

SYSTEMATIC REVIEW

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Effectiveness of intramedullary nails in Tibiototalcalcaneal arthrodesis for Charcot neuroarthropathy: a systematic review and meta-analysis

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Abstract

Objective To systematically evaluate the efficacy and safety of intramedullary nails (IMNs) in tibial-talocalcaneal arthrodesis (TTCA) for treating Charcot neuroarthropathy (CN).

Methods A comprehensive search for relevant literature was conducted in the PubMed, Embase, Cochrane Library, Web of Science, Scopus and SinoMed databases, covering studies from 2014 to October 30, 2024. The inclusion criteria were based on the PICOS framework: the study population consisted of CN patients, the intervention was TTCA with IMNs, and the outcomes assessed included bone union rate, complication rate, and limb salvage rate. Statistical analysis was performed using Stata 17.0 software. Literature quality was assessed using the Newcastle–Ottawa Scale (NOS) for cohort studies and case series. This systematic review was prospectively registered with the International Prospective Register of Systematic Reviews (PROSPERO; registration number: CRD42025644983).

Results A total of seven studies involving 147 patients with a mean follow-up of one year were included. The meta-analysis revealed a combined standardized mean difference (SMD) of -4.99 (95% CI: -6.70 to -3.28) for the AOFAS score, with high heterogeneity ($I^2 = 90.7\%$). Sensitivity analyses were conducted to assess the stability of the results. The combined estimate for the bone nonunion rate was 3.3% (95% CI: 0.1% to 8.9%), with moderate heterogeneity ($I^2 = 33.2\%$). The combined estimate for the infection rate was 12.9% (95% CI: 2.0% to 29.2%). A comparison of preoperative and postoperative scores showed significant improvements in patients' function and quality of life, highlighting the critical role of the TTCA procedure in improving prognosis.

Conclusion IMNs in TTCA demonstrate high efficacy for CN, with significant functional improvement, low nonunion rates, and favorable limb salvage outcomes. However, infection risks and heterogeneity across studies highlight the need for standardized protocols and larger controlled trials to optimize patient selection and postoperative management.

Keywords Charcot Neuroarthropathy, Tibiototalcalcaneal Arthrodesis, TTCA, Intramedullary Nails, Meta-analysis

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Introduction

Charcot neuroarthropathy (CN) is a serious and potentially disabling condition. It occurs mainly in patients with diabetes mellitus, especially in patients with diabetes-induced peripheral neuropathy [1]. Other common causes of CN include neurosyphilis, spinal cord



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injuries, leprosy, spinal cord cavernous malformations, hereditary neuropathies, smoking, and alcoholism. The disease leads to progressive destruction of the bones, joints, and soft tissues of the foot and ankle, resulting in dislocations, peripheral fractures, or both, and ultimately causing instability, deformity, and an increased risk of ulcers and infections. Currently, many scholars argue that the core pathogenesis of CN is neurogenic arthropathy. Sensory nerve damage prevents patients from perceiving joint abnormalities, leading to joint lesions caused by repeated pressure [2]. Jeffcoate et al. [3] suggest that inflammation and activation of the RANKL/OPG pathway are central to the development and persistence of acute CN. Managing CN is particularly challenging in its advanced stages, where involvement of the ankle and hindfoot often necessitates surgical intervention to restore stability and enable ambulation. Common surgical approaches include exostectomy, fusion, external fixation, amputation, and Achilles tendon lengthening [4].

Tibiototalcalcanal arthrodesis (TTCA) is a salvage procedure that fuses the ankle and subtalar joints [5] to treat conditions such as progressive deformity or severe arthritis [6], and has become a key surgical approach for treating advanced CN involving the hindfoot. Among the various fixation methods for TTCA, retrograde Intramedullary Nails (IMNs) fixation provides stable metatarsal mechanics and reliable biomechanical support, making it a focal point in the treatment of CN [7]. As technology advances, the design and modification of various new IMNs have led to further improvements in the safety and efficacy of this procedure.

Despite the widespread use of IMNs in clinical practice, studies on their application in CN have limited sample sizes and are mostly retrospective analyses or case studies, lacking high-quality randomized controlled trials. In addition, individual patient differences and the diversity of surgical techniques increase the heterogeneity of the research results, and there is a lack of systematic comprehensive analysis. Therefore, there is an urgent need for a systematic review and meta-analysis of the existing literature to comprehensively evaluate the effectiveness and safety of IMNs in the treatment of CN with TTCA.

This study aims to fill gaps in current research through systematic review and meta-analysis, clarifying the role and potential benefits of IMNs in treating CN with TTCA. The study focuses on postoperative functional scores, bone union rate, complication rates, and the applicability and limitations of intramedullary nails. By systematically reviewing and analyzing existing literature, this study aims to provide an evidence-based foundation for guiding clinical decision-making.

Materials and methods

Search strategy

The study followed the PRISMA 2020 guidelines and systematically searched for relevant literature in the following databases: PubMed, Embase, Cochrane Library, Web of Science, Scopus and SinoMed, from 2014 to October 30, 2024. It was registered in the PROSPERO database (CRD42025644983), ensuring methodological transparency and adherence to international standards. All methods—including eligibility criteria, data extraction, risk of bias assessment, and statistical analyses—were predefined and are comprehensively reported. This ensures that the study remains transparent, reproducible, and adheres to high methodological standards. The search terms included: "Tibiototalcalcanal Arthrodesis," "Hindfoot Arthrodesis," "Charcot arthropathy," "Charcot neuroarthropathy," "intramedullary nail," and "fusion rates," among others. Boolean logic operators (AND, OR, NOT) were used to ensure the comprehensiveness and specificity of the search. Additionally, manual searches were conducted to identify potentially missed studies, particularly treatment options for TTCA and CN, as well as citation chasing. All manually retrieved literature was screened by two independent researchers to minimize omissions and bias.

Specific search strategies combined free text terms and MeSH terms, such as (Tibiototalcalcanal Arthrodesis [Title/Abstract]) OR (TTC Arthrodesis [Title/Abstract]) AND ((Arthropathy, Neurogenic [MeSH Terms]) OR (Neurogenic Arthropathy [Title/Abstract]) OR (Charcot Joint [Title/Abstract])). The search strategy for each database was adapted to its specific characteristics.

Information sources included all databases, registration platforms, reference lists, and other methods of searching or consultation (e.g., referrals from experts in relevant fields). The search and query date were October 2024, and detailed search strategies for all sources are provided in the Appendix.

