study/level IV	N = 20	Stage II	Surgical arthrodesis by illizarove frame	Patient interview, examination and radiography	20 months	10% success All patients show solid union and correction of deformities
6) Pinzur et al., (2007)	Prospective study/level IV	N = 9	Unspecified	Arthrodesis with retrograde intramedullary nailing	Patient interview, examination and radiography	32 months	100% success 9 patients show union fusion
7) Pinzur et al., (1997)	Prospective study/level IV	N = 20	Unspecified	Retrograde locked intramedullary	Patient interview, examination and radiography	12-31 months	19 patients achieved bony fusion: 1 patient: Amputation 1 patient: Died
8) Caravaggi et al., (2006)	Prospective study/level IV	N = 14	Stage II	Intramedullary compressive nail fixation	Patient interview, examination and radiography	18 [±] 4 months	Success rate 92.2% 10 patients achieved solid arthrodesis returning to walking with protective shoes 3 patients develop fibrous union that allowed walking with brace 1 patients: below knee amputation
9) Paola et al., (2007)	Prospective study/level IV	N = 1	Stage IV	Panarthrodesis of ankle using intramedullary retrograde transcaneal mailing	Patient interview, examination and radiography	14 [±] 10.1 months	The percentage of limb salvage 100% due to control patient selection 14 patients: complete bony union of ankle arthrodesis and were able to wear shoes 4 patients: fibrous union and still walking with a pneumatic walker – custom molded ankle foot orthosis was prescribed which allowed shoes wear
10) Yousry and Abdalhady (2010)	Prospective study/level IV	N = 12	Stage II/III	Tibiocalcaneal and tibitalar fusion using an illiazrove frame	Patient interview, examination and radiography	19.3 months	Success rate 75% Fusion was confirmed in 9 patients (75%) 2 patients had pseudoarthrosis 1 patient had unstable pseudoarthrosis
11) Siebachmeyer et al., (2015)	Prospective study/level IV	N = 20	Unspecified	Retrograde intramedullary nail	Patient interview, examination and radiography	26 months	21 feet: All achieved limb salvage 100% 19 feet show bony fusion 1 feet shows stable fibrous union 1 feet shows non-union
12) Zarutsky et al., (2005)	Retrospective analysis/level III	N = 11	Unspecified	Circular wire external fixator	Patient interview examination and radiography	27 months	Bony union: 7 patients Fibrous union: 3 patients Amputation: 1 patient

Article	Study design/level of evidence	No of patients	Stage of disease	Non-surgical technique	Follow up data.	Follow up period	Results
13) Shah and De (2011)	Retrospective analysis/level III	N = 11	Stage II/III	6 patients used external fixator 5 patients used retrograde intramedullary nail	Patient interview, examination and radiography	4 months	Regarding intramedullary nail all 5 patients achieved bony union (100%) Regarding external fixator 6 patients: 1 patient bony union 4 patients non-union 1 patient amputation
14) Myerson et al., (2010)	Retrospective case series/level IV	N = 26	Unspecified	Tibicalcaneal arthrodesis using a condylar blade plate	Patient interview, examination and radiography	48 months	All achieved limb salvage 24 patients showed bony union 2 patients showed fibrous union
15) Çinar et al., (2010)	Retrospective case series/level IV	N = 4	Unspecified	Tibicalcaneal arthrodesis using posterior blade plate	Patient interview, examination and radiography	24 months	All achieved limb salvage 3 patients showed bony union 1 patient showed fibrous union
16) DeVries et al., (2012)	Retrospective cases series/level IV	N = 52	Various stages	45 patients used retrograde intramedullary nail 7 patients used external fixator	Patient interview, examination and radiography	24 months	Regarding intramedullary nail: 32 patients stable bony union 3 patients showed fibrous union 10 patients undergoing amputations Regarding external fixator: 5 patients showed bony union 2 patients showed amputation

4. Discussion

The management of patients with foot and ankle diabetic neuroarthropathy is challenging. Patient education about prevention, early recognition of arthropathy and prompt institution of protective treatment is clearly crucial factor that determine the outcome of this problem. The mainstay of treatment for ankle Charcot neuroarthropathy is prolonged immobilization in the form of plaster cast, brace or using antiresorptive medication during the acute stage. However, some patients already have disabling deformity or sever instability at the time of presentation in which conservative treatment alone is destined to failure. For such patients, reconstruction of the foot and ankle is a valuable technique (**Yousry and Abdalhadry, 2010**).

