Reconstructive Foot Surgery in Neuropathic Diabetic Foot Ulcers [NDFU]

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ABSTRACT

Introduction: NEuropathic Diabetic Foot Ulcer [NDFU] is a challenging problem for both patients and surgeons. Peripheral neuropathy has an important role in diabetic foot lesions. Sensory neuropathy causes loss of protective sensations. Motor neuropathy causes foot deformities, biomechanical imbalance and change of weight bearing areas. Autonomic neuropathy causes callus, charcot neuroarthropathy and loss of sympathetic tone to peripheral resistance. Those interplaying factors can lead to increased planter pressure, foot deformities, soft tissue damage and ulcerations. Management of NDFU should cure the present condition and prevent recurrences.

Patients and Methods: 120 Patients with diabetic foot ulcers complained of painless non-healed ulcer and deformed foot with or without loss of digits. General and local examination, routine investigations, wound cultures, foot X-ray and wound care were done. Control of diabetes was crucial. Reconstructive foot surgery was done. Plantar pressure was re-assessed postoperatively.

Results: 84 patients (70%) were males and 36 (30%) were females. All patients have diabetic neuropathy. All patients have decreased or lost 2-point discrimination, pain sensation and proprioception. Plantar pressure assessment methods revealed abnormal patterns of weight bearing areas. Reconstructive foot surgery achieved restoration of better function and gait.

Conclusion: Reconstructive foot surgery aims to preserve foot structure and restore foot function and shape as much as possible. It is important to eliminate the areas of pressure, correct the deformity and prevent recurrence. Strict use of this regimen can avoid foot or toe amputations which are very stressful for the diabetic patient.

Key Words: *Diabetic foot – Neuropathic ulcer – Pathology – Reconstructive foot surgery.*

INTRODUCTION

Diabetes may predispose to the development of foot lesions. Twenty five to fifty percent of diabetic patients will develop diabetic foot ulcers, [1-3] and between 14% and 20% of patients with diabetic foot ulcers require amputation [3]. The onset of foot complications could be unpredictable and irreversible. Thus when they occur, the foot becomes vulnerable to ulceration. Pathogenesis of diabetic foot ulceration involves two processes interplaying with each other; first, progressive peripheral neuropathy, and second, progressive reduction of blood supply. Although both are major contributing factors, neuropathic or ischemic foot does not ulcerate spontaneously. Thermal or mechanical forces will be the main trigger.

Peripheral neuropathy has an important role in diabetic foot lesions and is present in 80% of diabetic patients with foot problems [4-6]. It was found that patients who are admitted with foot problems due to painless trauma are approximately three times as many patients who are admitted for ischemic pain [7,8]. Incidence of Diabetic Neuropathy [DN] in patients with diabetes increases with poor control of diabetes and prolonged duration of the disease. Thus after 25 years of diabetes, 50% of all patients show clinical evidence of neuropathy [9]. DN is classified into; sensory-motor neuropathy, autonomic neuropathy, and mononeuropathy. Sensory neuropathy causes loss of protective sensations as; pain, temperature sensation and proprioception. Paresthesia and dysesthesia may occur. It starts distally and then spreads proximally in a stoking distribution. Lazaro-Martinez et al., 2011 stated that sensory neuropathy renders the foot "deaf and blind" to stimuli that would normally elicit pain or discomfort [10]. Motor neuropathy may cause foot deformities due to the biomechanical imbalance between extrinsic and intrinsic musculature with predominance of long flexors of the foot [11]. Small muscles atrophy [12] with altered foot biomechanics leads to foot deformity and redistribution of foot pressures, which can eventually predispose to foot ulcers [4]. Structural deformities such as claw toes lead to prominence of the metatarsal heads with subsequent ulceration. Also, loss of abduction, varus deformity

of the heel, and hammering of toes, may occur exposing more areas to pressure and thus to their ulcerations [4]. Autonomic neuropathy causes decreased sweating, dry skin with thick plaques of hard callus in the sole with cracks, fissures and subsequent ulceration [12]. It may also cause loss of sympathetic tone to peripheral resistance which leads to increased blood flow and A-V shunting [13]. This will cause increased venous capillary pressure [14], skin temperature [13,15] and neuropathic edema [4,16-18]. Charcot Neuroarthropathy [CN] is one of the most challenging late complications of the diabetic foot which characterized by bone and joint destruction, fragmentation, and remodeling [9]. Pathogenesis of charoct neuroathropathy includes; autonomic neuropathy with increased blood flow and bone resorption and; sensory neuropathy with repetitive insensitive trauma [19-21]. It may affect 0.8% to 10% of diabetic populations [22-27]. Diagnosis of acute CN in the early stages is crucial to avoid fractures and foot deformities. A unilateral, clinically uninfected, warm, often swollen, and sometimes painful foot, in a DN patient should be managed as acute CN until proven otherwise [28]. MRI is the most sensitive imaging technique for acute CN [20,29-32]. The best treatment for acute CN is immediate effective offloading, typically with total contact casting [33]. There are several manifestations of charcot deformities which include; forefoot supinatus, forefoot abduction, hind foot medial translation, ankle contracture, varus calcaneus, equinus and the rocker-bottom foot deformity with midfoot collapse [3].

Mechanism of ulcer formation is formed of two factors; increased planter pressure and Decreased cushioning property. Increased planter pressure is caused by; biomechanical deformities (as Charcot's deformities, hammer toe, claw toe, and pes-cavus). They allow the foot to become highly susceptible to trauma, which can lead to weakening and breakdown of the integument. Elevated plantar dynamic pressures, together with neuropathy, can eventually lead to ulcer formation [34]. Decreased cushioning property of plantar soft tissue is due to glycozilation of collagen fibrils which causes fragmentation, distortion and plantar heel-pad stiffness [35,36]. Also, there is a shift of the metatarsal fat pad forward of the metatarsal head, exposing the metatarsal head to the increased plantar pressure, and eventually ulceration [4]. Thus, increased planter pressure leads to high and localized stress and continuous pressure applied over a changed plantar pad for long time. Bony prominences with repeated moderate pressure will finally cause broken skin with resulting infection.

The traditional management of diabetic ulceration was directed primarily to controlling diabetes, ameliorating painful neuropathy and local wound management. The usual surgical management includes; debridement, amputations, skin grafts and local flaps. The condition usually recurs which may affect the patient's quality of life adversely. Diabetic patients are very sensitive to amputations even the little toe. Thus much effort must be done to save foot from amputations. Surgical treatment of diabetic ulcers should cure the present condition, and prevent the occurrence of future ulcerations. This work aims not only to reconstruct plantar defect but to restore foot structure and eliminate the trigger that induces ulceration and its recurrence.

PATIENTS AND METHODS

120 patients with diabetic foot have been presented to outpatient clinic at Ain Shams University Hospitals and Dar Al-Shifa Hospital from 2010 to 2015. Patients' age ranged between 55 to 68 years of age. 84 patients were males and 36 patients were females. Patients came to the clinic with non-healing ulcer. Many of them were on daily dressings with no improvement. Their main complaints were; painless non-healed ulcer, infection and deformed foot with or without loss of digits. 30% of patients were referred from endocrinologists. 60% of patients were referred from vascular surgeons. 18 patients had vascular revascularization. Complete history and general physical examination were performed to identify comorbidities and history of medications. Vascular examination of lower limbs and feet was done. Neurological examination and gait assessment was performed. Foot examination was done. Foot wear was inspected to see whether; is it appropriate for the foot. Table (1) shows important signs which can be found in diabetic foot examination.

Foot ulcers are assessed for number, site, size, depth, discharge, sloughs, redness and cellulitis of adjacent skin. Planter pressure is assessed using; harris beath mat, white powder on black sheet and Plantar scope Fig. (1). Routine investigations as; complete blood picture, blood glucose, hemoglobin A1c, renal function tests were requested. Wound cultures were taken. Foot X-ray was requested and evaluated closely for any plantar prominences or deformity of the foot and ankle. Consultation of Endocrinologists was done for control of diabetes. Medications were given to control neuropathy. Daily dressings with limb elevation were done. Patient's cardiac condition was carefully evaluated and echo was requested if needed.

Surgical technique:

The main principle is to excise the ulcer completely and to remove bony prominences and any osteomyeltic bone.

• *Claw toe:* The aim is to relax the long extensor tendons; which can be done by removal of the segment containing the metatarso-phalengeal joint, thus turning the claw foot deformity into a straight normally shaped fore foot. Local transposition skin flap is designed to be away from the weight bearing areas to cover the defect.

• *Hammer toe:* First trying to straighten the digits followed by physiotherapy. If it is not possible, reduction of distal phalanx is done to give a space for tendons to glide and prevent toes from touching the floor. Later on psudoarthrosis occurs with better gait.

• *Midfoot collapse:* Excision of the ulcer with removal of all destructed bones is done. Local skin flap is used with decreasing the plantar surface width.

• *Heel ulceration:* The ulcer and callus are excised. The bone spur is removed. Skin flap from the non-weight bearing area which is usually new instep area.

Follow-up:

The patient is not allowed to step on his/her foot for two weeks postoperatively. Plantar pressure is assessed to detect the new weight bearing areas. New plantar map is used as a guide for design of foot wear. Plantar pressure is reassessed every three months with the help of physical medicine. Patient is educated to self-examine his/her feet with meticulous pedicure. Once the patient notices a minimal ulceration should re-consult.

