



DIABETIC FOOT ULCER AND ITS MANAGEMENT

Medical Surgical Nursing

Ms. Mathivathani M

Assistant Professor, LPS Institute Of Cardiology & Cardiovascular Thoracic Surgery, G.S.V.M Medical College, Kanpur, UP.

Ms. Priyanka Singh

Assistant Professor, Autonomous State Medical College, Basti, UP.

ABSTRACT

Diabetes-related foot care is one of the most ignored aspects of diabetes care in India. Due to social, religious, and economic compulsions, many people walk barefoot. Poverty and lack of education lead to the usage of inappropriate footwear and late presentation of foot lesions. Hence, this article aims to highlight the knowledge to understand the barriers and facilitators specific to the population. Foot treatments include diabetes-related foot education, therapeutic footwear, and routine foot care. Patients' attention to foot care and self-management is the key to success among all the aspects that might aid in these duties. A combination of healthcare personnel and patient education, multidisciplinary foot ulcer treatment, prevention, and regular monitoring can lower amputation rates by 49–85%⁸. As a result, the IDF (International Diabetes Federation) and WHO have set aims to cut amputation rates by up to 50%².

KEYWORDS

Diabetic foot ulcers (DFUs), Foot care, Elastography, podiatrist.

INTRODUCTION

According to the International Diabetes Federation, India ranks second in the world and first in Southeast Asia, with around 74 million people with diabetes in 2021, accounting for one in every seven people worldwide.¹ Diabetes management costs approximately USD 114.40 per person per year in India. The theme for World Diabetes Day 2021-23 is 'Access to Diabetes Care'⁴ emphasizing the significance of diabetes treatment access.

In India, Diabetic foot ulcers (DFUs) affect 15% of patients with diabetes during their lifetime. Evidence from the published literature showed 100,000 leg amputations/year due to diabetes-related problems. In India, 25% of the diabetic population develops DFUs, of which 50% become infected, requiring hospitalization, while 20% need amputation. DFUs contribute to approximately 80% of all non-traumatic amputations in India annually.

In addition, India is the most expensive country for DFU care, as 5.7 years (68.8 months) of an average patient's income is required to pay for complete DFU therapy. In total, 50% of DFU patients who have one amputation suffer another amputation within the next 2 years.⁵ The mortality rate following amputation rises from 13–40% in 1 year to 39–80% in 5 years.^{4,5,6}

This scenario necessitates a routine examination of the foot for the existence of any abnormalities. The problem is to properly adopt foot care while keeping costs in mind.

Indication

All patients with diabetes should receive education on proper diabetic foot care. Prevention of diabetic foot complications includes identifying the at-risk foot, daily exam and inspection, patient/family/healthcare provider education, appropriate shoe gear, and proper and early treatment of pre-ulcerative lesions. Higher risk patients should obtain a referral to podiatry for management and monitoring. The International Working Group on Diabetic Foot (IWGDF) classification recommends diabetic foot screening by a medical professional

- Once a year for individuals without peripheral neuropathy
- Every six months for individuals with peripheral neuropathy
- Every 3 to 6 months for individuals with peripheral neuropathy, peripheral arterial disease and/or foot deformity
- Every 1 to 3 months for individuals with peripheral neuropathy and a history of pedal ulceration or lower extremity amputation⁶²

Barriers

Lack Of Awareness

Patients who visit the foot care facility for the first time are unaware of the diabetes-related foot issues that might emerge and the associated difficulties. The importance of foot care and frequent foot examination is often overlooked. This is confirmed by the research of Soumya et al.

and Saurabh et al.^{7,8} People aren't aware that ill-fitting shoes, harsh bottoms, and going barefoot can lead to diabetes-related foot issues. Patients ignore foot examinations and only glance at their feet when there is blood on the floor or the cut becomes painful. This is confirmed by a statistical test that shows that persons with diabetes for a longer period retain more foot care knowledge.

Religious Practices

Men and women throughout most of the country go barefoot to local sites and temples, as is customary with any religious activity, as recorded in Vibha et al.⁹ and Guell et al.¹⁰ Few men and women, particularly in South India, do not wear footwear even for a month when on pilgrimage to specific temples. They consider it a religious activity. Fasting during Ramzan (a religious festival) contributes to poor diabetes control and, as a result, poor diabetes-related foot outcomes.

Time and Cost Factor

Most patients arrive early in the morning to perform fasting glucose testing, post-prandial sugar tests, diet counselling, ECG checks, and then meet with a diabetes-related expert if necessary. They may also be requested to perform eye examinations and foot assessment tests. It takes two days to conduct all of the tests and meet the podiatrist.

The foot examination tests take at least 30 minutes for each patient. The International Working Group on the Diabetic Foot (IWGDF)¹¹ advises foot evaluation at least once a year for diabetes patients without current difficulties and once every 6 months or 3 months for individuals at risk, depending on the risk or complication involved. Patients going from adjacent communities must factor in travel time and expense, which is a significant obstacle to efficient wound treatment.

Socio-Economic Factor

People in the educated middle and upper middle classes had higher levels of awareness and foot care knowledge. When a patient's financial situation is bad, individuals begin to ignore foot issues due to the lack of financial assistance. People are also less alert when they live in places where there is a dearth of understanding about the complications and how to prevent them. This is similar to what Agha et al. discovered in¹². Household income and the total number of daily medications statistically significantly predicted foot self-care behavior in HF-comorbid T2D adults.

Working Environment Factor

Diabetes-related foot sufferers have additional problems in the workplace. For example, a man working in the construction business had blisters on his foot as a result of contact with cement and sharp things such as steel, while another man developed a web space infection as a result of continual soaking of his foot due to

housekeeping activities. Depicts the visual and infrared thermal images that were captured.¹³

Access To Specialized Foot Care And An Increasing Number Of Patients

In Bangalore, there are three specialized foot care facilities where the same type of test is performed. There are no specialized centers in adjacent areas; thus, individuals from a 100 km radius in Karnataka come to this facility. The facility serves patients not just from Karnataka but also from neighbouring states, including Andhra Pradesh and Tamil Nadu. The number of patients continues to rise, putting a strain on podiatrists.

When an operation to amputate a foot or toe is scheduled, patient waiting times increase, forcing the facility to limit the number of new patients enrolled. This is a major concern for patients who travel significant distances (approximately 100 km from Hindupur in Andhra Pradesh and Krishnagiri in Tamil Nadu) to see the podiatrist.¹²

Dependency By The Patient

Patients with diabetes, particularly women, expect someone to accompany them to the facility. Owing to this dependency, the visit gets delayed, and hence, the wound becomes infected. This further causes a delay in the therapeutic procedure. Similarly, patients with limited mobility also expect a member of their family to accompany them to the care facility. Such dependencies postpone effective treatment at the appropriate moment, resulting in poor wound care outcomes.

Communication Gap

In total, 75% of patients see both a diabetes specialist and a foot care specialist and receive medical prescriptions from both. When the foot care professional instructs the patient to discontinue the drug after a certain length of use, some individuals misinterpret it as the complete set of prescriptions and stop taking all medications, including diabetes medicines. This is a serious issue since it raises blood glucose levels, causing nerve damage. Certain people quit taking their drugs abruptly before the time limit because they have produced some undesired side effects without informing their doctor. This, once again, impedes successful therapy. Few people do not finish their antibiotic course, and as a result, they develop resistance to some of the antibiotics, requiring the doctor to provide a larger dose of another potent and expensive antibiotic to combat the infection.

Poor Blood Glucose Level Monitoring

Many patients only check their blood glucose levels once a year, and others go even longer periods. Diabetes management failure results in poor diabetes-related foot care outcomes. Despite the fact that the aforementioned hurdles impede good foot care treatment and wound management, some facilitators attempt to enhance foot care and wound management at the centre, as shown in the next section.¹⁴

Facilitators

- The presence of highly experienced surgeons and nurses for quick action—limb salvage surgery and vascular surgery—is a facilitator, as is assessment of various diabetes problems such as nephropathy, retinopathy, and cardiology under one roof.
- Self-foot care and patient education, as documented in, are also major facilitators here, resulting in a decreased proportion of high-risk patients.
- Diet counselling to keep blood glucose levels under control, physiotherapy to alleviate discomfort and promote mobility, provision for purchasing specialist diabetes-related footwear within the facility, and the surgeons' attitude and degree of care and concern for patients are also facilitators.¹⁵

Potential Facilitators

- Emerging technologies [such as laser Doppler flowmetry, elastography, infrared thermography, plantar pressure, and pressure gradient system for DFUs, as well as other rehabilitation modalities such as off-loading devices and electrotherapy] might be useful.
- Also available are foot care education experts, in addition to podiatric doctors, to give information and instruction to patients. Furthermore, as indicated, health education on diabetes by school instructors would have a significant influence on the awareness of diabetes as a disease, as well as its prevention and treatment, which would enhance the results of diabetes-related complications.¹⁶

- During a pandemic, digital/virtual diabetes clinics potentially enhance diabetes-related foot care outcomes.
- Monitoring self-care activities by delivering automated SMS reminders to examine the feet regularly will also be helpful. Healthcare on the go, such as mHealth, might be investigated because it has been demonstrated to be possible and acceptable. Identifying patients who might serve as foot care education specialists would improve diabetes-related foot outcomes.¹⁷
- The authors reported using a non-invasive and non-contact screening technology, such as an infrared thermal image-based diagnostic system, as part of their larger investigation.¹⁸
- Infrared thermography and visual systems are used in remote monitoring systems to save time and travel, as documented in Rural foot care camps are being organized.
- In addition, new specialist foot care clinics with suitable resources could be established in the surrounding rural regions.²⁰

Nail And Skin Care

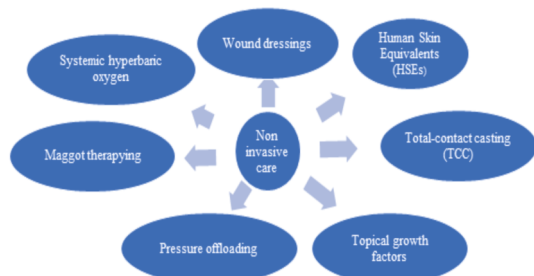
- Diabetic patients should examine their feet on a daily basis. The maceration, especially between the toes, is usually caused by a fungal infection and should be observed carefully. It is recommended to use a mirror to better observe the plantar surface of the foot. If the diabetic patient's vision is compromised due to retinopathy or the patient is unable to perform their daily foot examination, another fully trained individual should perform the task on their behalf.
- The feet should be washed and dried at least once a day. It is important to dry the inter-digital spaces between the toes very carefully.
- The temperature of the water used for rinsing the foot should be less than 37 centigrade. It is recommended to use the elbow or the forearm in order to estimate the temperature of water. This method helps to prevent accidental burning of the extremities due to characteristic glove-stocking neuropathy in diabetic patients.
- The diabetic patients, especially the ones with sensory neuropathy, should not use the heating pads over their bodies. It is also recommended to warn the patient not to place their feet close to the heaters during the winter.
- All the patients, especially those with diabetic neuropathy or high-risk diabetic foot, should be instructed to use footwear both indoors and outdoors. It is recommended to wear special shoes with adequate size when the patient is walking indoors on the carpet. The use of shoes without stockings in diabetic patients should be discouraged. In patients with neuropathy, it is also recommended to use footwear with an enclosed frontal part to prevent minor trauma to the forefoot.
- It is recommended to observe and physically examine the inside of the patient's shoes daily. This recommendation is given to detect any external objects inside the shoes and to look for pressure effects on different surfaces of the patient's feet. The lateral engorgement of the shoes is an indication of pressure exerted by the first and fifth metatarsals, and the swelling observed in the frontal part of the shoes is caused by the pressure of the distal phalanges of the first digit.
- Diabetic patients due to autonomic neuropathy present with increased perspiration in the upper thorax and lower extremities, and perspiration. As a result, the dryness of the plantar surfaces of the feet and heels is common. The minor trauma combined with the dry skin creates cracks which facilitate the entrance of microorganisms into the skin, and consequently, foot infection is inevitable. It is recommended to apply lubricants containing urea or salicylates with the ability to penetrate dry and hyperkeratotic skin. However, the use of lubricants in the inter-digital spaces is discouraged.
- In diabetic patients, it is recommended to change and put on clean socks on a daily basis.
- The patients should be discouraged from wearing tight socks, and the seams should be toward the outside. In diabetic patients, it is not advisable to wear stockings up to the knee.
- Especially in female diabetics, any kind of manipulation of the nails is not recommended. The nails should not be cut in a rounded fashion; the straight across cut is recommended.
- The patient should be instructed not to use any kind of chemical substances or commercial pads, or plasters in order to treat the calluses of the feet.^{27,28}
- The global patient and economic burden of diabetic foot disease can be considerably reduced when evidence-based preventative treatment is implemented in the foot care of people with diabetes

who are at risk of developing a foot ulcer. Reducing the risk of ulceration also reduces the risk of infection, hospitalization, and lower-extremity amputation in these patients. While not drawing most attention from clinicians and researchers, foot ulcer prevention is the best way to prevent severe morbidity and mortality in people with diabetes. We think that following the recommendations for preventative treatment in this guideline will help health care professionals and teams provide better care for diabetic patients who are at risk of ulceration.²⁸

Management Modality

Non-invasive Care

The most prevalent management modality for DFU is local care, in which many potential avenues of treatment can be utilized. These includes



Wound Dressings

Wound dressings are the most basic and common treatment measure, and although they serve a vital purpose in the management of DFU, other methods have proven vastly more effective in comparison to or in conjunction with wound dressings.

Human Skin Equivalent (HSE)

HSE is more effective compared to the standard treatment of saline-moistened gauze in reducing the rates of amputation and infection and in improving the rate of ulcer healing. One randomized controlled trial (RCT) assessed the effectiveness of Graft skin, a living skin equivalent indicated for use in noninfected, nonischemic DFU. Graft skin was applied weekly for a maximum of 4 weeks or until complete healing occurred. The results of the trial highlighted the increased effectiveness of HSE in comparison to the control group, in which ulcers were treated only with saline-moistened gauze. The use of HSE resulted in an 18% increase in complete wound healing when compared to the control group³³. Despite these impressive results, one limitation to this treatment is that HSE may have limited availability or accessibility.

Offloading, TCC

Pressure offloading serves as one of the primary treatments of DFU, primarily in ulcers accompanied by neuropathy, with many variants being utilized. For ischemic DFUs, however, revascularization is more commonly used. Common methods of offloading include bed rest, wheelchair use, implementation of a crutch-assisted gait, total contact casting, use of felted foam, use of therapeutic shoes, and use of removable cast walkers.³⁴ The most effective offloading treatment is TCC, in which full casts are applied by an experienced physiotherapist and are changed weekly for 2-3 weeks or until healing has occurred. One RCT found that TCC was extremely effective in increasing ulcer healing and reducing infection when compared to traditional dressing changes and other offloading methods. The study reported a 91% rate of healing within the TCC population, compared to a 32% rate of healing in the control group. This rate was reported following 65 days. Furthermore, the TCC group reported a 0% incidence of infection, while the same in the control group was reported as 26%³⁵. Multiple other studies have reported similar results, with TCC being an extremely effective treatment for DFU, particularly when compared to traditional dressing changes. One adverse effect of this treatment, however, is fungal infection, but this was addressed with topical treatment and did not prevent continued casting. TCC requires an experienced physiotherapist, constant replacement, and care.

Hyperbaric Oxygen Therapy

Another treatment for DFU is systemic hyperbaric oxygen therapy (HBOT), which is reserved for advanced cases and aimed at reducing the risk of amputation. This treatment is prevalent, particularly in the treatment of infected DFU, where a systematic review identified 6 RCTs that evaluated chronic DFU. Systemic HBOT sessions are

usually conducted in 45 to 120-minute sessions once or twice daily at pressures between 1.5-3.0 ATA. This method resulted in significantly reduced rates of major amputation compared with the usual care of DFU. HBOT is typically used as an adjunctive therapy to normal wound care measures³⁶. However, this treatment modality is quite expensive, is still not fully researched, and may warrant further trials.

Larvae Therapy (Maggot Therapy)

Maggot therapy is another well-researched technique concerning the treatment of chronic wounds in which maggots are placed on the wound area. This treatment method has been shown to significantly facilitate debridement. Maggot therapy also enabled faster development of granulation tissue and more significantly decreased wound surface area compared to other topical treatments such as hydrogel dressings. Maggot therapy also did not affect disinfection or complete healing rate for the wound.³⁷

Topical Growth Factors

Topical growth factors, particularly platelet-derived growth factors, have also proven effective in increasing ulcer healing rates when compared with placebo. Growth factors serve as principal immediate mediators of wound healing, and when applied in the setting of DFU, accelerate ulcer healing. Meta-analysis evaluated 26 RCTs with 2088 participants and focused on recombinant epidermal growth factor, autologous platelet-rich plasma, and recombinant human platelet-derived growth factor. Overall, each of the 3 treatments significantly improved the rate of healing when used alongside standard treatment, with recombinant human epidermal growth factor slightly favoured when compared to other growth factors.³⁸

Shock Wave Therapy

Extracorporeal shockwave therapy (ESWT) has been reported to accelerate the healing of soft tissue wounds when treating DFU. ESWT is utilized to stimulate osteoblasts and, in turn, facilitate soft tissue healing. There have been promising clinical trial results, indicating that ESWT is more effective in the treatment of DFU when compared to traditional methods. Two multi-national RCTs were conducted to compare the efficacy of ESWT when used adjunctively with standard care and other DFU treatments. The trials both lasted 12 weeks and showed a reduction of wound volume by more than 50% with the use of ESWT when compared to standard treatment alone³⁹.

Stem Cell Therapy

The cornerstone of available treatment options currently includes treatment of infection, surgical debridement, and revascularization⁴⁰. Better understanding of the tissue remodelling process, which comprises inflammation, cell migration, neovascularization, and tissue proliferation, has paved the way for stem cell-based therapy to become viable for the treatment of DFU⁴¹. Stem cells aid wound healing by secretion of cytokines that play an important role in cell migration, angiogenesis, remodelling of extracellular matrix, and regeneration of nerves.⁴² Also, stem cell capacity for differentiation into various cell types, including myofibroblasts and endothelial cells, optimizes wound healing.⁴³

The stem cell types that have been studied to aid in diabetic foot treatment are mainly adult stem cells (ASCs). Bone marrow-derived mesenchymal stem cells (BM-MSC) are the most extensively studied among the different ASCs; other types include adipose-derived stem cells, umbilical cord-derived mesenchymal stem cells (UC-MSC), and peripheral blood-derived mesenchymal stem cells⁴⁴. The use of BM-MSC in the treatment of DFU demonstrated more effective ulcer healing, with improvements in Ankle-Brachial Index (ABI), angiogenesis, and blood flow when compared to local treatment.^{47,48} Even functional improvement with a decrease in rest pain and an increase in claudication distance was demonstrated. Decreased amputation when compared to conventional treatment was also seen. Furthermore, combining UC-MSC stem cell therapy with traditional angioplasty resulted in improvements in ABI, claudication distance, and skin temperature.⁴⁸

Invasive Treatment Strategies

Debridement

Debridement is a major component in the treatment of DFU, particularly due to its ability to alter the environment of the chronic wound through the removal of necrotic and nonviable tissue and foreign debris, which impede the healing process. Debridement may not always lead to complete healing of the DFU, but it serves as an

important preliminary step in the treatment. Following debridement, the wound is further analysed, and if necessary, other treatment paths are pursued.⁵⁵ Debridement is commonly used in conjunction with other treatment modalities.

Revascularization (Angioplasty)

When patients with DFU also have a history of peripheral arterial disease (PAD), delayed healing, higher complication rates, and an increased chance of potential amputation may be observed. Thus, when patients have both DFU and chronic limb ischemia, revascularization can serve as a promising treatment option. According to various studies, the ulcer healing rate following revascularization ranges from 46% to 91%, representing a higher rate of healing compared to PAD patients who do not undergo revascularization.⁵⁶ Revascularization options include stenting and surgical bypass if other interventions are not possible. Atherectomy, shockwave treatment for calcified lesions, and balloon revascularization (cutting, drug-coated, cryoplasty) can also be used alone or with stenting.⁵⁷ In a clinical trial in which 80 patients who underwent foot revascularization procedures, promising results were also shown. All patients in this study underwent an endovascular procedure (balloon angioplasty). The patients were followed for 12 months after the procedure, and results showed that 56.2% of the patients fully recovered, 58.7% had minor amputations, and only 16.2% required major amputations. Overall, revascularization is an effective treatment for DFU, especially when the patient is at risk of amputation.⁵⁸ However, the effectiveness of the vascular procedure differs among patients, and it also does not reduce the risk of death associated with PAD. It is important to consider the role of complex therapy (including medical management) in conjunction with revascularization in the treatment of DFU. This includes close monitoring of glucose, lipids, and blood pressure, and the use of antiplatelet therapy following the surgical procedure. Compared with initial supervised exercise training (SET) alone, endovascular therapy in combination with SET is associated with significant improvements in total walking distance, ABI, and risk of future revascularization or amputation. On the other hand, endovascular therapy alone was not associated with an improvement in functional capacity.⁵⁹ It is also important to note that post-endovascular procedure patients must be started on dual antiplatelet therapy, including aspirin plus clopidogrel or ticagrelor for several months. Statins therapy has also been proven to stabilize any plaques present before and after revascularization.