Eligibility criteria

Inclusion criteria were: 1) studies conducted on patients who underwent TTCA for CN and used IMNs for fixation; 2) retrospective and prospective cohort studies, case series, and clinical studies; 3) reports with clear outcome metrics, such as the rate of bone fusion, complication rates, and functional scores; and 4) literature published in English and Chinese. Exclusion criteria were: 1) other treatments; 2) pathology reports or studies with fewer than 5 participants; 3) literature with unclear or unextractable data.

Data extraction and management

Literature extraction was conducted by two senior authors (Zhang and Zhao), who independently screened titles and abstracts. The full text was thoroughly examined according to predetermined inclusion criteria, with disagreements resolved by a third-party investigator. Extracted data included: authors and year of publication, country, type of study, patient characteristics (e.g., age, gender, hobbies, comorbidities), sample size, surgical method, duration of follow-up, and assessment measures (e.g., AOFAS scores, FFI scores, SF-36 scores, rates of limb preservation, infections, and bone nonunion). To ensure consistency across all studies, extracted data was stored in Microsoft Excel, and double entry was performed to minimize errors.

Assessment of methodological quality

Literature quality screening was conducted independently by two authors. The quality of the included studies was assessed using the Newcastle–Ottawa Scale (NOS) [8], with disagreements resolved through discussion. The assessment results, summarized in Table 1. The assessment results will be used in subsequent sensitivity analyses to evaluate the impact of study quality on overall outcomes.

Statistical analysis

Statistical analyses were performed using Stata 17.0 software. For continuous variables, effect sizes were assessed using standardized mean differences (SMD) with 95% confidence intervals (CI); for dichotomous variables, odds ratios (OR) with 95% CI were used. Heterogeneity was assessed using the I² statistic, with sensitivity analyses performed for I² > 50%, indicating

significant heterogeneity. Additionally, sensitivity analysis plots were used to assess the impact of individual studies on overall results and explore sources of heterogeneity. The significance level for all statistical tests was set at $p < 0.005$.

Results

Study selection

A systematic search of five databases was conducted, retrieving a total of 146 papers. Ultimately, seven studies met the inclusion criteria for the meta-analysis [9–15]. The screening process is detailed in the PRISMA flowchart (Fig. 1). The seven included studies involved a total of 147 patients with Charcot neuroarthropathy treated with TTCA. Baseline characteristics of patients are summarized in Table 2.

Study quality assessment

The analysis included six case studies and one cross-sectional study, all evaluated using the Newcastle–Ottawa Scale (NOS) [8]. All included studies were of high quality. Details of the included studies are provided in Table 1. The NOS assessment score indicates that six studies are of high quality (score ≥ 7); however, they lack a control group and fail to adequately control for confounding factors. Rastegar et al. received a slightly lower score of 6 points, primarily due to issues with exposure selection. Despite the overall high score, it is important to note the absence of a control group and the significant issue of confounding factors. Future studies should prioritize designing rigorous control groups and addressing confounding factors to minimize bias in the results.

Table 1 The Newcastle–Ottawa Scale

Study	Selection				Comparability		Exposure			NOS评分
	①	②	③	④	①	②	①	②	③	
Rastegar et al. [9]	1	0	1	1	1	0	1	1	0	6
Bajuri et al. [10]	1	0	1	1	1	0	1	1	1	7
Moonot et al. [11]	1	0	1	1	1	0	1	1	1	7
Ma et al. [12]	1	1	1	1	1	0	1	1	0	7
Ersin et al. [13]	1	0	1	1	1	0	1	1	1	7
Chraim et al. [14]	1	0	1	1	1	0	1	1	1	7
Siebachmeyer et al. [15]	1	0	1	1	1	0	1	1	1	7

NOS Newcastle–Ottawa Scale. The NOS score for case–control studies includes: Selection of the study population ① proper identification of cases, ② representativeness of cases, ③ selection of controls, ④ identification of controls), comparability between groups ① control of major confounding factors, ② control of minor confounding factors), measurement of exposure ① identification of exposure, ② consistent methods for exposure identification in both cases and controls, ③ response rate). The NOS score for cohort studies includes: selection of the study population ① representativeness of the exposed group, ② selection of the non-exposed group, ③ determination of exposure factors, ④ outcome indicators not observed at the time of the study), comparability between groups ① control of major confounding factors, ② control of secondary confounding factors), outcome measurement ① adequate evaluation of the outcome, ② sufficient follow-up period, ③ completeness of follow-up)

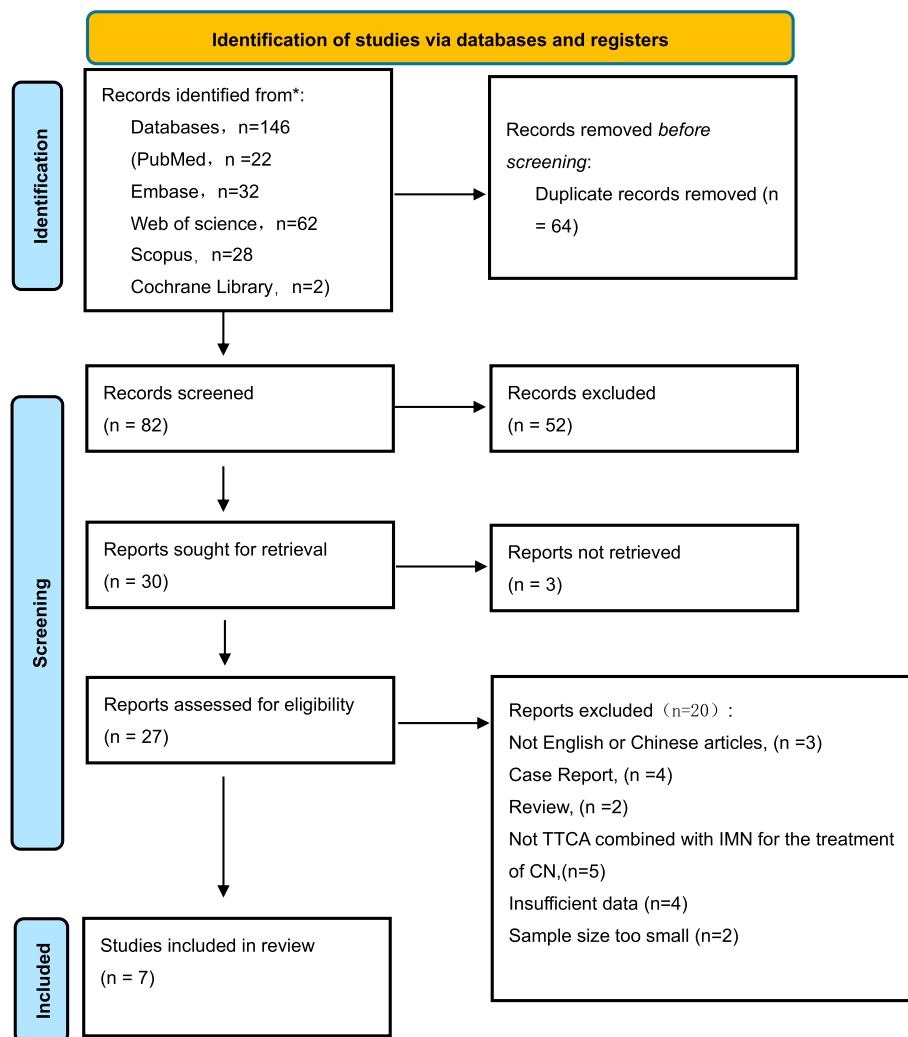


Fig. 1 Screening flowchart

Meta-analysis results

AOFAS score

American Orthopaedic Foot and Ankle Society (AOFAS) scores were reported in six studies involving 127 patients (128 feet) with a mean follow-up of 12 months. The forest plot indicated a standardized mean difference (SMD) of -4.99 (95% CI: -6.70 to -3.28), $P < 0.001$, showing that postoperative scores were significantly higher than preoperative scores. Since the AOFAS score is a positive scale, a negative SMD indicates a significant improvement in foot and ankle function after surgery. However, the high heterogeneity ($I^2 = 90.7\%$) in this meta-analysis suggests substantial variability between studies, likely due to the large differences in sample sizes between the studies of Bajuri et al. and Moonot et al., which may impact the stability of effect estimates. Therefore, a sensitivity analysis was performed in Fig. 2, revealing that the overall effect size

range (approximately -5.16 to -3.41) remained stable after removing any single study. This suggests that the results of the meta-analysis were robust, with no single study exerting an excessive influence on the overall findings, thereby mitigating the potential risk of bias.

Nonunion rate

This meta-analysis included seven studies, and a combined estimation using a random effects model yielded an effect size (ES) of 0.033 (95% CI: 0.001 to 0.089) (Fig. 3), indicating a low overall non-convergence rate. Heterogeneity analysis revealed a p -value of 0.174 and an I^2 of 33.2% , suggesting moderate but non-significant heterogeneity. Overall, the combined estimated nonunion rate was 3.3% , indicating that intramedullary nailing in TTCA for Charcot neuroarthropathy has a low risk of nonunion, supporting its role as a reliable surgical fixation method.

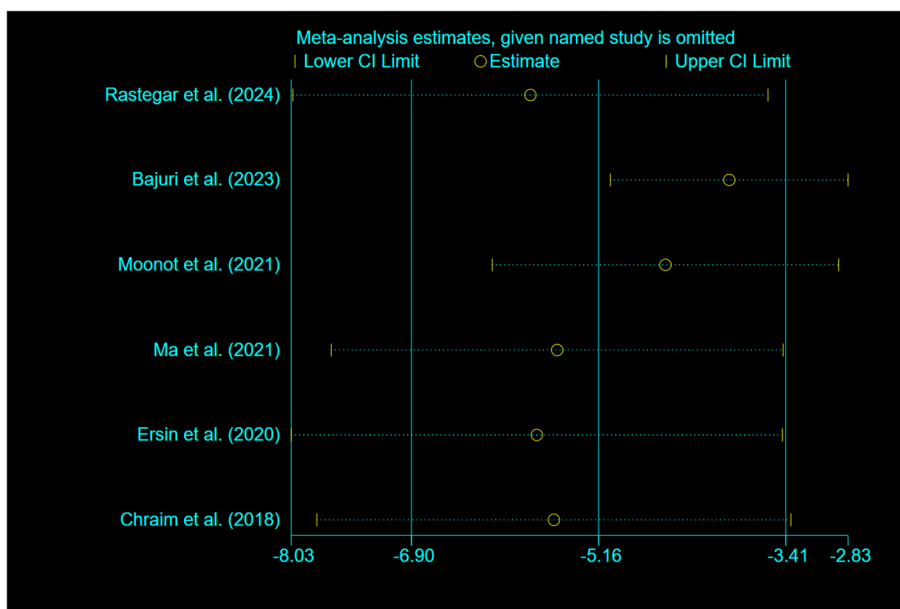


Fig. 2 Sensitivity analysis for AOFAS score. This figure presents the sensitivity analysis for AOFAS scores, showing the effect size stability after excluding individual studies. The results remained significant, confirming the robustness of the meta-analysis