In our review, 405 patients underwent different treatment modalities of which: 110 underwent non-surgical treatment with variable conservative modalities. While the remaining 295 underwent surgical treatment with different fixation modalities and operative techniques.

Regarding non-surgical treatment, **Jude et al. (2001)** and **Anderson et al. (2004)**, studied the effect of bisphosphonate on 62 patients as regards its role in the clinical signs improvement during the acute stage. Thirty-four patients received bisphosphonate while the other 28 took placebo (control group). All patients who received bisphosphonate showed a 100% decrease in the clinical signs and symptoms of Charcot arthropathy compared to the placebo group.

The exact mechanisms by which bisphosphonates inhibit bone resorption are unknown. It is known that pamidronate is taken up by bone, bound to hydroxyapatite crystal of the bone matrix and then acts to prevent osteoclast precursors from attaching to bone. Pamidronate also directly inhibits mature, already active, osteoclasts, and promotes osteoclast apoptosis. Finally, pamidronate decreases osteoblast-mediated osteoclast activation. Although pamidronate inhibits osteoclasts via several mechanisms, it has not been shown to impair mineralization (**Russell and Graham, 2007**).

Inflammation regression in the form of temperature drop is clinically recorded in the Charcot

ankle arthropathy group who received pamidronate. A decrease of alkaline phosphatase is also noted in the same group. The single infusion of 60 - 90 mg intravenously over 4-24 hours was the selected regimen as Jude et al and Anderson et al reported in their studies.

There was no complication of bisphosphonate treatment reported by Jude et al., while Anderson et al., used a post-administration systemic fever of 1-3 degrees, which lasted only hours and subsided within 24 hours after slow infusion, this accounted for 9.67% of study population (6 patients only out of 62 patients). Transient nausea and gastrointestinal upset were also observed amounting to 8.06% of their patients, which was also short lived. There were no major side effects related to pamidronate in any of the study patients. In spite of the effect of pamidronate on the acute process of Charcot, there are several concerns regarding their methodology for limitations discussed by Jude et al and Anderson et al in this review. First the pamidronate group and placebo group were in different institutions and were not concurrent; second the number of patients in their review was 62 patients, which was small. So, large trials would be necessary to show sufficient power of the results. Lastly calibration of sensor devices was not done, because the tool was actually a different one at each site, some variability may have existed.

Weight-bearing total contact cast (TCC) and orthosis were evaluated as another modality of conservative treatment by Leo which included 27 patients with Charcot arthropathy (7 patients with bilateral ankle involvement). The involved 34 feet showed no deleterious effect from weight-bearing in 100% of cases, so TCC is considered a safe immobilization technique in Eichenholtz stage-1 Charcot arthropathy of the ankle. Ulcer was noted in 10 out of 34 feet (29.41%). Yet, none of them was complaining during TCC application period (14 weeks). They all developed after the limb had been placed in an orthosis (at with a freehand technique with image intensification monitoring).

Solid fusion was achieved in 152 feet out of 183 feet (83.06%) and stiff fibrous union was obtained in 13 feet (7.1%), and only 16 feet (8.74%) underwent below knee amputation. One patient showed non-union (0.54%) and one patient died. The complications noted by the authors in our review when using intramedullary nail fixation were variable. Infection is the most common complication reported in their patients at the rate of 45.85% presented in the form of superficial wound infection or loosening and breakage of proximal or distal screws. Pawar et al., had overcome the infection problem by using antibiotic coated intramedullary nail and all their patients did well and showed 100% complete healing.