Skin Grafting

Skin grafting may serve as a solution when DFUs become more severe, offering a chance to replace the infected skin and promote the healing process. There are a variety of skin grafting techniques that may be used, including bioengineered or artificial skin, autografts (taken from the patient), allografts (taken from another person), or xenografts (taken from animals). A review article that analyzed 17 RCTs concluded that skin grafting and tissue replacement, when used in conjunction with standard treatment, led to an increase in the healing rate of DFU and slightly lowered the chance of amputation. However, evidence of long-term effectiveness is uncertain.⁶⁰

Amputation

Amputation represents the final management option when treating DFU and is reserved for the most chronic levels of infection or deformity that render the foot non-functional. Amputation can be classified as either minor or major, with minor amputation being the removal of a smaller area (e.g., removal of a toe or a part of the foot). Major amputation, however, can be performed above or below a major joint such as the knee or elbow. In a clinical trial, minor amputation was performed for 38.4% and major amputation was performed for 6.8% of patients with DFU.⁶¹

CONCLUSION

Although there has been much progress in our understanding of the etiopathogenesis and management of diabetic foot disorders over the last 30 years, much of what we use in clinical practice today still lacks an evidence-base. This is particularly true for example for dressings. The International Working Group on the Diabetic Foot has reported on the details required in the planning and reporting of intervention studies in the prevention and management of diabetic foot lesions. Details of the necessary trial design, conduct, and reporting should be taken into account when assessing published studies on interventions in the diabetic foot. Most important of all however in the management of patients with diabetic foot disorders, is to remember that the patient

has frequently lost the “gift of pain” that protects most of us from developing significant foot problems but, when absent, can lead to devastating consequences.