RESULTS

84 patients (70%) were males and 36 (30%) were females presented with NDFU. Mean age was 62.3 years. 44% have history of poor control of diabetes. Mean duration of diabetes is 20 years. Mean fasting blood glucose was (200mg/dl), mean postprandial blood glucose was (320mg/dl), and mean hemoglobin A1c was (9.8). 94 patients (78.3%) have previous debridement and 44 patients (36.6%) have one or more digit amputations. Comorbidities (cardiac, renal, ophthalmologic) were present in 23% of patients. The time of presentation as regards duration of the ulcer ranges between 4 months to 12 months. Patients have foot ulceration in one foot; however, the other foot may show signs of risk for ulceration. Ulcer formation was preceded by hyperkeratosis and tissue breakdown

deep to the plaque with cavity formation. Most patients have decreased or lost longitudinal arches. Five patients have reversed longitudinal arches with Rocker-bottom deformity. Fig. (2) shows decreased longitudinal arch of both feet with hyperkeratosis. Fig. (3) shows pre-ulcer stage with classic claw toe deformity. Fig. (4) shows an ulcer over head of first metatarsal bone with callosities, decreased longitudinal and transverse arch and subsequent change in plantar pressure distribution.

Numbers of ulcers per foot was one ulcer in 108 patients (90%) and 2-3 ulcers in 12 patients (10%). Those ulcers were located on the toe tips. Ulcer site varies between heads of metatarsals, forefoot, midfoot and hind foot. Fig. (5) shows a diagrammatic presentation of percentage of locations of NDFU in the study group. Table (2) shows the different sites of NDFU.

Foot ulcers were circular, with a punched out appearance. All ulcers were deep except those on the toe tips. Table (3) shows classification of NDFU according to ulcer size.

Neurological examination revealed decreased or lost 2-point discrimination, decreased pain sensations and decreased vibration perception in 108 patients (90%) of the affected feet. Ankle reflex was lost in 84 patients (70%).

All patients with NDFU have foot deformities. However, foot deformities could be present in pre-ulcer stage.

Plantar pressure assessment using; harris beath mat; walking with white powder over black surface; and plantar scope; revealed abnormal patterns of weight bearing areas. This was very much related to foot deformity.

Foot X-ray findings include; joint distension and destruction; bone fragmentation, demineralization and bone debris; and soft tissue swelling. Destroyed MTP joints extended to metatarsal head and proximal phalanx in some cases with ulceration over metatarsal heads. Foot X-rays in patients with midfoot collapse showed signs of foot structure disorganization as decreased calcaneal angle, disruption of talo-first metatarsal line, increased intertarsal spaces and shifted subtalar joints area to a lower position explaining loss of longitudinal arch and rocker-bottom deformity. Calcaneal spur was present in cases with heel ulcerations.

Vascular status was evaluated in all patients. Vascular surgery was done prior to foot reconstruc-

tive surgery. Continuous assessment of lower limbs vessels was incorporated in the follow-up protocol.

Postoperative outcome:

Excision of ulcer and coverage eliminated any portal for deep infection. Restoration of foot shape helped restoration of better function and gait, for example; in claw toe, resection of the area of metatarso-phalengeal joint eliminated the higher pressure point, lowered plantar pressure and relieved the tension on the long extensors. Also, straightening of the affected hammer toe gave space for tendon and could prevent recurrence of the condition. Patients' plantar pressure is reassessed after three months for follow-up and to help designing of foot wear. Ulcer recurrence didn't

occur at the same plantar areas. Patients could tolerate walking for a longer period as it became pain free and ulcer free.

Fig. (6) shows diagrammatic illustration of excision of metatarsophalangeal joint area. Fig. (7) shows a case with an ulcer over the metatarsal head with claw deformity of second toe. It shows postoperative coverage of the defect after ulcer excision and correction of the claw deformity. Fig. (8) shows diabetic foot with a large ulcer over midfoot with amputated two lateral toes, Charcot arthropathy and midfoot collapse. It shows reconstructive foot surgery with ulcer excision, removal of destructed bone, coverage with local flap and restoration of foot shape.

Table (1): Diabetic foot examination.

Vascular examination	Neurological examination	Foot structure & biomechanics	Foot ulcerations
Palpating dorsalis pedis and posterior tibial arteries A Doppler may be used	*Sensory examination:* 2-point discrimination; pin-prick test: - Normal - Decreased - Lost	Status of longitudinal foot arches: - Normal - Lost - Reversed	*Number:* - One - Multiple
Skin Colour changes	*Proprioception examination:* Vibration sense; - Present - Absent *Ankle reflex:* - Present - Absent - Exaggerated	Status of transverse foot arch	*Site:* - Toe tips - Forefoot - Midfoot - Hind foot *Relation to metatarsophalangeal joints:* - Related - Non-related
	Motor examination: Motor power reflexes	*Foot deformities:* - Claw toe - Hammer toe - Hallux valgus - Hallux rigidis - Rocker-bottom - Deformity - Others	*Size:* - Small; <1cm. - Intermediate; 1-3cm. - Large; >3cm.
Skin temperature: Normal Warm Cold	*Skin temperature:* Normal Warm Cold [Edematous warm foot may indicate charcot foot]	*Amputations:* None Loss of one digit Loss of multiple digits	*Depth:* Superficial Deep
Atrophic changes	*Signs of autonomic neuropathy:* Hair loss Brittle nails Dry skin Scales, hyperkeratosis Callus	*Plantar pressure measurements:* - Harris beath mat - Foot print using white powder on black sheet - Plantar scope	Floor Necrotic tissue, sloughs Discharge
Scars of previous vascular surgeries		Scars, grafts, ..	*Adjacent skin:* Normal Signs of cellulitis

Main areas of diabetic foot examination and important signs which can be found in diabetic foot examination.

Table (2): Different sites of NDFU and related foot deformity.

Anatomical location of the ulcer	No. of patients	%	Foot deformity
Toe tips	12*	10	Hammer toe or/mallet toe
First metatarsal head	42	35	Hallux valgus ± hallux regidus hallux malleus
Second, third, fourth and fifth metatarsal heads	39	32.5	Claw toes
Medial midfoot	12	10	Loss of transverse arch
Hind foot	24	20	Calcaneal spur
In-step area	3	2.5	Charcot foot with midfoot collapse

*: 12 patients have one main ulcer and associated with ulcers over one or more tips of the toes.

Table (3): Different sizes of foot ulcers.

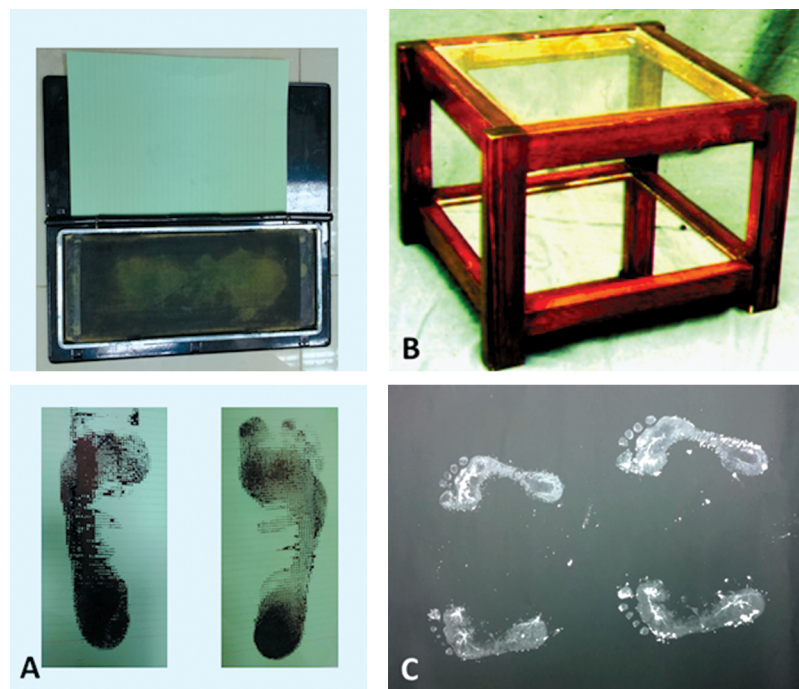| Size	No. of ulcers (137)
Small; <1cm.	12 (8.75%)
Intermediate; 1-3cm.	60 (43.80%)
Large; >3cm.	65 (47.45%)

Fig. (1): Plantar pressure assessment methods, (A) Harris beath mat, (B) Simple hand-made plantar scope, (C) Foot print using white powder on black sheet.
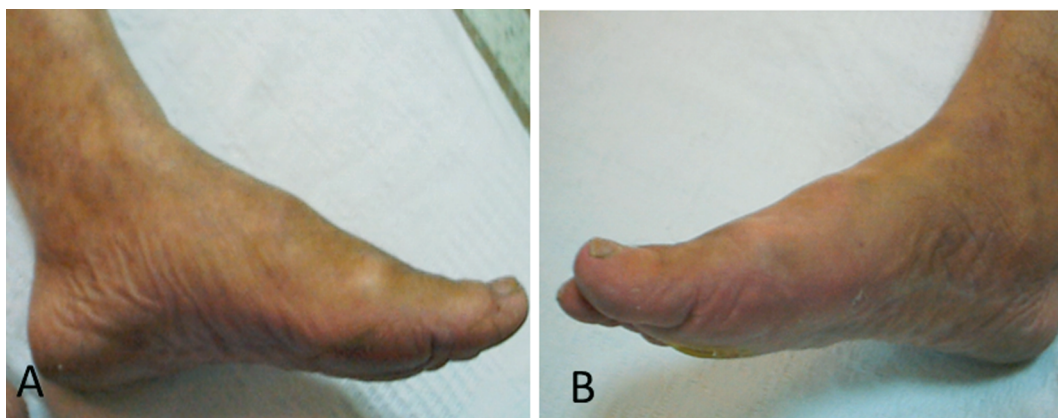

Fig. (2): Decreased longitudinal arch and hyerkeratosis in diabetic patient.

Fig. (3): Pre-ulcer stage with classic claw toe deformity.

Fig. (4): Left foot ulceration, (A) Plantar view shows an ulcer over head of first metatarsal bone, callosities, decreased transverse arch and old STSG used for previous foot ulcer. (B,C) Medial and Lateral views show hallux malleus deformity and decreased longitudinal arch. (D) Foot print shows abnormal plantar pressure distribution.
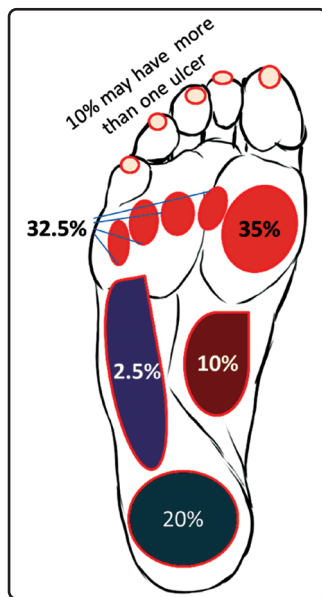

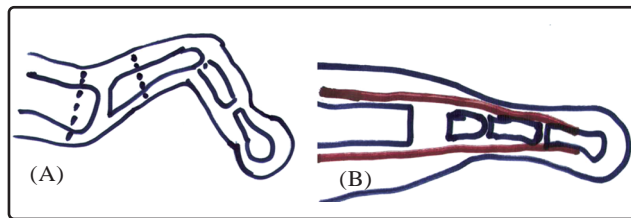Fig. (5): Sites of neuropathic diabetic foot ulcer.

Fig. (6): (A) Claw deformity of a toe, (B) Resection of the area of metatarso-phalengeal joint to straighten joint and eleminate pressure effect.
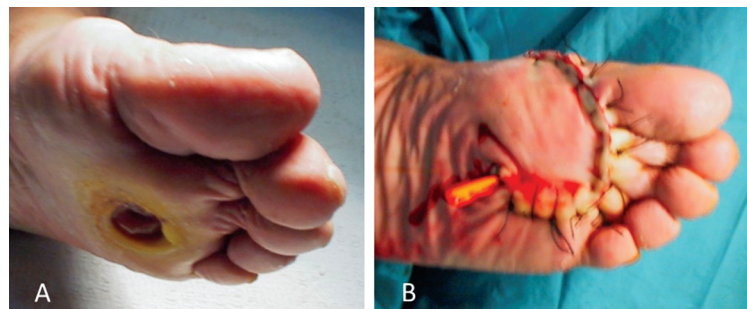

Fig. (7): (A) Typical neuropathic diabetic ulcer with claw toe deformity, (B) After reconstructive foot surgery; resection of MPJ and local flap.

Fig. (8): (A) Neuropathic diabetic ulcer with midfoot collapse, (B) X-ray foot shows charcot arthropathy, (C) Reconstructive foot surgery with local flap

DISCUSSION

NDFU may lead to devastating consequences. It is a serious problem as it predicts future infection, sepsis, amputations and limb loss. Prevention, rather than treatment, decreases patient morbidity and lowers care expenses [37]. The overall risk of a plantar ulcer in diabetic patients has been estimated as high as 25%, and the recurrence is 50% at three years despite best practices [1,2], up to 85% of diabetic patients with amputations had previous ulcerations [38,39]. Although the diagnosis of diabetes is improved, up to 10% of patients initially diagnosed with diabetes will be presented with ulceration [41]. The mean duration of diabetes in our study is 20 years.

Khanolkar et al., 2008 stated that after 25 years of diabetes, 50% of all patients show clinical evidence of neuropathy [9]. Peripheral neuropathy with loss of protective sensations, foot deformity, and thermal or mechanical trauma can form a triad which may put the foot at risk for ulceration. We found that all patients have signs of peripheral neuropathy and foot deformities with history of repeated neglected trauma. So this triad can be interrupted to help prevention and/ or recurrence of foot ulceration. Many authors recommended screening for sensation loss, detecting risk factors and preventive measures to reduce incidence of ulcerations [37,42].

In this study; 35% of patients had ulcers at the first metatarsal heads, 32.5% of patients had ulcers over the other metatarsal heads, 10% of patients had ulcers over mid foot, over hind foot in 20% of patients and over 2.5% of patients had ulcers over instep area. 10% of patients had associated ulcers over toe-tips. Edmond et al., 1986 stated that the classical site of NDFU is under the metatarsal heads. It can occur frequently on the tips of the toes and occasionally on the dorsum of the toe, between the toes and on the heel [43]. Plantar Pressure [PP] was assessed using; harris beath mat; walking with white powder over black surface; and plantar scope. All showed abnormal patterns with change of weight bearing areas which explained the occurrence of ulceration or prediction of inevitable ulceration. Ulcer locations in patients can be explained with the corresponding foot deformity and foot pattern. For example; patients who had claw toe deformity may have ulceration over the metatarsal heads and patient who had midfoot collapse, may have ulceration over instep area.

Principle treatment of ulcers includes; weight offloading, and local wound dressings to enhance healing [44,45]. Zimny et al., 2004 and Zimny et al., 2005 found that healing may take 2-3 months or even longer than 4 months in severe cases [46,47]. Oyibo 2001 found that healing will not occur in presence of osteomyelitis and the case may end into eventual amputation [48]. In our study, patients gave history of wound dressings for months with no real improvement in intermediate and large ulcers. As all patients have the full triad; wound dressing and weight offloading would not be efficient treatment. Debridement is done first with control of diabetes. We planned for reconstructive foot surgery. Care should be taken to preserve as much of the foot structure as possible, to allow functional weight bearing. Restoration of natural dynamic plantar pressure is crucial. We agreed with Garapati et al., 2004, Shen et al., 2013 and Schade and Andersen 2015 [49-51] that main principles of reconstructive foot surgery are; resection of all bony prominences, correcting deformities, removal of osteomyelitic bones and coverage. In case of claw toe deformity; resection of metatarsophalengeal joint area eliminates the pressing heads and lowers the plantar pressure. This helps in prevention of ulcer recurrence. We may resect the neighbor metatarsphalngeal joint through one incision as prophylactic procedures to straighten the fore foot. We also recommend tenotomies to be done in preulcer stage as prophylactic procedure. In case of Midfoot collapse; excision of the ulcer with removal of all destructed bones is done. Decreasing the plantar surface width could be achieved. In case of heel ulceration; the ulcer and callus are excised. The bone spur is removed.

Classic instep flap may not be the classic solution anymore in NDFU as the weight bearing areas are changing. The original instep area would be a new weight bearing area. The chosen flap is designed away of weight bearing areas. We do not recommend the use of intrinsic foot muscle flap, as they are involved in the pathology of NDFU and may be atrophied. In recurrent cases with previous use of small muscle flaps as flexor digitorum brevis, skin flaps as instep flap are compromised and susceptible to necrosis because of midline incision.

Plantar pressure was assessed postoperatively to help designing the proper foot wear. As Saccoa et al., 2014 emphasized on the importance of identifying load shifting in the early stages of the disease [52], we recommend reassessment of plantar pressure postoperatively and to be repeated monthly to detect any plantar pressure change and taking the preventive procedures. Postoperative results showed better functional and cosmetic outcome.

Patients are educated to self-examine his/her feet with meticulous pedicare. Once the patient notices a minimal ulceration, he/she should re-consult. Glycaemic control remains at the forefront of diabetes management and to reduce all diabetes-related complications [53,54]. Patient compliance is mandatory to prevent de novo ulcerations.

Conclusion:

NDFU may lead to devastating consequences. Excision of ulcers and soft tissue reconstruction may not be the best modality for diabetic ulcers. It is important to preserve foot structure and restore foot function as much as possible. Reconstructive foot surgery aims to eliminate the areas of high and localized pressure, correct the deformity and prevent recurrence of foot ulcerations. Strict use of this regimen can avoid foot or toe amputations which are very stressful for the diabetic patient. This will have a positive psychosocial and better quality of life.

REFERENCES

1- Young M.J., Breddy J.L., Veves A. and Boulton A.J.: The prediction of diabetic neuropathic foot ulceration using vibration perception thresholds. A prospective study, Diabetes Care, 17: 557-60, 1994.

2- Reiber G.E., Vileikyte L., Boyko E.J., Del Aguila M., Smith D.G., Lavery L.A. and Boulton A.J.: Causal pathways for incident lower-extremity ulcers in patients with diabetes from two settings, Diabetes Care, 22: 157-62, 1999.

3- Malhotra S., Bello E. and Kominsky S.: Diabetic Foot Ulcerations: Biomechanics, Charcot Foot, and Total Contact Cast, Semin. Vasc. Surg., 25: 66-9, 2012.

4- Edmonds M.E.: The Diabetic Foot: Pathophysiology and Treatment, Clinics in Endocrinology and Metabolism-Vol. 15. No. 4. November, 1986.

5- Boulton A.J.M.: The diabetic neuropathic foot: Neuropathic in Aetiology? Diabetes Med., 7: 852-8, 1990.

6- Pecoraro R.E., Reiber G.E. and Burgess E.M.: Pathways to diabetic limb amputation. Basis for prevention. Diabetes Care, May; 13 (5): 513-21, 1990.

7- Levin M.E., O'Neal L.W. and Bowker J.H. (eds): The diabetic foot, 5th ed. Mosby-Year Book, St Louis, 1994.

8- Pirart J.: Diabetes mellitus and its degenerative complications: A prospective study of 4400 patients observed between 1947 and 1973 (third and last part). Diabetes Metab., 3: 245-56, 1977.

9- Khanolkar M.P., Bain S.C. and Stephens J.W.: The diabetic foot. Q. J. Med., 101: 685-795, 2008.

10- Lazaro-Martinez J.L., Argon-Sanchez F.J., Beneit-Montesinos, et al.: Foot biomechanics in patients with diabetes mellitus. J. Am. Podiatr. Med. Assoc., 101: 208-14, 2011.

11- Harrison M.J.G. and Faris I.I.I.: The neuropathic factor in the aetiology of diabetic foot ulcers. Journal of Neurological Sciences, 28: 217-23, 1976.

12- Brand P.W.: The diabetic foot. In: Ellenberg M. & Rifkin I.I. (cds) Diabetes Mellitus, pp 803-28. New York: Medical Examination Publishing, 1983.

13- Ward J.D., Simms J.M., Knight G., Boulton A.J.M. and Sandler D.A.: Venous distension in the diabctie neuropathic foot (physical sign of arteriovenous shunting). Journal ofthe Royal Society of Medicine, 76: 1011-4, 1983.

14- Boulton A.J.M., Scarpello JlIIl and Ward J.D.: Venous oxygenation in the diabetic neuropathic foot: Evidence for arteriovenous shunting? Diabctologia, 22: 6-8, 1982.

15- Archer A.G., Roberts V.C. and Watkins P.l.: Blood flow patterns in painful diabetic neuropathy. Diabetologia, 27: 563-7, 1984.

16- Scarpello J.H., Martin T.R. and Ward J.D.: Ultrasound measurements of pulse wave velocity in the peripheral arteries of diabetic subjects. Clinical Science J.D., 58: 53-7, 1980.

17- Edmonds M.E., Roberts V.C. and Watkins I'.J.: Blood now in the diabetic neuropathic foot. Diabctologia, 22: 9-15, 1982.

18- Rayman G., Hassan A. and Tooke J.E.: Blood flow in the skin of the foot related to posture in diabetes mellitus. British Medical Journal, 292: 87-90, 1986.

19- Mascarenhas J.V. and Jude E.B.: Pathogenesis and medical management of diabetic Charcot neuroarthropathy. Med. Clin. North Am., 97: 857-72, 2013.

20- Rogers L.C. and Frykberg R.G.: The Charcot foot. Med. Clin. North Am., 97: 847-56, 2013.

21- Papanas N. and Maltezos E.: Etiology, pathophysiology and classifications of the diabetic Charcot foot. Diabet Foot Ankle, 4, 2013.

22- Schon L.C. and Marks R.M.: The management of neuroarthropathic fracture-dislocations in the diabetic patient. Orthop. Clin. North Am., 26: 375-92, 1995.

23- Schon L.C., Easley M.E. and Weinfeld S.B.: Charcot neuroarthropathy of the foot and ankle. Clin. Orthop., 349: 116-31, 1998.

24- Myerson M.S. and Edwards W.H.: Management of neuropathic fractures in the foot and ankle. J. Am. Acad. Orthop. Surg., 7: 8-18, 1999.

25- Myerson M.: Diabetic neuroarthropathy. In: Myerson M., ed. Foot and Ankle Disorders. Philadelphia: W.B. Saunders, 439-65, 2000.

26- Stuck R.M., Sohn M.W., Budiman-Mak E., Lee T.A. and Weiss K.B.: Charcot Arthropathy Risk Elevation in the Obese Diabetic Population, November, Volume 121, Issue 11, Pages 1008-14, 2008.

27- Gouveri E. and Papanas N.: Charcot osteoarthropathy in diabetes: A brief review with an emphasis on clinical practice. World J. Diabetes, 2 (5): 5965, 2011.

28- Markakis K., Bowling F.L. and Boulton A.J.M.: The diabetic foot in 2015: An overview, Diabetes Metab. Res. Rev., 32 (Suppl. 1): 169-78, 2016.

29- Ergen F.B., Sanverdi S.E. and Oznur A.: Charcot foot in diabetes and an update on imaging. Diabet Foot Ankle, 4, 2013.

30- Ledermann H.P. and Morrison W.B.: Differential diagnosis of pedal osteomyelitis and diabetic neuroarthropathy: MR imaging. Sem. Musculoskelet. Radiol., 9: 272-83, 2005.

31- Schweitzer M.E. and Morrison W.B.: MR imaging of the diabetic foot. Radiol. Clin. North Am., 42: 61-71, 2004.

32- Tan P.L. and Teh J.: MRI of the diabetic foot: Differentiation of infection from neuropathic change. The Br. J. Radiol., 80: 939-48, 2007.

33- Rogers L.C., Frykberg R.G., Armstrong D.G., et al.: The Charcot foot in diabetes. Diabetes Care, 34: 2123-9, 2011.

34- Boulton A.J.M., Meneses P. and Ennis W.J.: Diabetic foot ulcers: A framework for prevention and care. Wound Repair Regen, 7: 7-16, 1999.

35- Hsu T., Lee Y. and Shau Y.: Biomechanics of the heel pad for type 2 diabetic patients. Clinical Biomechanics (Bristol, Avon), 17: 291-6, 2002.

36- Paul R. and Bailey A.: Glycation of collagen: The basis of its central role in the late complications of ageing and diabetes. The International Journal of Biochemistry and Cell Biology, 28: 1297-310, 1996.

37- Pinzur M.S., Slovenkai M.P., Trepman E. and Shields N.N.: Diabetes Committee of American Orthopaedic F, S. Ankle, Guidelines for diabetic foot care: recommendations endorsed by the Diabetes Committee of the American Orthopaedic Foot and Ankle Society, Foot Ankle Int., 26: 113-9, 2005.

38- Adler A.I., Boyko E.J., Ahroni J.H. and Smith D.G.: Lower extremity amputation in diabetes. The independent effects of peripheral vascular disease, sensory neuropathy, and foot ulcers, Diabetes Care, 22: 1029-35, 1999.

39- Adler A.I., Erqou S., Lima T.A. and Robinson A.H.: Association between glycated haemoglobin and the risk of lower extremity amputation in patients with diabetes mellitus-review and meta-analysis, Diabetologia, 53: 840-9, 2010.

40- Reiber E.: The epidemiology of diabetic foot problems, Diabet. Med., 13 (Suppl. 1), S6-S11, 1996.

41- Boulton A.J., Vileikyte L., Ragnarson-Tennvall G. and Apelqvist J.: The global burden of diabetic foot disease, Lancet, 366: 1719-24, 2005.

42- Singh N., Armstrong D.G. and Lipsky B.A.: Preventing foot ulcers in patients with diabetes, J.A.M.A., 293: 217-28, 2005.

43- Edmonds M.E., Blundell M.P., Morris H.E., et al.: Improved survival of tile diabetic foot: The role of a special foot clinic. Quarterly Journal of Medicine, 1986.

44- Armstrong D.G., Nguyen H.C., Lavery L.A., Van Schie C.H., Boulton A.J. and Harkless L.B.: Off-loading the diabetic foot wound: A randomized clinical trial, Diabetes Care, 24: 1019-22, 2001.

45- Mueller M.J., Diamond J.E., Sinacore D.R., Delitto A., Blair V.P. III, Drury D.A. and Rose S.J.: Total contact casting in treatment of diabetic plantar ulcers. Controlled clinical trial, Diabetes Care, 12: 384-8, 1989.

46- Zimny S., Schatz H. and Pfohl M.: The effects of ulcer size on the wound radius reductions and healing times in neuropathic diabetic foot ulcers, Exp. Clin. Endocrinol. Diabetes, 112: 191-4, 2004.

47- Zimny S. and Pfohl M.: Healing times and prediction of wound healing in neuropathic diabetic foot ulcers: A prospective study, Exp. Clin. Endocrinol. Diabetes, 113: 90-3, 2005.

48- Oyibo S.O., Jude E.B., Tarawneh I., Nguyen H.C., Harkless L.B. and Boulton A.J.: A comparison of two diabetic foot ulcer classification systems: The Wagner and the University of Texas wound classification systems, Diabetes Care, 24: 84-8, 2001.

49- Garapati R. and Weinfeld S.B.: Complex reconstruction of the diabetic foot and ankle, the American Journal of Surgery 187 (Suppl to May 2004) 81S-86S, 2004.

50- Shen W. and Wukich D.: Orthopaedic surgery and the diabetic Charcot foot. Med. Clin. North Am., 97: 873-82, 2013.

51- Schade V.L. and Andersen C.A.: A literature based guide to the conservative and surgical management of the acute Charcot foot and ankle. Diabet Foot Ankle, 6: 26627, 2015.

52- Saccoa I.C.N., Hamamotoa A.N., Tonicellia L.M.G., Wataria R., Ortegab N.R.S. and Sartora C.D.: Abnormalities of plantar pressure distribution in early, intermediate, and late stages of diabetic neuropathy, Gait & Posture, 40: 570-4, 2014.

53- The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N. Engl. J. Med., 329: 977-86, 1993.

54- Inzucchi S.E., Bergenstal R.M., Buse J.B., et al.: Management of hyperglycemia in type 2 diabetes, 2015: A patient centered approach: update to a position statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care, 38: 140-9, 2015.