In spite of these good results the limitation of their study was the small patients' number (five patients only). So, future studies with larger numbers of are required.

The other complications of intramedullary nail are development of ulcers 8.27% (15 out of 181 patients), postoperative hematoma reported in one patients (8.74%) underwent knee amputation.

This review suggests that treatment of arthrodesis with retrograde nailing is a safe and effective treatment option for ankle instability in patients with Charcot arthropathy.

Another internal fixation method is ankle arthrodesis using crossed screws. Ayoub et al., gave the results of an attempt to salvage the limbs of 17 patients using cannulated screws to obtain tibiotalar fusion. A solid fusion was achieved in nine patients (53%) and higher fusion rates were achieved with three screws. A stiff fibrous union was obtained in five patients (29.4%). Only three patients (18%) developed unstable pseudoarthroses, which lead to below knee amputation. The complications shown on their patients were superficial wound infection in four patients (23.5%) and avascular necrosis of talus and hind foot ulceration in three patients (17.6%).

Blade plate ankle arthrodesis technique was evaluated by Murat Çinar et al., and Myerson et al., in an attempt to salvage the limbs of 30 patients to obtain tibiotalar fusion.

The patients were positioned in a lateral decubitus position. A 15- to 20-cm longitudinal incision was performed on the lateral border of Achilles' tendon. The Achilles' tendon was cut at the insertion to the calcaneus. After posterior capsular resection, the tibiotalar and subtalar joints were exposed. In order to correct the deformity, subtotal or total talectomy was performed. Simultaneously, a second central anterior incision was performed. A flat cut, denuding the tibial articular cartilage is made, with an oscillating saw. The appropriate size of AO 95-degree-angled blade plate was chosen (usually a 4-5 holes plate 50 to 60 mm in length). Under the control of an image intensifier the foot was placed in neutral position relative to the tibia, and the hole in which the blade plate was going to be placed in the posterior calcaneus was opened with a slot. An appropriate plate was placed on the calcaneus. At this stage, the plate was sloped as needed if there was incongruence between the posterior tibial cortex and the plate. The compression was applied via the DCP holes of the plate. The bone graft from the lateral malleolus was packed around the plate from the posterior tibia to the dorsum of the calcaneus.

All patients achieved limb salvage (100%): either by solid fusion in 27 patients (90%) or stiff fibrous union in three patients (10%). Infection was

the most common complication reported on 18 out of 30 patients (60%). Another complication seen was developing stress fracture at the proximal end of blade (6.66%). The limitation of their study is the population number (30 patients only); so future studies with larger numbers are still required. This review suggested that treatment by arthrodesis using blade plate constitutes a safe and effective treatment option for ankle instability in patients with Charcot arthropathy. However, open correction with internal fixation for Charcot osteoarthropathy is associated with a high rate of complications and failure because of infection, bone softening, resorption, fragmentation and breakage of implants. Complex reconstructive procedures with arthrodesis are more frequently reserved for realignment and stabilization of severely deformed feet and ankles in an effort to avoid amputation.

The choice of internal or external fixation depends on the quality of bone. Generally, in Charcot disease, the bone stock is poor and external fixation provides better compression with fewer fixation failures and soft tissue complications. Due to its ability to correct multiplanar deformities in osteopenic bone, even in presence of open wounds, the circular (Ilizarov) external fixator is preferred for most Charcot foot and ankle reconstructions.

