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ARTICLE REVIEW

Diabetic foot: a current review of diagnosis and treatment

Pie diabético: una revisión actual del diagnóstico y tratamiento

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ABSTRACT

Introduction: diabetic foot is a complication of diabetes mellitus that requires exhaustive follow-up by physicians and nurses, as well as attitudinal changes by patients, family members and daily caregivers.
Objective: to describe the current criteria for the diagnosis and treatment of diabetic foot.
Methods: to conduct this article, PRISMA methodology was used to examine studies published between 2018 and 2023. Forty scientific articles obtained through a digital search in various databases were reviewed: Pubmed, SciELO, Redalyc and Google Scholar, with inclusion criteria of full articles published between 2018-2023, in English and Spanish.
Results: the selected articles allowed obtaining updated data on therapeutic modalities, as well as care strategies for the patient with diabetic foot. The need for systematic review of the patient's lower limbs was detailed, as well as the need to pay attention to predisposing epidemiological factors such as hypertension, peripheral neuropathy, smoking and lack of foot hygiene.
Conclusions: timely diagnosis according to epidemiological situational identification, allows to resort to appropriate treatments, applying care strategies with resources that prevent the incidence and complications of diabetic foot ulcers, allowing physicians and nurses to guide clinical practice towards improving the quality of care, integrality of assistance, self-management, quality of life and patient satisfaction.

Keywords: Diabetic Foot; Diabetes Mellitus; Uality Of Life.

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RESUMEN

Introducción: el pie diabético es una complicación de la diabetes mellitus que necesita seguimiento exhaustivo por médicos y enfermeros, así como cambios actitudinales de pacientes, familiares y personal de cuidado diario.
Objetivo: describir los criterios actuales para el diagnóstico y tratamiento del pie diabético.
Métodos: para la realización de este artículo se empleó la metodología PRISMA para examinar los estudios publicados entre 2018 y 2023. Se revisaron 40 artículos científicos obtenidos a través de una búsqueda digital en diversas bases de datos: Pubmed, SciELO, Redalyc y Google Académico, con criterio de inclusión de artículos completos publicados entre 2018-2023, en inglés y español.
Resultados: los artículos seleccionados permitieron obtener datos actualizados sobre las modalidades terapéuticas, así como estrategias de cuidados para el paciente con pie diabético. Se detalló la necesidad de la revisión sistemática de los miembros inferiores del paciente, así como se debe prestar atención a factores epidemiológicos predisponentes como son la hipertensión, neuropatía periférica, el tabaquismo y la falta de higiene en los pies.
Conclusiones: el diagnóstico a tiempo según identificación epidemiológica situacional, permite recurrir a tratamientos adecuados, aplicando estrategias de cuidados con recursos que previenen la incidencia y complicaciones de ulceras en pie diabético, permitiendo a médicos y enfermeros orientar la práctica clínica hacia mejorar la calidad de atención, integralidad de asistencia, autogestión, calidad de vida y satisfacción del paciente.

Palabras Clave: Pie Diabético; Diabetes Mellitus; Calidad De Vida.

INTRODUCTION

Foot ulceration, as indicated by Miranda C,[1] is the most common and costly late complication of diabetes, with morbidity and mortality rates worse than those of many cancers, with data suggesting that one in three people with diabetes will develop a diabetic foot ulcer (DFU) at some point in their life. Non-healing DFUs are a leading cause of hospitalization, amputation, disability, and death among the diabetic population.

DFUs have a global prevalence of 6,3 % and are higher in type 2 diabetics (6,4 %) than in type 1 diabetics (5,5 %). It is estimated that between 9,1 and 26,1 million people worldwide will develop DFUs each year, with an estimated lifetime incidence of 15 % to 25 % in diabetic patients. Due to the associated diabetic neuropathy, patients with DFUs are often unable to feel or relieve pressure on their extremities, which can lead to vascular complications, vascular denervation, and decreased oxygen supply to the wound area, resulting in impaired healing. The associated mortality rate in patients with DFUs is twofold higher than that of diabetics without ulcerations after living with an ulceration for five years. For Bardill et al.,[2] unfortunately many of the factors that contribute to chronic wounds coexist with other comorbidities, such as hypertension, diabetic retinopathy and a history of smoking.

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Similarly, Castro argues,[3] that diabetic foot is a complication of diabetes mellitus (DM), whose risk factors for the development of the disease are grouped into two large groups: modifiable and non-modifiable factors. In this regard, the author indicates that modifiable factors are all those that can be corrected to stop the progression of the disease, such as metabolic imbalance, deformities, inadequate footwear and overweight; while non-modifiable factors such as sex, age, previous history of ulcers or amputation, cannot be modified, constituting an added risk for the patient's foot.

On the other hand, the periodic assessment of the feet to detect signs of neuropathy, circulation disorders and skin disorders in people with DM, is a basic principle of comprehensive care for the prevention of diabetic foot (PD) in the opinion of Delabra et al.,[4] when they indicate that, in addition to the good management of symptoms or early manifestations, it presupposes patient education for hygiene, foot care and the disease through diet, exercise, adherence to treatment and glycemic control.

Traditional treatment of DFUs as reported by Boulton et al.,[5] includes treatment of infections with antibiotics, application of dressings to promote moist environments for wound healing, surgery to resolve infections, biomechanical alterations, and restoration of vascularization. While several treatment options exist for these wounds and may provide some relief to patients, statistics demonstrate the current magnitude of the problem highlighting the limited effectiveness of treatments and the substantial need for improved therapies.

In this sense, as Moreno et al.,[6] argue, approximately 148 million diabetic patients suffer from foot injuries, with 50 % of these patients suffering from neuropathy, which is the most common complication of diabetes. Furthermore, diabetic foot has an annual incidence of 2 % worldwide, and in Latin America it is responsible for 3,7 % of hospitalizations and 20 % of injuries in hospitalized patients. Due to this, diabetic patients have an estimated risk of 19-34 % of presenting with DFU, where infection increases the risk of hospitalization by 50 %.

In Ecuador, there is no available evidence on the knowledge and practice of diabetic foot care among medical students. There is a pressing need to clarify the current status of the disease based on studies conducted over the last five years. This is intended to identify strengths and weaknesses that will allow for improvements in professional training, prevent future complications in patients with diabetic foot care, and achieve a positive impact on their quality of life. With this in mind, this review was conducted to describe the current criteria for the diagnosis and treatment of diabetic foot care.

METHODS

The literature review focused on providing a comprehensive update on the diabetic foot, addressing relevant aspects of diagnosis and treatment based on recent evidence. