REVIEW

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Current surgical interventions of Charcot neuroarthropathy of the foot and ankle: a systematic review

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ABSTRACT

Introduction: Charcot neuroarthropathy (CN), also known as Charcot's foot, is consequently causing a reduction in quality of life, high disability, and an increased risk of mortality that poses many clinical challenges in its diagnosis and management. Common surgical interventions typically include ulcer debridement, exostectomy, deformity correction, and minor and major amputations.

Methods: This systematic review was conducted using the PRISMA guideline. Literature research incorporating PubMed/MEDLINE database for English language studies published in the last 5 years with the key terms defined using the PICO framework, which includes: Charcot, neuroarthropathy/arthropathy, neurogenic, and surgery, which were used interchangeably. A further set of keywords within the topic were then identified, including ankle, hindfoot, foot, fore-foot, and mid-foot.

Result: 221 feet undergone surgical reconstruction. Bony fusion occurred in 154 of 221 feet (71%), 79 of 128 feet (62%) in internal fixation, 47 of 58 feet (81%) in external fixation, and 29 of 34 feet (85%) in the utilization of both internal and external fixation.

Conclusion: Charcot neuroarthropathy poses many clinical challenges in its diagnosis and management. Many experts have proposed the implementation of different strategies to manage this complex condition depending on the acute and chronic phases of its nature. Delayed diagnosis can result in a severe deformity that can act as a gateway to ulceration, and infection and, in the worst case, can lead to limb loss. Further studies aimed at determining selection criteria and treatment algorithms are required for greater standardization of outcomes.

Keywords: *Charcot neuropathy, diabetes mellitus, surgical reconstruction*.
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INTRODUCTION

Charcot neuroarthropathy (CN), also known as Charcot's foot, is a debilitating, chronic, progressive condition of weight-bearing joint deterioration, most commonly in the foot and ankle as a result of peripheral neuropathy. It is characterized by progressive bone deformity and osteoarticular instability, which then leads to ulceration, osteomyelitis, an elevated risk of amputation, and consequently, a reduction in quality of life, high disability and an increased risk of mortality.[1-6] CN was first reported in 1831 by physician John Kearsley Mitchell in patients with tuberculosis-induced spinal damage. Then a French neurologist, Jean-Martin Charcot, described a chronic progressive neuroarthropathy resulting in joint destruction in patients with *tabes dorsalis*.[7] However, it was not until William Riely Jordan described the first case of neuropathic arthropathy in a patient with diabetes mellitus (DM) in 1936.[8] Though the etiology of CN is not fully known, it has been well accepted that neuropathy precedes the disease, which DM is the most common cause in a developed country. Other plausible risk factors include syphilis, HIV, leprosy, syringomyelia, meningomyelocele, spina bifida, amyloid neuropathy, neuropathies secondary to alcoholism, and renal dialysis and postrenal transplant arthropathy.[9-10]

Current literature on CN indicated a limited number of studies on the CN prevalence. The available literature is focused mostly on the western population. The American Diabetes Association has made an estimation of 9.8% of the United States population have been diagnosed with DM, of which 4.9% of these patients will develop peripheral neuropathy. Lavery *et al.*, in their study of diabetic foot syndrome prevalence, stated that it might affect 8.5 per 1000 populations with DM annually.[11] In addition, Sohn *et al.*, in their recent study, showed the development of foot ulceration in 34% of patients as a complication of CN. This study showed a risk of amputation 7 times higher in patients with ulceration in the absence of CN but 12 times higher in CN patients with ulceration when compared with patients with CN alone.[12]

Charcot neuroarthropathy poses many

clinical challenges in its diagnosis and management. Therefore many experts have proposed the implementation of different strategies to manage this complex condition, depending on the acute and chronic phases of its nature. The treatment goal is to achieve a plantigrade foot with osseous stability, which could reduce the likelihood of ulcer formation and eventually reduce the rate of infection and amputation. The initial management has often been conservative, involving the use of casting, bracing, and other loading devices such as Charcot restraint orthotic walker devices, allowing patients to functional ambulation without invasive interventions. However, due to its nature of refractory to conservative care, a considerable number of patients would eventually result from the requirement of surgical management. Common surgical interventions typically include ulcer debridement, exostectomy, deformity correction, and minor and major amputations. Yet, there is still no general consensus on the proper timing or method of surgical intervention, owing to the characteristic heterogeneity of the patient's clinical presentation and pathology.[13]

A systematic review by Lowery *et al.* examined all published data regarding surgical management of CN from 1960 to 2009, and then an updated study was done by Schneekloth from 2009 to 2014.[14,15] This study aims to systematically review the updated literature published within the current five years regarding the current surgical interventions used in the treatment of diabetes-related Charcot neuroarthropathy of the foot and ankle. The present systematic review also aimed to analyze the occurrence of common outcomes associated with each intervention.

METHODS

This systematic review was conducted using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guideline, and Figure 1 shows the PRISMA flow diagram. Literature research was primarily done by incorporating PubMed/MEDLINE database for English language studies published in the last 5 years. The key terms were defined using the PICO framework (population, intervention, comparison, outcome), which include: Charcot, neuroarthropathy/arthropathy, neurogenic, and surgery, which were used interchangeably. A further set of keywords within the topic were then identified, including ankle, hindfoot, foot, fore-foot, and mid-foot.

Inclusion criteria

The inclusion criteria were any report written in English discussing the surgical management of CN of the foot and ankle secondary to DM. Case reports and retrospective case series were also included. In terms of the surgical outcomes, several parameters have been recorded, including quality of life, foot function score, complications, radiographic measurements, numbers of amputations, weight-bearing ability and time, and other associated surgical complications. Some information on these outcomes was missing; thus, the number of ambulation and other complications are reported for those patients for whom the data were available.

Exclusion criteria

The criteria excluded from the study group was any report written not in English and that did not discuss the surgical management of CN. Studies discussing patients with nondiabetic causes of CN (leprosy, syringomyelia, syphilis, and alcohol) were also excluded, as were those describing CN in areas of the body other than the foot and ankle.

RESULTS

The electronic search resulted in a total of 109 reports cited during a 5-year period (2015-2020). After titles and abstracts analysis, 84 records were excluded, and of these, five studies met the full inclusion criteria and underwent further

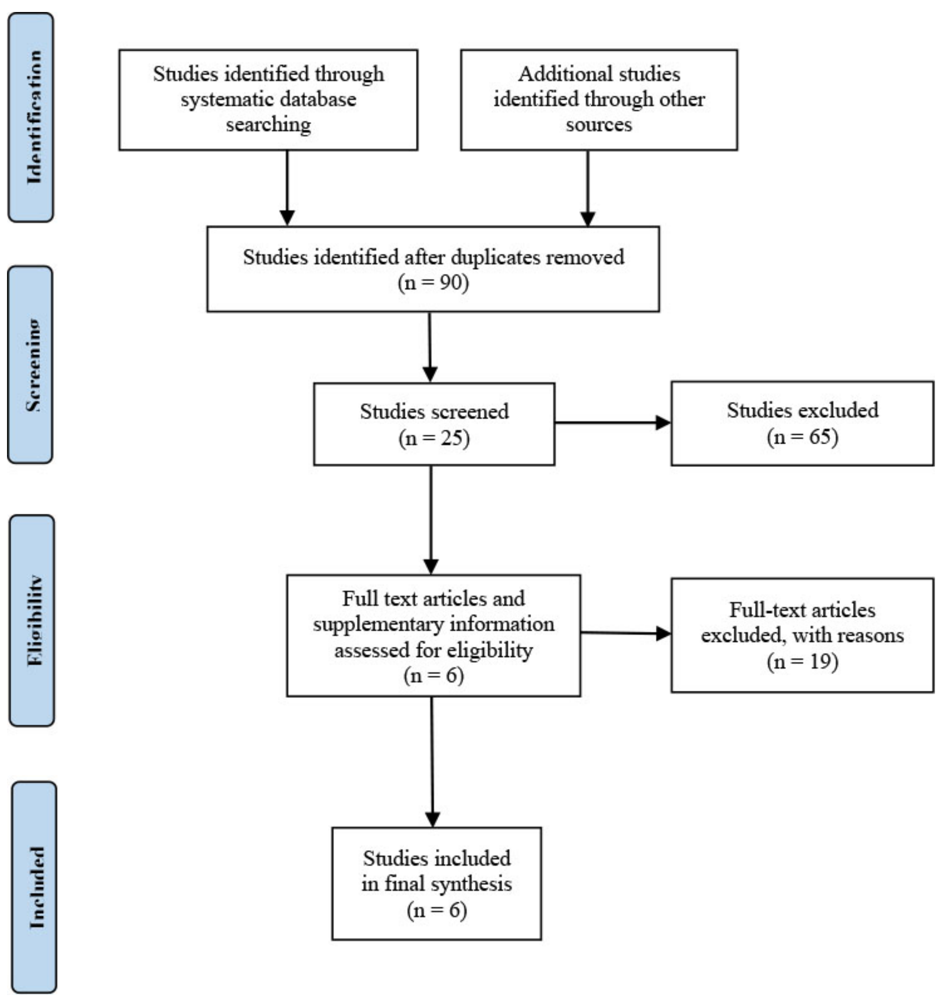

Figure 1. Articles selection with PRISMA guideline.

Table 1. Statistical Description of Reports (N=6) and Patients Demographic Features (n=218).

Author, Year, Country	Participants	Study	No. of Feet	Age	Age Range	Mean F/U (Months)	Fixation Type
Richter *et al*., 2015, Germany	47	Clinical Multi-Centre Study	48	60.1	(35-78)	12 (1-35)	Midfoot Fusion Bolt
Hegewald *et al*., 2015, USA	23	Systematic review	23	54	(31-75)	15 (4-41)	Plate and Ilizarov Ex Fix
Matsumoto *et al*., 2015, USA	10	Therapeutic Case Series	11	52.2	(35-78)	29 (12-44)	Plate and MAC Ex Fix
Ettinger *et al*., 2016, Germany	58	Case-Control Studies	58	59.1	(26-81)	31.3 (12-57)	IMN 38 Ex Fix 19
Harkin *et al*., 2017, USA	56	Case Series	56	57.9	(28-77)	90 (12-168)	IMN 17 Circular Ex Fix 39
Ford *et al*., 2018, USA	25	Retrospective case series	25	58	(25-79)	18 (12-24)	Intramedullary Beaming

Table 2. Outcomes of each Reports Post Charcot Reconstruction.

Author, Year, Country	No. of Feet	Fixation Type	Complications	Favorable Clinical Outcome	No. of Amputation
Richter *et al*., 2015, Germany	48	Midfoot Fusion Bolt	30 (10 wounds, 6 deep infections, 5 amputations)	21 (40.4%)	5 (10.4%)
Hegewald *et al*., 2015, USA	23	Plate and Ilizarov Ex Fix	12 (10 infections, 2 BKA)	18 (81.82%)	2 (9.09%)
Matsumoto *et al*., 2015, USA	11	Plate and MAC Ex Fix	3 (2 ulcers 1 superficial wound)	11 (100%)	0 (0%)
Ettinger *et al*., 2016, Germany	58	IMN 38 Ex Fix 19	3 (infections requiring amputation)	55 (94.8%)	2 ((3.4%)
Harkin *et al*., 2017, USA	56	IMN 17 Circular Ex Fix 39	39 (26 infections, 6 recurrent deformities, 2 non-union, 5 hardware failures)	28 (50.0%)	8 (14.2%)
Ford *et al*., 2018, USA	25	Intramedullary Beaming	15 (6 deep infections, 4 recurrent ulceration, 3 recurrent deformities, 1 hardware failure, 1 wound dehiscence)	21 (84%)	4 (16%)

Table 3. Summary of Outcomes of Surgical Intervention Major Methods.

	Overall	Internal	External	Both
Complications %	46	45	55	45
Fusion %	71	62	81	85
Time to WB (weeks)	13.5	12.8	12	15

analysis (Figure 1). All six studies were retrospective case series and were all classified as levels of evidence IV. A total of 218 patients were eventually included in the present systematic review, which has undergone surgical reconstruction in 221 feet (Table 1). The mean age of patients was 56.8 (35-81) years.

The surgical interventions techniques performed included internal fixation in 128 feet (48 fusion bolts only and 80 with an intramedullary nail/beaming), external fixation in 58 feet, and combined internal and external fixation in 34 feet (plate with either Ilizarov or MAC/multiaxial correction fixator) (Figure 2).

Outcomes

The reported post-surgical outcomes were collected from each study in the referenced literature that had available data. Not all studies were consistent in providing data regarding fusion utilizing radiographic or clinical parameters; thus, determining a determination of favorable outcome rate would be difficult. Bony fusion, based on radiographic and clinical examination, occurred in 154 of 221 feet (71%) (Table 2 and 3). Of these, 79 of 128 feet (62%) were in the internal fixation, 47 of 58 feet (81%) were in the external fixation, and 29 of 34 feet (85%) were in the utilization of both internal and external fixation.[16-21]

Weight-bearing was documented in all studies, with a mean of 13.5 weeks to start weight-bearing ambulation. A mean duration of 12.8 weeks was recorded in the internal fixation group, 12 weeks with external fixation and 15 weeks with a combined fixation method (Table 3). Favorable clinical outcomes varied in numbers and parameters for each study (Table 2). Richter *et al.* recorded that 21 patients (40%) recovered without persistent damage, with a union rate of 98%. While Hegewald *et al.*[16] reported that successful radiographic osseous union was proved by bridging trabeculation on final post-operative radiographs in 18 patients

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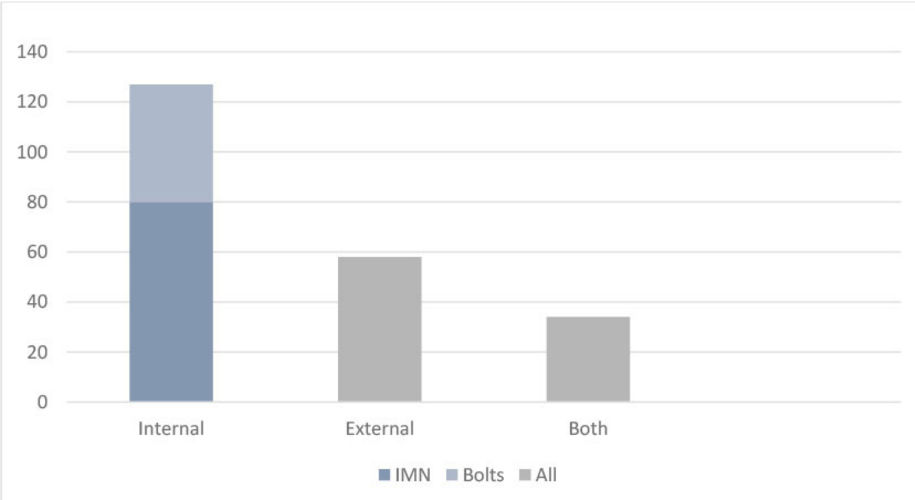

Figure 2. Number of feet and fixation type reported in studies.

(81.82%), with total limb salvage achieved in almost all patients (90.91%). Matsumoto also reported excellent outcomes with all patients (n=11) who achieved successful solid union and correction of rocker bottom deformity, as well as in Ettinger *et al*. study with a 94.8% rate of limb salvage and bone fusion achieved. Whereas Harkin *et al*. identified only half the total patients (n=28) went ulcer- or infection-free and were able to bear weight either with therapeutic footwear alone or in combination with an ankle brace/short ankle-foot orthosis walker (CROW). And Ford *et al*. reported 21 of 25 patients (84%) in their study to have had restoration of stable, plantigrade, and ulcer-free feet.[16-21]

The overall complication rate was 102 in 221 (46%) feet. Further analysis for each specific type of fixation showed complications to be 58 of 128 (45%) in the internal fixation, 32 of 58 (55%) in the external fixation, and 15 of 34 (45%) in groups of combined fixation. Complications were divided into local and systemic complications. The local complications recorded were hardware failure, post-operative infections (consisting of superficial, deep, and pin tract infections), revisional surgery, as well as wound dehiscence. As for systemic complications, observed were 2 mortalities due to unrelated causes to surgical procedures.[16-21]

Furthermore, the overall amputation rate was 21 out of 221 feet (9.5%), consisting of 12 out of 128 (9.4%) in the internal fixation (5 solid bolts, 4 intramedullary beaming, and 3 retrograde locked intramedullary nailing), 7 of 58 (12.1%) in the external fixation, and 2 of 34 (5.9%) in the combined fixation group.

DISCUSSION

Charcot neuroarthropathy (CN) is a debilitating and often underdiagnosed condition resulting from nerve injury, with diabetes mellitus being the most common underlying cause. The condition believed to play a critical role in the pathogenesis of CN is enhanced osteoclastogenesis in the presence of neuropathy. Several classification systems have been proposed to help treatment decision-making of CN, among which these were the two widely quoted classifications; the Eichenholtz classification and the Sanders and Frykberg classification. The modified Eichenholtz classification (including a stage 0) is a summary of theoretical stages of CN radiographic progression from inflammation without skeletal damage to skeletal damage and possibly to resolution.[22] The Sanders and Frykberg classification classified the disease on the basis of the affected joints, which identified five patterns of damage in the foot and ankle associated with different anatomical patterns.[23] Delayed diagnosis can result in a severe deformity that can act as a gateway to ulceration, and infection and, in the worst case, can lead to limb loss. Therefore, in recent decades, two central advances have been proposed in investigating and reporting on Charcot neuroarthropathy, including research on and findings of the epidemiologic pathways and surgical approach to manage severe deformities, which eventually would provide the patients with opportunities to preserve the foot and achieve improved function, especially where conservative measures fall short to manage this condition.

Surgical intervention of Charcot neuroarthropathy has been increasingly considered an option for achieving functional limb salvage, and this has been proved by the increasing number of reported studies over the last 5 years compared to the previous 15 years. However, the cohort size of the studies was still relatively small, which could be caused by the diverse difficulties of each particular patient's condition, the complexity of the procedures and the associated high complication rates. Based on the studies by Burns and Wukich, as well as Siddiqui and Laporta, the surgical interventions could be indicated in such cases of unstable joints, infected or nonhealing ulcers with or without osteomyelitis, equinus deformities, and also unbraceable deformities, which all would be expected to create a plantigrade foot by reducing deformity, restoring stability and alignment, thus, providing an ambulatory, braceable foot ultimately preventing ulceration and potential amputation.[29,30]

The aforementioned Eichenholtz classification has been of any assistance to decision-making regarding the surgical management timing. Past treatment algorithms have recommended non-operative management (immobilization) during the acute phases, and thus the late chronic stage is to be treated surgically. It has been historically contraindicated for stage 0 or 1 to be surgically treated due to the concerns of more wound-healing complications, implant failure, as well as nonunions. While stage 3 has been traditionally thought to be the most optimal time for reconstruction surgery due to lessened risks of soft-tissue and osseous complications with a resolution of osseous destruction and soft tissue inflammation. But with the increasing understanding of Charcot pathophysiology and the improved surgical techniques, surgical intervention is deemed amenable to be implemented earlier in Charcot progression. A study by Simon *et al*. reported arthrodesis utilized in stage 1 Charcot to have had promising results, including no short-term nor long-term complications, and all patients achieved their respective prior ambulation capabilities. Despite encouraging literature support, however, evidence for the acute-phase surgical management remains inconclusive till the present since there has been no direct comparison performed yet during the past five years on comparing early and late surgery.[13]

Regarding the methods of fixation used in the present systematic review, there was no particular technique found with a higher frequency of outcome reported compared to others, nor did the clinical outcomes vary considerably between each different method of fixation. While the historical fixation method was no longer considered adequate to fulfill the high mechanical demands the Charcot foot needed, several authors who utilized internal fixation techniques preferred the concept of a superconstruct, abandoning the traditional principle of fixation to improve the stability of fixation.

The term "superconstruct" defined by Sammarco is a concept of 4 factors, including a fusion extending proximally and distally beyond the injury zone to include the unaffected joints, a bony resection shortening the extremity allowing adequate reduction of the deformity without increasing tissue tension, the use of the strongest implant that could be tolerated by the soft tissue envelope, and a device applied in a position to maximize mechanical function.[24] Sammarco also demonstrated 3 superconstructs in the reconstruction of midfoot Charcot foot deformity, including plantar plating, locking plate technology, axial fixation with screw or bolt and external fixation, which are warranted in cases with a high likelihood of failure and appropriate in the setting of dysvascular bone, bone loss, deformity correction, and severe osteoporosis as well as in patients with multiple medical comorbidities leading to delayed healing.[24]

The present systematic review recorded most of the studies have preferred internal fixation either alone or with a combination of external fixators for the intervention of CN, consisting of solid fusion bolt, intramedullary nailing/beaming, and plating combined with external fixation of Ilirazov and MAC/multiaxial correction system.[16-21] Garchar *et al*. in their study analyzed the biomechanical aspect of medial column plantar plating, showing a superior result.[25] But the technique required a long incision and extensive exposure for plate placement, leading to significant soft tissue trauma. Meanwhile, the progression of locked plating might enable medial plate placement, reducing the extensivity of exposure; however, the increasing tension on the overlying skin might create a bulky construct, which could be a problem.[24] A study by Richter *et al*. reported fewer hardware breakage with the utilization of solid fusion bolts as an intramedullary device, with a 98% union rate.[16] Nevertheless, this method has been associated with a high rate of implant migration which might require additional revisional surgery. Furthermore, the use of intramedullary devices is reported to have allowed surgeons to decrease the amount of hardware required to achieve instability, provide improved compression, and do so with less soft tissue stripping as well as a lower chance of hardware exposure in the event of wound breakdown. Ford *et al*. examined the clinical outcome of patients with midfoot CN managed with realignment arthrodesis and stabilization using intramedullary beams alone, showing ulcer-free, stable, plantigrade feet obtained in 84% of patients.[21] Others study by Ettinger *et al*. reported fusion of all patients treated with intramedullary nailing (100%) compared to the fusion rate of 84.2% of patients treated with an external fixator.[19]

Roukis *et al*. stated that external fixation might offer several advantages over internal fixation, allowing stable fixation while ensuring access to open wounds as well as allowing weight bearing at an earlier stage, and the present study's findings support this statement. A combined method of internal and external fixation was used in both studies of Hegewald *et al*. (plate arthrodesis and Ilizarov external fixation) and Matsumoto *et al*. (plate arthrodesis and MAC external fixation), showing excellent functional outcomes: 81.82% osseous union and 100% solid union and ambulation, respectively. In addition, a study by Harkin *et al*. reported 39 patients of CN with infections treated with circular external fixation to have had 52% of patients whose ulcer- and infection-free and also able to walk with commercially therapeutic footwear.[20] Circular-type external fixator has gained recognition for its advantages of stable fixation, ability to correct deformity gradually in cases of infections, and possible earlier mobilization.[26-31] However, some downsides of this circular frame are that it might be costly, bulky, the possibility of a steep learning curve, and sometimes might be intimidating to use.

The outcome parameters that are commonly used in the present systematic review were weight bearing and amputation. The overall mean time of weight bearing was 13.5 weeks. While the overall amputation rate was 21 out of 221 feet (9.5%), similar to the 8.9% rate reported in a previous study by Schneekloth *et al*.[15] A study by Sohn *et al*. reported CN patients with foot ulcers were 12 times more likely to require a major amputation than were the CN patients without foot ulcerations.[12] Furthermore, Wukich and Pearson examined amputation as the primary option in patients with non-reconstructable CN showing significant improvement in the physical component self-reported outcomes after transtibial amputation as well as the self-reported mental quality of life.[28] In addition to that, fusion rate is also seen as an important surgical outcome measure. The overall fusion rate in the present study was 71%. However, the calculation for fusion rates was based on a significant heterogeneity between each methodology used, making it unable to firmly conclude if one surgical technique was superior to the other in achieving such outcomes. Especially the worth noting truth that multiple studies have reported adequate foot stability with good functional outcomes achieved in fibrous non-unions, despite the aim of achieving full bone fusion, eliminating the need for revisional surgery.

The overall complications within this group of patients were high at 46%. And as expected, the complication rate in those treated with external fixation was higher at 55% compared to the internal fixation patients at 45%. In circumstances when a combination of internal and external fixation techniques was used, the complication rates were as high as 45%, similar to the internal fixation. However, the number of subjects was too small to derive any definitive as well as representative conclusions. As for the particular factors associated with the overall outcomes of this condition, there were still no studies found that identified specifically the role of delayed wound closure, the types of dressings used, the utilization of incisional negative pressure wound therapy or the use of necessary antibiotics; which would be of importance in future research.

CONCLUSION

Charcot neuroarthropathy poses many clinical challenges in its diagnosis and management. Therefore many experts have proposed the implementation of different strategies to manage this complex condition, depending on the acute and chronic phases of its nature. Delayed diagnosis can result in a severe deformity that can act as a gateway to ulceration, and infection and, in the worst case, can lead to limb loss. Therefore, in recent decades, advances have been achieved in investigating and reporting on Charcot neuroarthropathy, including the utilization of a surgical approach to manage severe deformities, which eventually would provide the patients with opportunities to preserve the foot and achieve improved functional outcomes, especially where conservative measures fall short to manage this condition.

However, there have been no randomized, prospective, multicentre trials published yet regarding the topic, as well as the proper timing of surgery. Therefore, further studies aimed at determining selection criteria and treatment algorithms are required for greater standardization of outcomes.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

FUNDING

None.

ETHICAL CLEARANCE

Not required.

AUTHORS CONTRIBUTION

All authors contribute to the study from the conceptual framework, data acquisition, and data analysis until reporting the study results through publication.

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