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CASE SERIES

Electrodiagnostic evidence of nerve regeneration in patients with diabetic Charcot foot treated with proximal tibial cortex transverse distraction

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ABSTRACT

Objectives: The aim of this study was to investigate whether proximal tibial cortex transverse distraction (PTCTD) could result in nerve regeneration in diabetic Charcot foot via electromyography (EMG).

Patients and methods: Between March 2015 and June 2021, a total of six patients (4 males, 2 females; mean age: 58.8±15.5 years; range, 32 to 75 years) with diabetic Charcot foot treated with PTCTD were retrospectively analyzed. Electromyography was performed preoperatively and six months postoperatively to evaluate nerve regeneration. Healing time, wound area and limb salvage rates were also recorded.

Results: The mean time to wound healing in all patients was 155.17±19.13 (range, 135 to 189) days. The mean wound area was 4.44±2.58 (range, 2.52 to 9.52) cm^2. No cases of low limb amputation occurred, with a limb salvage rate of 100%. The EMG revealed spontaneous potentials and decreased recruitment in all patients preoperatively. Motor unit potentials were found only in some of the tested muscles. At the final follow-up, the extensor digitorum brevis in four patients (67.7%) had a simple recruitment phase. Three patients (50%) and four patients (67.7%) had increased compound muscle action potential (CMAP) amplitudes in muscles innervated by the nervus peroneus communis and tibial nerve, respectively. In one patient (16.7%), the CMAP was found only at the peroneal head segment of the nervus peroneus communis, but not at the distal end.

Conclusion: Our results indicate that nerve regeneration can be confirmed by EMG after PTCTD in patients with diabetic Charcot foot. However, further multi-center, large-scale, long-term prospective studies are needed to draw more reliable conclusions on this subject.

Keywords: Diabetic Charcot foot, Electromyography, nerve regeneration, proximal tibial cortex transverse distraction.

As an occasional and severe diabetic complication, Charcot foot usually manifests as aseptic inflammation and progressive bone degeneration in the unilateral or bilateral lower limbs, which may occur without any noticeable symptoms. It has an incidence of approximately 0.3%.[1] If untreated earlier, it may result in an ulceration, spontaneous fatigued bone fractures or even amputation. Below-knee amputation is often inevitable when foot ulcers occur.[2] Stuck et al.[3] reported that the risk of amputation increased 12-fold, if Charcot neuroarthropathy occurred along with ulceration. Early diagnosis plays an important role in successful

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treatment. However, this is still a great challenge even for experienced specialists.

Patients with diabetic Charcot feet usually have poor glycemic control and peripheral neuropathy, although the precise pathological mechanism is still unknown. Diabetes-related foot complications are typically caused by three major pathological processes: neuropathy, vasculopathy, and infection.[4] In general, neuropathy is regarded as a necessary predisposition, which can result in decreased sensation of the foot and eventual ulceration. Therefore, reversal or regeneration of the pathological process of neuropathy is considered critical for prognosis.

Achieving a stable lower extremity with no ulcer and eradication of infection is needed.[5] The technique of proximal tibial cortex transverse distraction (PTCTD) is a known surgical technique for diabetic foot and ulceration with favorable encouraging outcomes.[6] Longitudinal distraction of the proximal tibia induces the genesis and growth of new bone and surrounding soft tissues.[7] However, the literature regarding the effects of nerve regeneration in PTCTD is limited. Electromyography (EMG) can be used to objectively evaluate and quantify nerve regeneration.[8] In the present study, we aimed to investigate whether PTCTD could result in nerve regeneration in diabetic Charcot foot via EMG.

PATIENTS AND METHODS

This single-center, retrospective case series was conducted at Nanjing Hospital of Chinese Medicine, Affiliated to Nanjing University of Traditional Chinese Medicine, Department of Orthopaedics between March 2015 and June 2021. Six patients (4 males, 2 females; mean age: 58.8±15.5 years; range, 32 to 75 years) with diabetic Charcot foot treated with PTCTD were included. Exclusion criteria were not having the diagnosis of diabetes mellitus (DM), foot deformities, bilateral Charcot foot, prior foot surgery or amputation on either side. The diagnosis of diabetic Charcot foot was made based on the prespecified diagnostic criteria.[9,10] A written informed consent was obtained from each patient. The study protocol was approved by the Nanjing University of Traditional Chinese Medicine Ethics Committee (date: 30.12.2021, no: 2015-LL-0076). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Demographic data including age, sex, laterality, comorbidity and lower limb angiopathy were retrieved from the electronic hospital database.

Therapeutic regimen

The therapeutic regimen was tailored as previously described[6] and modified according to the required instructions. Briefly, off-loading and glucose control were prescribed immediately. Vascular patency and infection were subsequently evaluated and accompanied by necessary treatment to restore foot perfusion.[11] All surgeries were performed on a regular basis, and a schematic diagram is shown in Figure 1. The corticotomy fragment was a vertical rectangular area (about length 5 cm, width 2 cm) located at the medial upper tibia, about the junction of the upper one-third and middle one-third. A special monoliteral external fixator (Figure 2) was used for the transverse distraction. This fixator has a special designed linking device, allowing the corticotomy fragment to lift or descend by rotating the knob clockwise or counterclockwise. The maximum distraction height was 15 mm between the distracted cortex fragment and the tibia shaft. To minimally disrupt periosteal blood supply, several discontinuous incisions (2 to 4 mm) were made in periosteum for subperiosteal osteotomy. The fragment was separated with a small bone knife. Then, the external fixator was installed with incision sutured.

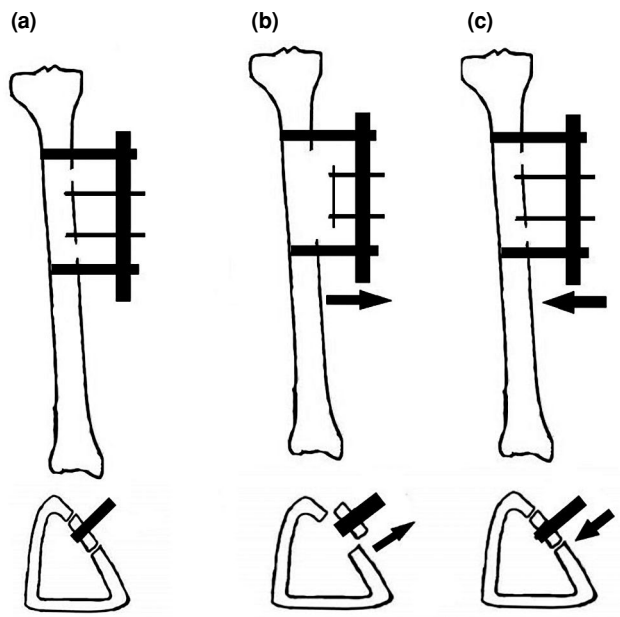

FIGURE 1. The schematic diagram of proximal tibial cortex transverse distraction. **(a)** Schematic diagram of tibial cortex transverse distraction. The corticotomy fragment was a vertical rectangular area (approximately 5 cm in length, 2 cm in width) located at the medial upper tibia. A special monoliteral external fixator was used for the transverse distraction. **(b)** Regular distraction. **(c)** Reverse distraction.