REFERENCES

- Akila, M.; Ramesh, R.S.; Kumari, M.J. Assessment of diabetic foot risk among diabetic patients in a tertiary care hospital, South India. *J. Educ. Health Promot.* **2021**, *10*, 14. [Google Scholar] [CrossRef] [PubMed]
- Apelqvist, J.; Bakker, K.; van Houtum, W.H.; Schaper, N.C. Practical guidelines on the management and prevention of the diabetic foot. *Diabetes/Metab. Res. Rev.* **2008**, *24* (Suppl. S1), S181–S187. [Google Scholar] [CrossRef]
- International Diabetes Federation. IDF Diabetes Atlas, 10th ed.; IDF: Brussels, Belgium, 2021; Available online: <https://www.diabetesatlas.org> (accessed on 20 January 2023).
- World Diabetes Day (WDD). Available online: <https://worlddiabetesday.org/about/theme/> (accessed on 20 January 2023).
- Ghosh, P.; Valia, R. Burden of Diabetic Foot Ulcers in India: Evidence Landscape from Published Literature. *Value Health* **2017**, *20*, A485. [Google Scholar] [CrossRef]
- Armstrong, D.G.; Wrobel, J.; Robbins, J.M. Guest editorial—are diabetes-related wounds and amputation worse than cancer? *Int. Wound J.* **2007**, *4*, 286–287. [Google Scholar] [CrossRef] [PubMed]
- Soumya, S.; Ajith, A.K.; Aparna, V.K.; Deepa, V.; Prajisha, V.; Rinsha, C.; Shinumol, V. Risk of Developing Diabetic Foot, Practice and Barriers in Foot Care among Clients with Type II Diabetes Mellitus. *Int. J. Health Sci. Res.* **2016**, *6*, 310–316. [Google Scholar]
- Saurabh, S.; Sarkar, S.; Selvaraj, K.; Kar, S.; Kumar, S.; Roy, G. Effectiveness of foot care education among people with type 2 diabetes in rural Pudukcherry, India. *Indian J. Endocrinol. Metab.* **2014**, *18*, 106–110. [Google Scholar] [CrossRef] [PubMed]
- Vibha, S.P.; Kulkarni, M.M.; Ballala, A.B.K.; Kamath, A.; Maiya, G.A. Community-based study to assess the prevalence of diabetic foot syndrome and associated risk factors among people with diabetes mellitus. *BMC Endocr. Disord.* **2018**, *18*, 43. [Google Scholar] [CrossRef]
- Guell, C.; Unwin, N. Barriers to diabetic foot care in a developing country with a high incidence of diabetes related amputations: An exploratory qualitative interview study. *BMC Health Serv. Res.* **2015**, *15*, 377. [Google Scholar] [CrossRef]
- Singh, N.; Armstrong, D.G.; Lipsky, B.A. Preventing foot ulcers in patients with diabetes. *JAMA* **2005**, *293*, 217–228. [Google Scholar] [CrossRef] [PubMed]
- Aga F, Dunbar SB, Kebede T, Guteta S, Higgins MK, Gary RA. Foot self-care behaviour in type 2 diabetes adults with and without comorbid heart failure. *Nurs Open.* **2022** Sep;9(5):2473–2485. doi: 10.1002/nop.2.1265. Epub 2022 Jun 9. PMID: 35678585; PMCID: PMC9374405.
- B. G., S., V., U., Shivaram, J. M., Belehali, P., M. A., S., H. C., C., Sikkandar, M. Y., & Briochi, M. L. (2023). Diabetic Foot Assessment and Care: Barriers and Facilitators in a Cross-Sectional Study in Bangalore, India. *International Journal of Environmental Research and Public Health*, *20*(11), 5929. <https://doi.org/10.3390/ijerph20115929>
- Reiber, G.E. Epidemiology of Foot Ulcers and Amputations in the Diabetic Foot. In Levin and O'Neal's The Diabetic Foot, 6th ed.; Bowker, J.H., Pfeifer, M.A., Eds.; Mosby: St Louis, MO, USA, 2001; pp. 13–32. [Google Scholar]
- Bakker, K.; Apelqvist, J.; Schaper, N.C.; International Working Group on the Diabetic Foot Editorial Board. Practical guidelines on the management and prevention of the diabetic foot, 2011. *Diabetes/Metab. Res. Rev.* **2012**, *28* (Suppl. S1), 225–231. [Google Scholar] [CrossRef]
- International Working Group on the Diabetic Foot (IWGDF). Available online: <https://iwgdfguidelines.org/wp-content/uploads/2019/05/IWGDF-Guidelines-2019.pdf> (accessed on 20 January 2023).
- Lung, C.-W.; Wu, F.-L.; Liao, F.; Pu, F.; Fan, Y.; Jan, Y.-K. Emerging technologies for the prevention and management of diabetic foot ulcers. *J. Tissue Viability* **2020**, *29*, 61–68. [Google Scholar] [CrossRef]
- Selvam, S.; Murugesan, N.; Snehalatha, C.; Nanditha, A.; Raghavan, A.; Simon, M.; Susairaj, P.; Ramachandran, A. Health education on diabetes and other non-communicable diseases imparted to teachers shows a cascading effect. A study from Southern India. *Diabetes Res. Clin. Pract.* **2017**, *125*, 20–28. [Google Scholar] [CrossRef]
- Phillip, M.; Bergenstal, R.M.; Close, K.L.; Danne, T.; Garg, S.K.; Heinemann, L.; Kovatchev, B.P.; Laffel, L.M.; Kovatchev, B.P.; Mohan, V.; et al. The digital/virtual diabetes clinic: The future is now—Recommendations from an international panel on diabetes digital technologies introduction. *Diabetes Technol. Ther.* **2021**, *23*, 146–154. [Google Scholar] [CrossRef]
- Ramachandran, A.; Kumar, R.; Nanditha, A.; Raghavan, A.; Snehalatha, C.; Krishnamoorthy, S.; Joshi, P.; Tesfaye, F. M. Diabetes initiative using text messages to improve lifestyle and health-seeking behaviour in India. *BMJ Innov.* **2018**, *4*, 155–162. [Google Scholar] [CrossRef]
- Sari, Y.; Yusuf, S.; Haryanto, A.; Sumeru, A.; Saryono, S. The barriers and facilitators of foot care practices in diabetic patients in Indonesia: A qualitative study. *Nurs. Open* **2021**, *9*, 2867–2877. [Google Scholar] [CrossRef]
- Viswanathan, V.; Shobhana, R.; Snehalatha, C.; Seena, R.; Ramachandran, A. Need for education on foot care in diabetic patients in India. *J. Assoc. Physicians India* **1999**, *47*, 1083–1085. [Google Scholar]
- Kanazawa, T.; Nakagami, G.; Goto, T.; Noguchi, H.; Oe, M.; Miyagaki, T.; Hayashi, A.; Sasaki, S.; Sanada, H. Use of smartphone-attached mobile thermography assessing subclinical inflammation: A pilot study. *J. Wound Care* **2016**, *25*, 177–182. [Google Scholar] [CrossRef]
- Raman, R.; Rajalakshmi, R.; Surya, J.; Ramakrishnan, R.; Sivaprasad, S.; Conroy, D.; Theethi, J.P.; Mohan, V.; Netuveli, G. Impact on health and provision of healthcare services during the COVID-19 lockdown in India: A multicentre cross-sectional study. *BMJ Open* **2021**, *11*, e043590. [Google Scholar] [CrossRef] [PubMed]
- Nather, A.; Cao, S.; Chen, J.; Low, A. Prevention of diabetic foot complications. *Singapore. Med. J.* **2018**, *59*, 291–294. [Google Scholar] [CrossRef] [PubMed]
- Amin, N.; Doupis, J. Diabetic foot diseases: From the evaluation of the “foot at risk” to the novel diabetic ulcer treatment modalities. *World J. Diabetes* **2016**, *7*, 153–164. [Google Scholar] [CrossRef] [PubMed]
- Iraj, B.; Khorvash, F.; Ebnesahidi, A., & Askari, G. (2013). Prevention of diabetic foot ulcer. *International journal of preventive medicine*, *4*(3), 373–376.
- Bakker K, Apelqvist J, Schaper NC. International Working Group on Diabetic Foot Editorial Board. Practical guidelines on the management and prevention of the diabetic foot, 2011. *Diabetes Metab Res Rev.* **2012**;28(Suppl 1):225–31. doi: 10.1002/dmrr.2253. [DOI] [PubMed] [Google Scholar]
- Al Abdralnabi, Fatimah Ahmed E, Shahad Abdulaziz S Alzahrani, Association Between Lipid Profile and Diabetic Foot Ulcer Volume 44 Issue S-6 Year 2023 Page 1253:1258. <https://www.researchgate.net/scientific-contributions/Shahad-Abdulaziz-S-Alzahrani-2267693968>
- Doughty KN, Del Pilar NX, Audette A, Katz DL. Lifestyle Medicine and the Management of Cardiovascular Disease. *Curr Cardiol Rep.* **2017** Oct;4;19(11):116. [

31. Patel R, Sina RE, Keyes D. Lifestyle Modification for Diabetes and Heart Disease Prevention. [Updated 2024 Feb 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK585052/>
32. Lim JZ, Ng NS, Thomas C. Prevention and treatment of diabetic foot ulcers. *J R Soc Med*. 2017;110:104–109. doi: 10.1177/0141076816688346. [DOI] [PMC free article] [PubMed] [Google Scholar]
33. Veves A, Falanga V, Armstrong DG, Sabolinski ML. Apligraf Diabetic Foot Ulcer Study. Graftskin, a human skin equivalent, is effective in the management of noninfected neuropathic diabetic foot ulcers: a prospective randomized multicenter clinical trial. *Diabetes Care*. 2001;24:290–295. doi: 10.2337/diacare.24.2.290. [DOI] [PubMed] [Google Scholar]
34. Wu SC, Jensen JL, Weber AK, Robinson DE, Armstrong DG. Use of pressure offloading devices in diabetic foot ulcers: do we practice what we preach? *Diabetes Care*. 2008;31:2118–2119. doi: 10.2337/dc08-0771. [DOI] [PMC free article] [PubMed] [Google Scholar]
35. Mueller MJ, Diamond JE, Sinacore DR, Delitto A, Blair VP 3rd, Drury DA, Rose SJ. Total contact casting in the treatment of diabetic plantar ulcers. Controlled clinical trial. *Diabetes Care*. 1989;12:384–388. doi: 10.2337/diacare.12.6.384. [DOI] [PubMed] [Google Scholar]
36. Roekel-Wiedmann I, Bennett M, Kranke P. Systematic review of hyperbaric oxygen in the management of chronic wounds. *Br J Surg*. 2005;92:24.32. doi: 10.1002/bjs.4863. [DOI] [PubMed] [Google Scholar]
37. Mohd Zubir MZ, Holloway S, Mohd Noor N. Maggot Therapy in Wound Healing: A Systematic Review. *Int J Environ Res Public Health*. 2020;17 doi: 10.3390/ijerph17176103. [DOI] [PMC free article] [PubMed] [Google Scholar]
38. Sridharan K, Sivaramakrishnan G. Growth factors for diabetic foot ulcers: Mixed treatment comparison analysis of randomized clinical trials. *Br J Clin Pharmacol*. 2018;84:434–444. doi: 10.1111/bcp.13470. [DOI] [PMC free article] [PubMed] [Google Scholar]
39. Galiano R, Snyder R, Mayer P, Rogers LC, Alvarez O, Sanuwave Trial Investigators. Focused shockwave therapy in diabetic foot ulcers: secondary endpoints of two multicentre randomised controlled trials. *J Wound Care*. 2019;28:383–395. doi: 10.12968/jowc.2019.28.6.383. [DOI] [PubMed] [Google Scholar]
40. Baltzis D, Eleftheriadou I, Veves A. Pathogenesis and treatment of impaired wound healing in diabetes mellitus: new insights. *Adv Ther*. 2014;31:817–836. doi: 10.1007/s12325-014-0140-x. [DOI] [PubMed] [Google Scholar]
41. Demidova-Rice TN, Hamblin MR, Herman IM. Acute and impaired wound healing: pathophysiology and current methods for drug delivery, part 1: normal and chronic wounds: biology, causes, and approaches to care. *Adv Skin Wound Care*. 2012;25:304–314. doi: 10.1097/01.ASW.0000416006.55218.d0. [DOI] [PMC free article] [PubMed] [Google Scholar]
42. Lopes L, Setia O, Aurshtina A, Liu S, Hu H, Isaji T, Liu H, Wang T, Ono S, Guo X, Yatsula B, Guo J, Gu Y, Navarro T, Dardik A. Stem cell therapy for diabetic foot ulcers: a review of preclinical and clinical research. *Stem Cell Res Ther*. 2018;9:188. doi: 10.1186/s13287-018-0938-6. [DOI] [PMC free article] [PubMed] [Google Scholar]
43. Sasaki M, Abe R, Fujita Y, Ando S, Inokuma D, Shimizu H. Mesenchymal stem cells are recruited into wounded skin and contribute to wound repair by transdifferentiation into multiple skin cell types. *J Immunol*. 2008;180:2581–2587. doi: 10.4049/jimmunol.180.4.2581. [DOI] [PubMed] [Google Scholar]
44. Ding DC, Shyu WC, Lin SZ. Mesenchymal stem cells. *Cell Transplant*. 2011;20:5–14. doi: 10.3727/096368910X. [DOI] [PubMed] [Google Scholar]
45. Chiang KJ, Chiu LC, Kang YN, Chen C. Autologous Stem Cell Therapy for Chronic Lower Extremity Wounds: A Meta-Analysis of Randomized Controlled Trials. *Cells*. 2021;10 doi: 10.3390/cells10123307. [DOI] [PMC free article] [PubMed] [Google Scholar]
46. Wu Q, Lei X, Chen L, Zheng Y, Huang H, Qian C, Liang Z. Autologous platelet-rich gel combined with in vitro amplification of bone marrow mesenchymal stem cell transplantation to treat the diabetic foot ulcer: a case report. *Ann Transl Med*. 2018;6:307. doi: 10.21037/atm.2018.07.12. [DOI] [PMC free article] [PubMed] [Google Scholar]
47. Dash NR, Dash SN, Routray P, Mohapatra S, Mohapatra PC. Targeting nonhealing ulcers of lower extremity in human through autologous bone marrow-derived mesenchymal stem cells. *Rejuvenation Res*. 2009;12:359–366. doi: 10.1089/rej.2009.0872. [DOI] [PubMed] [Google Scholar]
48. Qin HL, Zhu XH, Zhang B, Zhou L, Wang WY. Clinical Evaluation of Human Umbilical Cord Mesenchymal Stem Cell Transplantation After Angioplasty for Diabetic Foot. *Exp Clin Endocrinol Diabetes*. 2016;124:497–503. doi: 10.1055/s-0042-103684. [DOI] [PubMed] [Google Scholar]
49. Hikabe O, Hamazaki N, Nagamatsu G, Obata Y, Hirao Y, Hamada N, Shimamoto S, Imamura T, Nakashima K, Saitou M, Hayashi K. Reconstitution in vitro of the entire cycle of the mouse female germ line. *Nature*. 2016;539:299–303. doi: 10.1038/nature20104. [DOI] [PubMed] [Google Scholar]
50. Jiang XY, Lu DB, Chen B. Progress in stem cell therapy for the diabetic foot. *Diabetes Res Clin Pract*. 2012;97:43–50. doi: 10.1016/j.diabres.2011.12.011. [DOI] [PubMed] [Google Scholar]
51. Lee KB, Choi J, Cho SB, Chung JY, Moon ES, Kim NS, Han HJ. Topical embryonic stem cells enhance wound healing in diabetic rats. *J Orthop Res*. 2011;29:1554–1562. doi: 10.1002/jor.21385. [DOI] [PubMed] [Google Scholar]
52. Lipsky BA, Berendt AR, Cornia PB, Pile JC, Peters EJ, Armstrong DG, Deery HG, Embil JM, Joseph WS, Karchmer AW, Pinzur MS, Senneville E. Infectious Diseases Society of America. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. *Clin Infect Dis*. 2012;54:e132–e173. doi: 10.1093/cid/cis346. [DOI] [PubMed] [Google Scholar]
53. Kwon KT, Armstrong DG. Microbiology and Antimicrobial Therapy for Diabetic Foot Infections. *Infect Chemother*. 2018;50:11–20. doi: 10.3947/ic.2018.50.1.11. [DOI] [PMC free article] [PubMed] [Google Scholar]
54. Borys S, Hohendorff J, Frankfurter C, Kieck-Wilk B, Malecki MT. Negative pressure wound therapy use in diabetic foot syndrome from mechanisms of action to clinical practice. *Eur J Clin Invest*. 2019;49:e13067. doi: 10.1111/eci.13067. [DOI] [PubMed] [Google Scholar]
55. Lebrun E, Tomic-Canic M, Kirsner RS. The role of surgical debridement in healing of diabetic foot ulcers. *Wound Repair Regen*. 2010;18:433–438. doi: 10.1111/j.1524-475X.2010.00619.x. [DOI] [PubMed] [Google Scholar]
56. Vouillamet J, Bourron O, Gaudric J, Lermusiaux P, Millon A, Hartemann A. Lower-extremity arterial revascularization: Is there any evidence for diabetic foot ulcer-healing? *Diabetes Metab*. 2016;42:4–15. doi: 10.1016/j.diabet.2015.05.004. [DOI] [PubMed] [Google Scholar]
57. Tepe G, Brodmann M, Werner M, Bachinsky W, Holden A, Zeller T, Mangalmurti S, Nolte-Ernsting C, Bertolet B, Scheinert D, Gray WA Disrupt PAD III Investigators. Intravascular Lithotripsy for Peripheral Artery Calcification: 30-Day Outcomes From the Randomized Disrupt PAD III Trial. *JACC Cardiovasc Interv*. 2021;14:1352–1361. doi: 10.1016/j.jcin.2021.04.010. [DOI] [PubMed] [Google Scholar]
58. Meloni M, Morosetti D, Giurato L, Stefanini M, Loreni G, Doddi M, Panunzi A, Bellia A, Gandini R, Brocco E, Lazaro-Martinez JL, Lauro D, Uccioli L. Foot Revascularization Avoids Major Amputation in Persons with Diabetes and Ischaemic Foot Ulcers. *J Clin Med*. 2021;10 doi: 10.3390/jcm10173977. [DOI] [PMC free article] [PubMed] [Google Scholar]
59. Pandey A, Banerjee S, Ngo C, Mody P, Marso SP, Brilakis ES, Armstrong EJ, Giri J, Bonaca MP, Pradhan A, Bavry AA, Kumbhani DJ. Comparative Efficacy of Endovascular Revascularization Versus Supervised Exercise Training in Patients With Intermittent Claudication: Meta-Analysis of Randomized Controlled Trials. *JACC Cardiovasc Interv*. 2017;10:712–724. doi: 10.1016/j.jcin.2017.01.027. [DOI] [PubMed] [Google Scholar]
60. Santema TB, Poeyck PP, Ubbink DT. Skin grafting and tissue replacement for treating foot ulcers in people with diabetes. *Cochrane Database Syst Rev*. 2016;2:CD011255. doi: 10.1002/14651858.CD011255.pub2. [DOI] [PMC free article] [PubMed] [Google Scholar]
61. Kim SY, Kim TH, Choi JY, Kwon YJ, Choi DH, Kim KC, Kim MJ, Hwang HK, Lee KB. Predictors for Amputation in Patients with Diabetic Foot Wound. *Vasc Specialist Int*. 2018;34:109–116. doi: 10.5758/vsi.2018.34.4.109. [DOI] [PMC free article] [PubMed] [Google Scholar]
62. Song K, Chambers AR. Diabetic Foot Care. [Updated 2023 Jul 24]. In: StatPearls [Internet]. Treasure Island (FL): Stat Pearls Publishing; 2025 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK553110/>