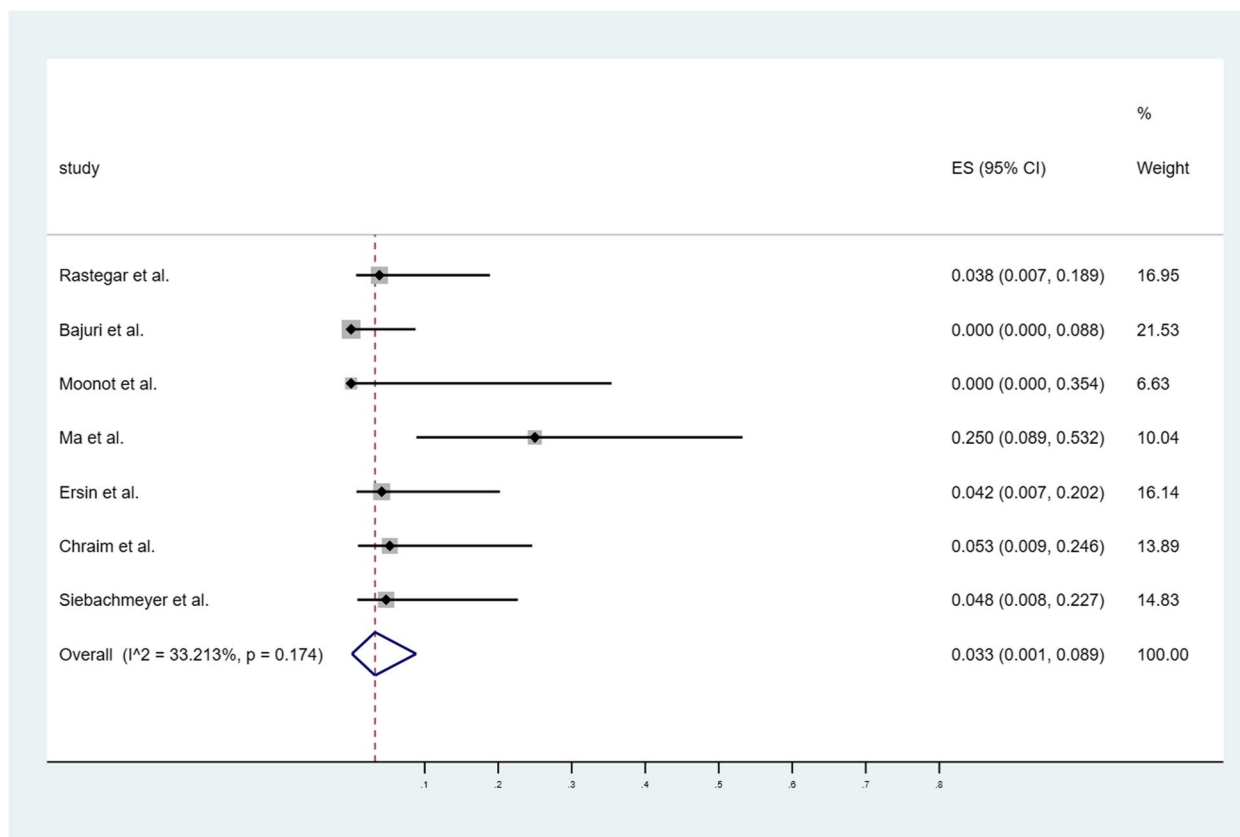


Fig. 3 Forest plot for nonunion rate. This forest plot shows the combined effect size (ES) for the nonunion rate across studies, with an overall nonunion rate of 3.3%. The analysis indicates a low overall nonunion rate with moderate heterogeneity (I² = 33.2%)

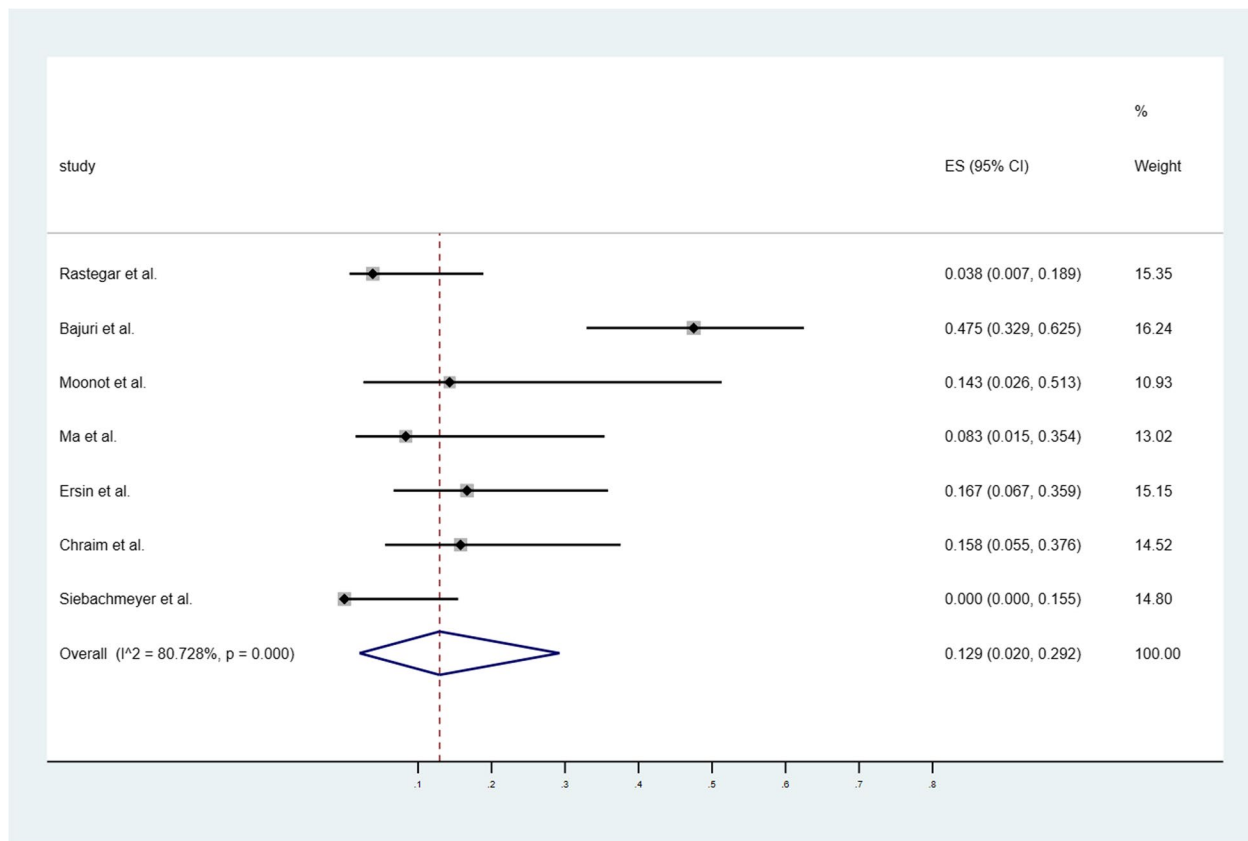


Fig. 4 Forest plot for infection rate. This plot represents the infection rates across studies, with a combined effect size of 0.129 (95% CI: 0.020 to 0.292), indicating a significant risk of infection in the treatment of Charcot neuroarthropathy using TTCA

Table 2 Patient Demographics and Baseline Characteristics

References	Country	Design	Year	Sample	Age(Year)	M/F	Follow-up(month)	Outcomes
Rastegar et al. [9]	Iran	Prospective case Series	2024	26	63	16/10	12	2, 7
Bajuri et al. [10]	Malaysia	Retrospective Case Series	2023	40	60.5	3/4	24	2, 6
Moonot et al. [11]	India, USA	Prospective cross-sectional study	2021	7	59.71	13/27	64	1, 2, 3, 4
Ma et al. [12]	China	Retrospective Case Series	2021	12	57.3	10/8	46	2, 3, 4, 5
Ersin et al. [13]	Turkey	Retrospective Case Series	2020	24	62	9/15	45	1, 2
Chraim et al. [14]	Austria	Retrospective Case Series	2018	19	63.43	12/8	26	1
Siebachmeyer et al. [15]	UK	Retrospective Case Series	2015	21	62.6	6/7	30	1, 2

1 = SF-36, 2 = AOFAS, 3 = FFI, 4 = FAOS, 5 = VAS, 6 = FADI, 7 = EQ-5D-5L, 8 = AAOS-FAO

Infection rate

In the meta-analysis of infection rates, heterogeneity was pronounced in Fig. 4, likely due to the higher infection rate observed in the study by Bajuri et al. This may be attributed to various factors, including surgical technique, patient characteristics (e.g., diabetes mellitus, alcoholism, smoking), and postoperative management. The overall effect size (ES) was 0.129 (95% CI: 0.020 to

0.292), indicating an overall infection rate of 12.9%. This indicates a certain risk of infection associated with TTCA for Charcot neuroarthropathy. Despite substantial variations in infection rates among studies, careful patient selection and stringent postoperative infection control measures are essential to minimize infection risk in clinical practice.

Limb salvage rate

Among the seven included studies, Chraim et al. reported a limb preservation rate of 84.2% (16 out of 19 patients successfully retained their limbs), indicating that some patients still required amputation. This may be attributed to factors such as disease severity, inadequate diabetes control, and postoperative infection management. These findings highlight the need for clinicians to thoroughly assess individual patient characteristics, particularly glycemic control and complication management, to minimize the risk of amputation. Overall, TTCA combined with intramedullary nailing achieved a high limb preservation rate in patients with Charcot neuroarthropathy, further confirming its effectiveness and reliability as a late-stage limb preservation approach. However, the risk of amputation remains in certain cases, indicating the need for future studies to investigate specific factors influencing limb preservation success. This will help optimize patient selection criteria and postoperative management strategies, ultimately improving treatment outcomes.

The summary of limb salvage rates, infection rates, and nonunion rates across the included studies is presented in Table 3.

Complications

Although IMNs have demonstrated significant benefits in treating CN patients with TTCA, they are associated with several complications, primarily poor bone fusion, infections, and delayed healing. Bajuri et al. reported that 40% of the patients' experienced complications, a notable proportion, with 37% of these patients having minor issues such as mild infections, delayed wound healing, and bone healing delays. Only 2% experienced serious complications, including fusion failure and hardware-related problems, typically observed in patients with more severe diseases or additional risk factors such as diabetes or neuropathy.

Other functional scores

An analysis of preoperative and postoperative functional scores from the included studies demonstrates that intramedullary nails (IMNs) significantly enhance patient function and quality of life following TTCA surgery for Charcot neuroarthropathy (CN). Postoperative improvements were particularly evident in the American Orthopaedic Foot and Ankle Society (AOFAS) scores, Short Form Health Survey (SF-36), and Foot Function Index (FFI). Bajuri et al. and Moonot et al. reported notable increases in SF-36 and AOFAS scores, highlighting significant functional recovery and improved quality of life post-surgery. In contrast, Siebachmeyer et al. observed more modest improvements, though their findings still support the efficacy of the procedure. Additionally, a significant reduction in postoperative pain, exemplified by the 1.9 Visual Analog Scale (VAS) score reported by Chraim et al., underscores the positive impact of IMNs on pain management. Specific details of the functional and pain scores are summarized in Table 4 and Table 5.

Discussion

This meta-analysis demonstrated that IMNs in TTCA for treating CN significantly improved functional outcomes (e.g., AOFAS scores, limb salvage rates), reduced complication rates, and increased fusion rates compared to preoperative levels. However, due to the limited number of studies on TTCA with IMNs for CN treatment, only seven studies met the inclusion criteria. This suggests the need for more high-quality randomized controlled trials or large-sample case studies to validate these findings. Furthermore, standardized procedures for surgical techniques and postoperative management should be further developed.

Advantages of intramedullary nails in TTCA

With advances in biomechanics, metallurgy, surgical techniques, and fluoroscopy, modern IMNs offer several advantages: low infection rates, minimal scarring,

Table 3 Summary of limb salvage, infection, and nonunion rates in the included studies

References	Year	Sample	Limb salvage	Infection	Nonunion
Rastegar et al. [9]	2024	26	100%	1	1
Bajuri et al. [10]	2023	40	100%	19	0
Moonot et al. [11]	2021	7	100%	1	0
Ma et al. [12]	2021	12	100%	1	3
Ersin et al. [13]	2020	24	100%	4	1
Chraim et al. [14]	2018	19	84%	3	1
Siebachmeyer et al. [15]	2015	21	100%	0	1

Table 4 Preoperative functional score

References	SF-36	AOFAS	FFI	FAOS	VAS	FADI	EQ-5D-5L	AAOS-FAO
Rastegar et al. [9]	—	49	—	—	—	—	65	—
Bajuri et al. [10]	2.25	16.28	76.65	58.93	—	—	—	—
Moonot et al. [11]	—	32.2	—	—	—	12.91	—	—
Ma et al. [12]	—	32	—	—	—	—	—	—
Ersin et al. [13]	—	40	—	—	—	—	—	—
Chraim et al. [14]	—	25.3	161.1	40.7	6.1	—	—	—
Siebachmeyer et al. [15]	—	—	—	—	—	—	—	50.7

Table 5 Postoperative functional score

References	SF-36	AOFAS	FFI	FAOS	VAS	FADI	EQ-5D-5L	AAOS-FAO
Rastegar et al. [9]	—	80	—	—	—	—	80	—
Bajuri et al. [10]	97.88	83.65	21.55	29.05	—	—	—	—
Moonot et al. [11]	—	67.6	—	—	—	70.7	—	—
Ma et al. [12]	63.02	74.74	—	—	—	—	—	—
Ersin et al. [13]	70	68	—	—	—	—	—	—
Chraim et al. [14]	—	71.5	87.2	51.5	1.9	—	—	—
Siebachmeyer et al. [16]	—	—	—	—	—	—	—	65.2

SF-36 Short Form Health Survey, AOFAS American Orthopaedic Foot and Ankle Society, FFI Foot Function Index, VAS Visual Analog Scale, FAOS Foot and Ankle Outcome Score, FADI Foot and Ankle Disability Index, EQ-5D-5L EuroQol 5-Dimension 5-Level, AAOS-FAO American Academy of Orthopaedic Surgeons Foot and Ankle Outcomes Questionnaire

excellent fracture stability [16], good biomechanical properties and osteointegration, minimal interference with the fracture site and surrounding soft tissues and vasculature, and a high success rate [17, 18]. IMNs provide strong axial and rotational stability, resulting in a fusion rate of over 80–90% [19–21]. IMNs are an excellent choice for complex tibial-talocalcaneal fusion, particularly for patients with CN [22].

Intramedullary nails versus other fixation modalities

In recent years, as research and clinical application of TTCA have advanced, increasing attention has been given to optimizing its fixation methods. Currently, TTCA fixation methods primarily include intramedullary nails, locking plates, external fixation frames, and hybrid fixation. Locking plates provide slightly less stability than intramedullary nails, whereas screws exhibit significantly weaker biomechanical properties and the poorest bone stability [23]. Zhang et al. [24] compared IMNs with locking plates and found that both significantly reduced postoperative VAS scores and increased AOFAS scores. IMNs had slightly shorter postoperative fusion times but showed a slightly lower fusion rate than locking plates. ElAlfy et al. [25] conducted a comparative study on Ilizarov external fixators and intramedullary nailing in TTCA, demonstrating that both methods have

distinct advantages. Ilizarov external fixators showed a slight advantage in promoting bone fusion and functional recovery but were associated with a higher complication rate, whereas intramedullary nailing was superior in complication control. El-Mowafi et al. [26] used a hybrid fixation method combining IMNs and the Ilizarov external fixator, yielding high fusion rates and functional improvement. DeVries et al. [27] explored using a prototype external fixator to assist IMNs for surgical stabilization and found similar results. Froelich et al. [28] compared the rotational stability of IMNs with locking plate fixation, finding that IMNs were superior overall. Berend et al. [20] compared IMNs with cross screws, finding that IMNs offered higher stability and fusion rates, further supporting IMNs as one of the preferred choices for TTCA in treating CN. Bajuri et al. [29] found that retrograde intramedullary nailing is the preferred approach for reconstructing Charcot neuroarthropathy before ulceration occurs, whereas hybrid fixation becomes more necessary in cases with ulceration or complex deformities.

Factors affecting the effectiveness of treatment

Multiple factors influence joint fusion following TTCA. Pitts et al. [30] analyzed the relationship between age, gender, diabetes mellitus, cardiovascular disease,

smoking, and other factors with postoperative complications by reviewing the charts of 101 TTCA patients. Their findings showed that diabetes remains a significant challenge for postoperative bone nonunion and infection, consistent with the results of Powers et al. [31]. Lee et al. [32] conducted a study to assess the impact of uncontrolled diabetes on surgical failure after TTCA, with all patients undergoing retrograde IMNs fixation (DLA nail; U & I Corporation, Seoul, Korea). The results showed that the surgical failure rate in uncontrolled diabetic patients was ten times higher than in nondiabetic patients, emphasizing the critical role of diabetes control in surgical success. Similarly, Kowalski et al. [33] studied risk factors for post-TTCA complications and found that diabetic neuropathy, higher ASA (American Society of Anesthesiologists) classification, Charcot neuropathy, and high HbA1C were significant risk factors for complications after TTCA. In contrast, factors such as smoking, age, and body mass index (BMI) did not show significant associations with postoperative complications. Wukich et al. [34] compared postoperative complication rates, fusion rates, and limb retention rates between diabetic and nondiabetic patients after TTCA. The study found that diabetic patients had a significantly higher incidence of superficial infections compared to nondiabetic patients, though the differences in deep infections and other complications were not significant. Despite the higher overall complication rate in diabetic patients (45.2%), approximately 95% of patients with complex deformities successfully retained their limbs. Additionally, Rana and Patel et al. [35] studied TTCA fusion in 32 cases of diabetic Charcot neuroarthropathy, finding a fusion rate of only 65%, significantly lower than the rest of the patient population. These findings suggest that diabetes, particularly diabetes-associated CN, significantly impacts the fusion rate and complications after TTCA. Clinicians may need to adopt more aggressive preoperative optimization and postoperative management strategies. For patients with diabetes mellitus and chronic kidney disease, a standardized glycemic control plan and renal function monitoring protocol should be developed.

Treatment options for CN

CN is a progressive disorder that compromises the musculoskeletal system. Studies on the expression of genes associated with CN and their early detection methods are still controversial and inconclusive [36, 37]. Pakarinen et al. [38] conducted a long-term follow-up of patients with CN over approximately 8 years. Their results showed that although conservative treatment may avoid surgery, early surgical intervention could improve long-term prognosis in some cases [39]. Wukich et al. [40] also

concluded that managing complex deformities in CN typically requires surgical intervention.

Additionally, Galhoum et al. [41] evaluated the clinical efficacy of non-surgical and surgical interventions by analyzing a comprehensive management plan for CN in a systematic review. Non-surgical treatment options included antiresorptive medications [42, 43], air cushion walking braces [44], and contact casts (TCC) [45]. Antiresorptive drugs perform better in the acute phase but have limited effect in patients with advanced deformity and instability. In contrast, air cushion support and plaster immobilization are less effective in managing patients with combined instability. Overall, treatment modalities should be selected based on the stage of the disease and the patient's specific situation to achieve the best therapeutic outcome. Arthrodesis is the most commonly used treatment for Charcot neuroarthropathy and is beneficial for patients who have failed conservative management, have late-stage instability, or experience recurrent ulcers [46, 47].

Limitations

This study has several limitations: 1. The small number of included studies [7] and the limited sample size may restrict the generalizability of the findings. 2. Some studies lacked comprehensive follow-up data, which may influence the evaluation of long-term outcomes. 3. Key indicators, such as specific postoperative infection control measures, were insufficiently described in the included studies.

Conclusion

This systematic evaluation and meta-analysis highlighted the substantial clinical benefits of IMNs in TTCA for treating CN. Our analysis revealed that IMNs significantly enhanced fusion rates, improved functional outcomes (e.g., AOFAS scores), and led to higher limb salvage rates. Furthermore, the technique was associated with a low overall complication and bone nonunion rate, underscoring its safety. However, the use of IMNs is accompanied by certain limitations, including an increased risk of postoperative infection in diabetic patients and considerable heterogeneity, suggesting that variations in patient characteristics and surgical techniques may impact efficacy.

Despite the many advantages of IMNs in treating CN, this study has limitations, including a small sample size and high heterogeneity. Future research should include high-quality randomized controlled trials and larger prospective studies to validate the efficacy and safety of IMNs across diverse patient populations, as well as to refine preoperative patient screening and postoperative management strategies.

Abbreviations

CN	Charcot Neuroarthropathy
TTCA	Tibiototalcalcaneal Arthrodesis
IMNs	Intramedullary Nails
NOS	Newcastle-Ottawa Scale
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
TCC	Total Contact Cast
ASA	American Society of Anesthesiologists Classification
RANKL/OPG	Receptor Activator of Nuclear Factor Kappa-B Ligand/Osteoprotegerin Pathway
GRADE	Grading of Recommendations, Assessment, Development, and Evaluations

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Authors' contributions

Hao Zhang: Conceptualization, data collection, statistical analysis, manuscript drafting, manuscript editing, Quality assessment, data interpretation. Ning Jiang: Methodology, literature review, data interpretation. Jun-Fei Zhao: Quality assessment, sensitivity analysis, manuscript revision. Xian-Tie Zeng: Supervision, project administration, final manuscript approval. All authors have read and approved the final manuscript.

Authors' information

Not applicable.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study is a systematic review and meta-analysis based on previously published studies. No new patient data were collected, and therefore, ethical approval and informed consent were not required.

Consent for publication

All authors have reviewed and approved the final version of this manuscript and consent to its publication.

Competing interests

The authors declare no competing interests.