We reviewed 67 patients who underwent surgical fixation by external fixator evaluated by Yousry and Abdalhady, El-Gafary et al, Jesper Fabrin et al., Zarutsky et al., George De Vries et al and Shah and De Solid fusion and anatomical reduction were obtained in 48 patients (71.64%), fibrous union was obtained in 10 patients (14.92%), nonunion occurred in 4 patients (5.97%) and below knee amputation in 6 patients (8.95%). Correction and stabilization of foot and ankle deformities with Ilizarov external, fixator were effective and allowed correction of deformities and avoid the complications of internal fixation. It also allowed early weight-bearing, care of soft tissue, prevention of skin ulceration and avoidance of amputation. However, it should be recognized that Ilizarov external fixation is not without some disadvantages since it involves lengthy duration of treatment with mean follow up period of 24 month as noted in our results, commonly associated with pin-tract infection 64.17 %. Ilizarov also required surgical expertise and dedicated instrumentation. Nevertheless, these problems are outweighed by the advantages of the technique.

In summary, early recognition and prevention of collapse are still the best options for the management of patients with diabetic Charcot arthropathy. Appropriate education, improved clinical evaluation and early intervention are required to control the disease. Once collapse is present, the use of an off-

loading TCC and anti-resorptive medication are recommended in the acute stage. In ensuing stages, salvage of the affected joint by tibiotalar arthrodesis is preferable either by internal fixation or external fixation.

Conclusion

According to this systematic review of clinical results of the Charcot arthropathy of ankle joint, the active process of Charcot neuro-arthropathy can be delayed with non-surgical technique. It also appears that the severe joint instability found in Charcot neuro-arthropathy of ankle can be treated successfully with intramedullary nail fixation and external fixation, yielding a high rate of limb salvage. However, future long-term, prospective randomized studies are needed and more non-surgical, surgical technique and outcomes measures needed.

References

1. Anderson JJ, Woelffer KE, Holtzman JJ, Jacobs AM. Bisphosphonates for the treatment of Charcot neuroarthropathy. *The Journal of foot and ankle surgery*, 2004; 43(5): 285-289.
2. Ayoub MA. "Ankle fractures in diabetic neuropathic arthropathy: can tibiotalar arthrodesis salvage the limb?." *The Journal of bone and joint surgery*. British volume 90, no. 2008; 7 (7): 906-914.
3. Balducci S, Sacchetti M, Haxhi J, Orlando G, D'errico V, Fallucca S, Pugliese G. Physical exercise as therapy for type 2 diabetes mellitus. *Diabetes/ metabolism research and reviews*, 2014; 30(S1): 13-23.
4. Caravaggi C, Cimmino M, Caruso S, Dalla Noce S. Intramedullary compressive nail fixation for the treatment of severe Charcot deformity of the ankle and rear foot. *The Journal of foot and ankle surgery*. 2006; 45(1):20-24.
5. Çinar M, Derincek A, Akpınar S. Tibiocalcaneal arthrodesis with posterior blade plate in diabetic neuroarthropathy. *Foot & ankle international*. 2010; 31(6):511-516.
6. DeVries JG, Berlet GC, Hyer CF. A retrospective comparative analysis of Charcot ankle stabilization using an intramedullary rod with or without application of circular external fixator—utilization of the Retrograde Arthrodesis Intramedullary Nail database. *The Journal of Foot and Ankle Surgery*. 2012; 51(4):420-425.
7. El-Gafary KA, Mostafa KM, Al-adly WY. The management of Charcot joint disease affecting the ankle and foot by arthrodesis controlled by an Ilizarov frame: early results. *The Journal of*