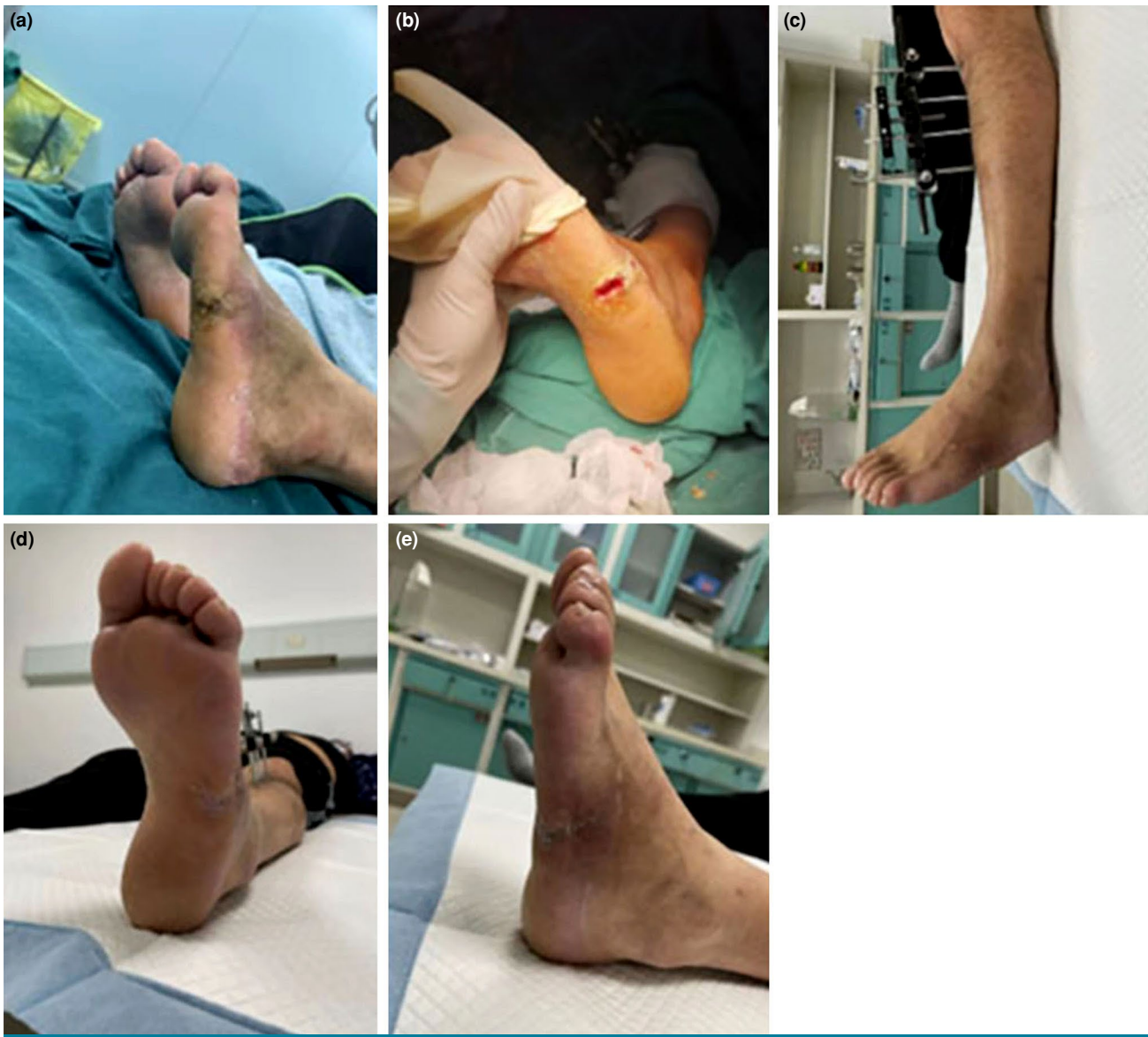

FIGURE 2. A patient in his 30s with diabetic Charcot foot was treated with PTCTD. He had a history of L5/S1 nerve root injury when he was young. **(a)** Preoperative image showed the existence of an ulcer (0.9×2.8 cm). **(b)** Intraoperative image showed the existence of the wound after debridement. **(c)** A 6-month postoperative image showed a special monoliteral external fixator was used for the transverse distraction. **(d)** and **(e)**: At final follow-up, the foot ulcer completely healed. And the patient walked freely with the healed foot.
PTCTD: Proximal tibial cortex transverse distraction.

The position of external fixator and corticotomy site were assessed by postoperative radiographs. All non-viable tissue including all infected and necrotic tissues, was aggressively debrided until it reached healthy tissue. If osteomyelitis was diagnosed, bone debridement was also performed. Daily dressing changes were applied to protect pin-site from infections. The tibial cortex transverse distraction (1 mm every day) was adjusted at a rate of 0.25 mm every 6 h after two to three days postoperatively. Earlier exercises were initiated, but full weight beating was allowed until the wound healed.

Clinical variables

Duration of DM was defined as the time from diagnosis to admission. Healing time was defined as the time from operation to healing of the foot ulcer. Healing was defined as the ulcer

TABLE I
The baselines were recorded at the first referral

			Comorbidity				Lower limb angiopathy	
No.	Laterality	DM duration (year)	CRI	CAD	HP	NRI	OS	S
1	L	5				Y		Y
2	L	25		Y	Y		Y	
3	L	3			Y			Y
4	R	12			Y			Y
5	L	9		Y	Y	Y		Y
6	R	11	Y	Y	Y		Y	

DM: Diabetes mellitus; CRI: Chronic renal insufficiency; CAD: Coronary artery disease; HP: Hypertension; NRI: nerve root injury; OS: Occlusion and stenosis; S: Stenosis only; L: left; R: right; Y: Yes.

completely epithelializing and not reoccurring.[12] Wound area was estimated by multiplying the two greatest diameters of the lesion at right angles.[13] Electromyography was performed preoperatively and six months postoperatively to evaluate nerve regeneration by one senior experienced physician majoring in electrodiagnostic medicine.

Statistical analysis

Statistical analysis was performed using the SPSS version 24.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean ± standard deviation (SD), median (min-max) or number and frequency, where applicable. The Kolmogorov-Smirnov test was used to evaluate the normal distribution of continuous variables. A p value of <0.05 was considered statistically significant.

RESULTS

Baseline characteristics of the patients are shown in Table I. The mean time to wound healing in all patients was 155.17±19.13 (range, 135 to 189) days (Figure 2). Three of six patients had osteomyelitis. After angiographic evaluation, two patients received stent implantation and four patients received balloon dilatation. The mean wound area was 4.44±2.58 (range, 2.52 to 9.52) cm^2. No cases of low limb amputation occurred, with a limb salvage rate of 100%. Five patients returned to their previous jobs uneventfully. No pin-site infection or other complications were reported.

The EMG revealed spontaneous potentials and decreased recruitment in all patients preoperatively. Motor unit potentials were found only in some of the tested muscles. Sensory nerve action potentials (SNAPs) in the sural nerve, superficial peroneal nerve and medial plantar nerve disappeared. No F-reaction and H-reflex in the tibial nerve were observed in any of the patients.

At the final follow-up, the extensor digitorum brevis in four patients (67.7%) had a simple recruitment phase. Three patients (50%) and four patients (67.7%) had increased compound muscle action potential (CMAP) amplitudes in muscles innervated by the nervus peroneus communis and tibial nerve, respectively. In one patient (16.7%), the CMAP was found only at the peroneal head segment of the nervus peroneus communis, but not at the distal end. The SNAPs in the sural nerve, superficial peroneal nerve and medial plantar nerve were still not detected. No F-reaction and H-reflex in the tibial nerve were observed postoperatively.

DISCUSSION

As a known clinical accepted technique, little is known about the biological mechanism of soft tissue regeneration, particularly the nerve regeneration. In this case series, we investigated whether PTCTD could result in nerve regeneration in diabetic Charcot foot via EMG. Our results showed nerve regeneration via EMG. A potential explanation for this phenomenon is that tibia cortex transverse distraction stimulates the angiogenesis and neovascularization, which provides proper metabolic support for nerve regeneration.

The central feature of the Charcot foot is the loss of sensory and sympathetic innervation. Koeck et al.[14] conducted a quantitative nerve density study and reported that the density of sympathetic nerve fibers significantly reduced in Charcot foot. The potential explanations for this pathological change are neurodegenerative factors such as oxidative

stress, nerve fiber apoptosis, and nerve fiber repulsion. Severe peripheral neuropathy results in sensory loss.[15] The loss of protective sensations (i.e., light touch, temperature, and pain perception) makes the foot vulnerable to minor unrecognized trauma.[16] In our study, the SNAPs in the sural nerve, superficial peroneal nerve and medial plantar nerve disappeared. No F-reaction and H-reflex in tibial nerve were observed in any of the patients.

The impaired vascular reflexes usually result in increased arterial perfusion, arteriovenous shunting and distal hyperemia of the lower extremities.[17] Christensen et al.[18] reported that local hyperemia increased the local inflammatory response, which promoted osteoclastic activity. Jansen et al.[19] measured the inflammatory biomarkers in Charcot foot and reported that the level of interleukin-6 significantly increased. Repeated local microtrauma and unregulated bone resorption initiate the inflammatory process in turn.

The increased local vascularity from neuropathy precipitates osteoclastic activation and changes local skeletal structures. In poor diabetic control, hyperglycemia usually increases the level of advanced glycosylation end products (AGEs).[20] The AGE upregulates the receptor activator kappa beta (RANK)-RANK ligand (RANKL) axis to activate osteoclasts.[20] The accumulation of AGEs within peripheral nerves confirmed the detrimental role of hyperglycemia.[21] Hyperglycemia often leads to irreversible disability by affecting neuronal and axonal degeneration. It not only destroys the ongoing regenerative plasticity, but also attempts to compensate for or reverse nerve damage. The intrinsic demineralization or osteoporosis is caused by sympathetic denervation of the bone vasculature. There is a significant relationship between peripheral sympathetic neuropathy and Charcot foot in individuals with diabetes.[22] Ultimately, if the cascade of these pathological changes is corrected in time, destruction can be minimized or avoided.

The exact mechanism of Charcot foot is still unclear. Chronic hyperglycemia causes neuropathy through changes in osmotic pressure. The peripheral nervous system and the autonomic system are impaired, manifesting as sensory loss and distal hyperemia.[23] As a serious and frequent problem, reversing or regenerating the pathological process of neuropathy is particularly critical. In this study, the extensor digitorum brevis had a simple recruitment phase in four patients (67.7%). Three patients (50.0%) and four patients (67.7%) had increased CMAP amplitudes in muscles innervated by the nervus peroneus communis and tibial nerve, respectively. These findings confirmed that nerve regeneration did exist.

The technique of tibial cortex transverse distraction provides a slow and continuous stretching to stimulate angiogenesis and neovascularization.[24] Computed tomography perfusion confirmed the existence of increased blood supply.[25] Intraneural revascularization is of utmost importance in peripheral nerve repair and regeneration.[26] The increased blood supply (including blood flow and capillary number) of surrounding soft tissues was redistributed, which provided proper metabolic support for nerve repair or regeneration.[27] Matsuyama et al.[28] reported angiogenesis during transverse distraction and reported that the average blood vessel volume ratio increased more than three-fold. The angiograms revealed that many proliferating arteries were widely distributed in the distracted limbs.

The axonal diameter and internodal length confirmed that gradual stretching could induce the axonal regeneration.[29] The same conclusion was also drawn from the structural analysis and ultrastructural analysis. Farhadieh et al.[30] examined the expression of nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF) in the inferior alveolar nerve (IAN), when distraction osteogenesis used in an ovine mandible model. They reported that distraction osteogenesis acts as a subacute injury to increase the expression of NGF and BDNF and facilitate Schwann cell proliferation. Electrophysiological evaluation in dogs also revealed stable evoked potential measurements after bifocal distraction osteogenesis with nerve regeneration.[31]

There are several limitations to this case series. First, it has a retrospective design with only six patients. Second, there is no control or comparison group to confirm whether the observed effects are solely due to PTCTD. Third, the long-term follow-up is needed to evaluate long-term effects on nerve regeneration or recurrence of symptoms.

In conclusion, our results indicate that nerve regeneration can be confirmed by EMG after PTCTD in patients with diabetic Charcot foot. However, further multi-center, large-scale, long-term prospective studies are needed to draw more reliable conclusions on this subject.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Wrote the main manuscript: J.X., K.L., K.Q.; Had undergone literature review and interpretation: Z.X., B.G.; Designed the study and managed overall process: J.Z., N.S.

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REFERENCES

1. Fabrin J, Larsen K, Holstein PE. Long-term follow-up in diabetic Charcot feet with spontaneous onset. Diabetes Care 2000;23:796-800. doi: 10.2337/diacare.23.6.796.
2. Karahan HG, Çetin O, Gök M, Akın HF, Vural A, Kayalı C. The effect of comorbid factors and amputation level on mortality in geriatric patients with diabetic foot. Jt Dis Relat Surg 2023;34:115-20. doi: 10.52312/jdrs.2023.818.
3. Stuck RM, Sohn MW, Budiman-Mak E, Lee TA, Weiss KB. Charcot arthropathy risk elevation in the obese diabetic population. Am J Med 2008;121:1008-14. doi: 10.1016/j.amjmed.2008.06.038. .
4. Ulusoy S, Kılınç İ, Oruç M, Özdemir B, Ergani HM, Keskin ÖH, et al. Analysis of wound types and wound care methods after the 2023 Kahramanmaras earthquake. Jt Dis Relat Surg 2023;34:488-96. doi: 10.52312/jdrs.2023.1128.
5. La Fontaine J, Lavery L, Jude E. Current concepts of Charcot foot in diabetic patients. Foot (Edinb) 2016;26:7-14. doi: 10.1016/j.foot.2015.11.001.
6. Jianda X, Maosheng B, Chenjian P, Xiaojing Y, Changhui W, Junhao L, et al. An novel and alternative treatment method for large heel ulceration in diabetic patients: Proximal tibial cortex transverse distraction. Int Wound J 2023;20:732-9. doi: 10.1111/iwj.13916.
7. Ilizarov GA. Clinical application of the tension-stress effect for limb lengthening. Clin Orthop Relat Res 1990;250:8-26.
8. Krarup C, Boeckstyns M, Ibsen A, Moldovan M, Archibald S. Remodeling of motor units after nerve regeneration studied by quantitative electromyography. Clin Neurophysiol 2016;127:1675-82. doi: 10.1016/j.clinph.2015.08.008.
9. Yousaf S, Dawe EJC, Saleh A, Gill IR, Wee A. The acute Charcot foot in diabetics: Diagnosis and management. EFORT Open Rev 2018;3:568-73. doi: 10.1302/2058-5241.3.180003.
10. Keukenkamp R, Busch-Westbroek TE, Barn R, Woodburn J, Bus SA. Foot ulcer recurrence, plantar pressure and footwear adherence in people with diabetes and Charcot midfoot deformity: A cohort analysis. Diabet Med 2021;38:e14438. doi: 10.1111/dme.14438.
11. Aiello A, Anichini R, Brocco E, Caravaggi C, Chiavetta A, Cioni R, et al. Treatment of peripheral arterial disease in diabetes: a consensus of the Italian Societies of Diabetes (SID, AMD), Radiology (SIRM) and Vascular Endovascular Surgery (SICVE). Nutr Metab Cardiovasc Dis 2014;24:355-69. doi: 10.1016/j.numecd.2013.12.007.
12. Larsson J, Agardh CD, Apelqvist J, Stenström A. Local signs and symptoms in relation to final amputation level in diabetic patients. A prospective study of 187 patients with foot ulcers. Acta Orthop Scand 1994;65:387-93. doi: 10.3109/17453679408995476.
13. Jeffcoate WJ, Price P, Harding KG. Wound healing and treatments for people with diabetic foot ulcers. Diabetes Metab Res Rev 2004;20 Suppl 1:S78-89. doi: 10.1002/dmrr.476.
14. Koeck FX, Bobrik V, Fassold A, Grifka J, Kessler S, Straub RH. Marked loss of sympathetic nerve fibers in chronic Charcot foot of diabetic origin compared to ankle joint osteoarthritis. J Orthop Res 2009;27:736-41. doi: 10.1002/jor.20807.
15. Young MJ, Marshall A, Adams JE, Selby PL, Boulton AJ. Osteopenia, neurological dysfunction, and the development of Charcot neuroarthropathy. Diabetes Care 1995;18:34-8. doi: 10.2337/diacare.18.1.34.
16. van der Ven A, Chapman CB, Bowker JH. Charcot neuroarthropathy of the foot and ankle. J Am Acad Orthop Surg 2009;17:562-71. doi: 10.5435/00124635-200909000-00003.
17. Vinik AI, Ziegler D. Diabetic cardiovascular autonomic neuropathy. Circulation 2007;115:387-97. doi: 10.1161/CIRCULATIONAHA.106.634949.
18. Christensen TM, Simonsen L, Holstein PE, Svendsen OL, Bülow J. Sympathetic neuropathy in diabetes mellitus patients does not elicit Charcot osteoarthropathy. J Diabetes Complications 2011;25:320-4. doi: 10.1016/j.jdiacomp.2011.06.006.
19. Jansen RB, Christensen TM, Bülow J, Rørdam L, Jørgensen NR, Svendsen OL. Markers of local inflammation and bone resorption in the acute diabetic Charcot foot. J Diabetes Res 2018;2018:5647981. doi: 10.1155/2018/5647981.
20. Yousaf S, Dawe EJC, Saleh A, Gill IR, Wee A. The acute Charcot foot in diabetics: Diagnosis and management. EFORT Open Rev 2018;3:568-73. doi: 10.1302/2058-5241.3.180003.
21. Sugimoto K, Yasujima M, Yagihashi S. Role of advanced glycation end products in diabetic neuropathy. Curr Pharm Des 2008;14:953-61. doi: 10.2174/138161208784139774.
22. Chantelau E, Onvlee GJ. Charcot foot in diabetes: farewell to the neurotrophic theory. Horm Metab Res 2006;38:361-7. doi: 10.1055/s-2006-944525.
23. Papanas N, Maltezos E. Etiology, pathophysiology and classifications of the diabetic Charcot foot. Diabet Foot Ankle 2013;4. doi: 10.3402/dfa.v4i0.20872.
24. Chen Y, Ding X, Zhu Y, Jia Z, Qi Y, Chen M, et al. Effect of tibial cortex transverse transport in patients with recalcitrant diabetic foot ulcers: A prospective multicenter cohort study. J Orthop Translat 2022;36:194-204. doi: 10.1016/j.jot.2022.09.002.
25. Chen Y, Kuang X, Zhou J, Zhen P, Zeng Z, Lin Z, et al. Proximal tibial cortex transverse distraction facilitating healing and limb salvage in severe and recalcitrant diabetic foot ulcers. Clin Orthop Relat Res 2020;478:836-51. doi: 10.1097/CORR.0000000000001075.
26. Caillaud M, Richard L, Vallat JM, Desmoulière A, Billet F. Peripheral nerve regeneration and intraneural revascularization. Neural Regen Res 2019;14:24-33. doi: 10.4103/1673-5374.243699.

27. Gubin AV, Borzunov DY, Marchenkova LO, Malkova TA, Smirnova IL. Contribution of G.A. Ilizarov to bone reconstruction: Historical achievements and state of the art. Strategies Trauma Limb Reconstr 2016;11:145-52. doi: 10.1007/s11751-016-0261-7.
28. Matsuyama J, Ohnishi I, Kageyama T, Oshida H, Suwabe T, Nakamura K. Osteogenesis and angiogenesis in regenerating bone during transverse distraction: Quantitative evaluation using a canine model. Clin Orthop Relat Res 2005(433):243-50. doi: 10.1097/01.blo.0000150562.24256.a4.
29. Saijilafu; Nishiura Y, Hara Y, Yoshii Y, Ochiai N. Gradual stretching of the proximal nerve stump induces the growth of regenerating sprouts in rats. J Orthop Res 2008;26:1012-7. doi: 10.1002/jor.20587.
30. Farhadieh RD, Nicklin S, Yu Y, Gianoutsos MP, Walsh WR. The role of nerve growth factor and brain-derived neurotrophic factor in inferior alveolar nerve regeneration in distraction osteogenesis. J Craniofac Surg 2003;14:859-65. doi: 10.1097/00001665-200311000-00007.
31. Isomura ET, Shogen Y, Hamaguchi M, Kogo M. Electrophysiologic evaluation of inferior alveolar nerve regenerated by bifocal distraction osteogenesis in dogs. Plast Reconstr Surg 2013;132:877-82. doi: 10.1097/PRS.0b013e31829fe49a.