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References

- Trepman E, Nihal A, Pinzur MS. Current Topics Review: Charcot Neuroarthropathy of the Foot and Ankle. *Foot Ankle Int.* 2005;26(1):46–63.
- Brown AW. Clinician's Guide to Diabetes Gadgets and Gizmos. *Clinical Diabetes.* 2008;26(2):66–71.
- Jeffcoate WJ. Charcot neuro-osteopathy. *Diabetes Metab Res Rev.* 2008;24(Suppl 1):S62–5.
- Lowery NJ, Woods JB, Armstrong DG, Wukich DK. Surgical Management of Charcot Neuroarthropathy of the Foot and Ankle: A Systematic Review. *Foot Ankle Int.* 2012;33(2):113–21.
- Manobianco A, Enketan O, Grass R. Tibiototalcalcaneal arthrodesis with an intramedullary nail: The functional and clinical outcome of a challenging patient group and its comparison to a below knee amputation. *Foot Ankle Surg.* 2024;30(3):268–72.
- Richman J, Cota A, Weinfeld S. Intramedullary Nailing and External Ring Fixation for Tibiototalcalcaneal Arthrodesis in Charcot Arthropathy. *Foot Ankle Int.* 2017;38(2):149–52.
- Jones JM, Schleunes SD, Marshall JE, Vacketta VG, McMillen RL. Tibiototalcalcaneal arthrodesis for the treatment of midfoot Charcot neuroarthropathy. *Foot & Ankle Surgery: Techniques, Reports & Cases.* 2023;3(1):100213.
- Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses [Internet]. Ottawa: Ottawa Hospital Research Institute; 2014.
- Rastegar S, Teymouri M, Sabaghi J. Association between the procedure of tibiototalcalcaneal arthrodesis by hindfoot nailing and quality of life in Charcot's joint. *J Orthop Surg Res.* 2024;19(1):332.
- Bajuri MY, Manas AM, Zamri KS. Functional outcomes of tibiototalcalcaneal arthrodesis using a hindfoot arthrodesis nail in treating Charcot's arthropathy deformity. *Front Surg.* 2022;9:862133.
- Moonot P, Sharma G, Kadakia A. Functional outcome in patients with Charcot neuropathy with almost complete loss of talus treated by tibiototalcalcaneal nail: A cross-sectional study. *Foot.* 2021;49:101833.
- Ma H, Yang R, Yang M. Comparison of locking plate and retrograde intramedullary nail for tibiototalcalcaneal arthrodesis in the treatment of Charcot ankle arthropathy. *Chinese Journal of Anatomy and Clinics.* 2021;26(5):529–34.
- Ersin M, Demirel M, Chodza M, Bilgili F, Kilicoglu OI. Mid-term results of hindfoot arthrodesis with a retrograde intra-medullary nail in 24 patients with diabetic Charcot neuroarthropathy. *Acta Orthop.* 2020;91(3):336–40.
- Chraim M, Krenn S, Alrabai HM, Trnka H-J, Bock P. Mid-term follow-up of patients with hindfoot arthrodesis with retrograde compression intramedullary nail in Charcot neuroarthropathy of the hindfoot. *Bone Joint J.* 2018;100-B(2):190–6.
- Siebachmeyer M, Boddu K, Bilal A, Hester TW, Hardwick T, Fox TP, et al. Outcome of one-stage correction of deformities of the ankle and hindfoot and fusion in Charcot neuroarthropathy using a retrograde intramedullary hindfoot arthrodesis nail. *Bone Joint J.* 2015;97-B(1):76–82.
- Lewis D, Lutton C, Wilson LJ, Crawford RW, Goss B. Low cost polymer intramedullary nails for fracture fixation: a biomechanical study in a porcine femur model. *Arch Orthop Trauma Surg.* 2009;129(6):817–22.
- Horn J, Linke B, Höntzsch D, Gueorguiev B, Schwieger K. Angle stable interlocking screws improve construct stability of intramedullary nailing of distal tibia fractures: A biomechanical study. *Injury.* 2009;40(7):767–71.
- Alfahd U, Roth SE, Stephen D, Whyne CM. Biomechanical Comparison of Intramedullary Nail and Blade Plate Fixation for Tibiototalcalcaneal Arthrodesis. *J Orthop Trauma.* 2005;19(10):703–8.
- Berend ME, Glisson RR, Nunley JA. A Biomechanical Comparison of Intramedullary Nail and Crossed Lag Screw Fixation for Tibiototalcalcaneal Arthrodesis. *Foot Ankle Int.* 1997;18(10):639–43.
- Chiodo CP, Acevedo JI, Sammarco VJ, Parks BG, Boucher HR, Myerson MS, et al. Intramedullary Rod Fixation Compared with Blade-Plate-and-Screw Fixation for Tibiototalcalcaneal Arthrodesis: A Biomechanical Investigation. *JBSJ.* 2003;85(12):2425–8.
- Pelton K, Hofer JK, Thordarson DB. Tibiototalcalcaneal Arthrodesis Using a Dynamically Locked Retrograde Intramedullary Nail. *Foot Ankle Int.* 2006;27(10):759–63.
- Trost M, Yarkin S, Knieps M, Frey S, Neiss WF, Eysel P, et al. Biomechanical comparison of different fixation methods in tibiototalcalcaneal arthrodesis: a cadaver study. *J Orthop Surg Res.* 2023;18(1):971.
- Zhang C, Shi Z, Mei G. Locking plate versus retrograde intramedullary nail fixation for tibiototalcalcaneal arthrodesis: A retrospective analysis. *Indian J Orthop.* 2015;49(2):227–32.
- ElAlfy B, Ali AM, Fawzy SI, Ilizarov External Fixator Versus Retrograde Intramedullary Nailing for Ankle Joint Arthrodesis in Diabetic Charcot Neuroarthropathy. *J Foot Ankle Surg.* 2017;56(2):309–13.
- El-Mowafi H, Abulsaad M, Kandil Y, El-Hawary A, Ali S. Hybrid Fixation for Ankle Fusion in Diabetic Charcot Arthropathy. *Foot Ankle Int.* 2018;39(1):93–8.
- 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. *J Foot Ankle Surg.* 2012;51(4):420–5.
27. Froelich J, Idusuyi OB, Clark D, Kogler GF, Paliwal M, Dyrstad B, et al. Torsional stiffness of an intramedullary nail versus blade plate fixation for tibiototalcaneal arthrodesis: a biomechanical study. *J Surg Orthop Adv.* 2010;19(2):109–13.
 28. Bekos A, Sioutis S, Kostrogrou A, Saranteas T, Mavrogenis AF. The history of intramedullary nailing. *Int Orthop.* 2021;45(5):1355–61.
 29. Mohd Yazid, Bajuri Shir Lee, Ong Srijit, Das Isa Naina, Mohamed IN. Charcot Neuroarthropathy: Current Surgical Management and Update. *Syst Rev Front Surg.* 9. <https://doi.org/10.3389/fsurg.2022.820826>.
 30. Powers NS, Leatham PR, Persky JD, Burns PR. Outcomes of Tibiototalcaneal Arthrodesis with a Femoral Nail. *J Am Podiatr Med Assoc.* 2021;111(3):1–7.
 31. Lee M, Choi WJ, Han SH, Jang J, Lee JW. Uncontrolled diabetes as a potential risk factor in tibiototalcaneal fusion using a retrograde intramedullary nail. *Foot Ankle Surg.* 2018;24(6):542–8.
 32. Kowalski C, Stauch C, Callahan R, Saloky K, Walley K, Aynardi M, et al. Prognostic risk factors for complications associated with tibiototalcaneal arthrodesis with a nail. *Foot Ankle Surg.* 2020;26(6):708–11.
 33. Wukich DK, Mallory BR, Suder NC, Rosario BL. Tibiototalcaneal Arthrodesis Using Retrograde Intramedullary Nail Fixation: Comparison of Patients With and Without Diabetes Mellitus. *J Foot Ankle Surg.* 2015;54(5):876–82.
 34. Rana B, Patel S. Results of Ankle and Hind foot arthrodesis in Diabetic Charcot Neuroarthropathy - A retrospective analysis of 44 patients. *Journal of Clinical Orthopaedics and Trauma.* 2021;23:101637.
 35. Diacogiorgis D, Perrin BM, Kingsley MIC. Factors impacting the evidence-based assessment, diagnosis and management of Acute Charcot Neuroarthropathy: a systematic review. *J Foot Ankle Res.* 2021;14(1):26.
 36. Rogers LC, Frykberg RG, Armstrong DG, Boulton AJM, Edmonds M, Van GH, et al. The Charcot Foot in Diabetes. *J Am Podiatr Med Assoc.* 2011;101(5):437–46.
 37. Pakarinen T-K, Laine H-J, Mäenpää H, Mattila P, Lahtela J. Long-term outcome and quality of life in patients with Charcot foot. *Foot Ankle Surg.* 2009;15(4):187–91.
 38. Patel A, Sivaprakasam M, Reichert I, Ahluwalia R, Kavarthapu V. Medium- and long-term outcomes of surgical reconstruction in acute charcot neuroarthropathy. *Orthop Proc.* 2024;106-B(SUPP_10):3-.
 39. Idusuyi OB. Surgical management of Charcot neuroarthropathy. *Prosthet Orthot Int.* 2015;39(1):61–72.
 40. Galhoum AE, Trivedi V, Askar M, Tejero S, Herrera-Pérez M, AlRashidi Y, et al. Management of Ankle Charcot Neuroarthropathy: A Systematic Review. *J Clin Med.* 2021;10(24):5923.
 41. Jude EB, Selby PL, Burgess J, Lilleystone P, Mawer EB, Page SR, et al. Bisphosphonates in the treatment of Charcot neuroarthropathy: a double-blind randomised controlled trial. *Diabetologia.* 2001;44(11):2032–7.
 42. Anderson JJ, Woelffer KE, Holtzman JJ, Jacobs AM. Bisphosphonates for the treatment of Charcot neuroarthropathy. *J Foot Ankle Surg.* 2004;43(5):285–9.
 43. Verity S, Sochocki M, Embil JM, Trepman E. Treatment of Charcot foot and ankle with a prefabricated removable walker brace and custom insole. *Foot Ankle Surg.* 2008;14(1):26–31.
 44. de Souza LJ. Charcot Arthropathy and Immobilization in a Weight-Bearing Total Contact Cast. *JBJS.* 2008;90(4):754–9.
 45. Papa J, Myerson M, Girard P. Salvage, with arthrodesis, in intractable diabetic neuropathic arthropathy of the foot and ankle. *JBJS.* 1993;75(7):1056–66.
 46. Zarutsky E, Rush SM, Schuberth JM. The use of circular wire external fixation in the treatment of salvage ankle arthrodesis. *J Foot Ankle Surg.* 2005;44(1):22–31.
 47. Pitts C, Alexander B, Washington J, Barranco H, Patel R, McGwin G, et al. Factors affecting the outcomes of tibiototalcaneal fusion. *BoneJoint J.* 2020;102-B(3):345–51.

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