- bone and joint surgery. *British volume*. 2009; 91(10):1322-5.
8. Fabrin J, Larsen K, Holstein PE. Arthrodesis with external fixation in the unstable or misaligned Charcot ankle in patients with diabetes mellitus. *The international journal of lower extremity wounds*. 2007; 6(2):102-7.
 9. Frykberg RG, Zgonis T, Armstrong DG, Driver VR, Giurini JM, Kravitz SR, Landsman AS, Lavery LA, Moore JC, Schuberth JM, Wukich DK. Diabetic foot disorders: a clinical practice guideline (2006 revision). *The journal of foot and ankle surgery*. 2006; 45(5): S1-66.
 10. Jude EB, Selby PL, Burgess, P. Lilleystone, E.B. Mawer, SR Page, M Donohoe, A VM Foster, ME Edmonds, AJM Boulton: Bisphosphonate in the treatment of charcot neuroarthropathy: a double-blind randomized controlled trial. *Diabetologia* 2001.
 11. Kaynak G, Birsel O, Fatih Güven M, Ögüt T. An overview of the Charcot foot pathophysiology. *Diabetic foot & ankle*. 2013; 4(1):211-17.
 12. Leo JS. Charcot Arthropathy and Immobilization in a Weight - bearing Total Contact Cast. *Journal of bone and joint surgery* 2008; 90(4):754-9.
 13. Lowery NJ, Woods JB, Armstrong DG, Wukich DK. Surgical management of Charcot neuroarthropathy of the foot and ankle: a systematic review. *Foot & ankle international*. 2012; 33(2):113-21.
 14. Myerson MS, Alvarez RG, Lam PW. Tibiocalcaneal arthrodesis for the management of severe ankle and hindfoot deformities. *Foot & ankle international*. 2000; 1(8):643-50.
 15. Paola LD, Volpe A, Varotto D, Postorino A, Brocco E, Senesi A, Merico M, De Vido D, Da Ros R, Assaloni R. Use of a retrograde nail for ankle arthrodesis in Charcot neuroarthropathy: a limb salvage procedure. *Foot & ankle international*. 2007; 8(9):967-70.
 16. Pawar A, Dikmen G, Fragomen A, Rozbruch SR. Antibiotic-coated nail for fusion of infected Charcot ankles. *Foot & ankle international*. 2013; 34(1):80-4.
 17. Pinzur MS and Kelikian A. Charcot ankle fusion with a retrograde locked intramedullary nail. *Foot Ankle Int*. 1997; 18:699-704.
 18. Pinzur MS and Kelikian A. Charcot ankle fusion with a retrograde locked intramedullary nail. *Foot Ankle Int*. 1997; 18:699-704.
 19. Pinzur MS. Ankle fusion with a retrograde locked intramedullary nail. *Techniques in Foot & Ankle Surgery*, 2007; 6(1): 38-43.
 20. Russell R and Graham G. "Bisphosphonates: mode of action and pharmacology." *Pediatrics* 119, no. Supplement 2 (2007): S150-S162.
 21. Shah NS and De SD. Comparative analysis of uniplanar external fixator and retrograde intramedullary nailing for ankle arthrodesis in diabetic Charcot's neuroarthropathy. *Indian journal of orthopaedics*. 2011; 45(4):359.
 22. Shen W and Wukich D. Orthopaedic surgery and the diabetic Charcot foot. *Medical Clinics*. 2013; 97(5):873-82.
 23. Siebachmeyer M, Boddu K, Bilal A, Hester TW, Hardwick T, Fox TP, Edmonds M, Kavarthapu V. Outcome of one-stage correction of deformities of the ankle and hindfoot and fusion in Charcot neuroarthropathy using a retrograde intramedullary hindfoot arthrodesis nail. *The Bone & Joint Journal*. 2015; 97(1):76-82.
 24. Verity S, Sochocki M, Embil JM, Trepman E. Treatment of Charcot foot and ankle with a prefabricated removable walker brace and custom insole. *Foot and ankle surgery*. 2008; 14(1):26-31.
 25. Yousry AH and Abdalhady AM. Management of diabetic neuropathic ankle arthropathy by arthrodesis using an Ilizarov frame. *Acta Orthopaedica Belgica*. 2010 Dec 1;76(6):821.
 26. Zarutsky E, Rush SM, Schuberth JM. The use of circular wire external fixation in the treatment of salvage ankle arthrodesis. *The Journal of foot and ankle surgery*. 2005; 44(1):22-31.

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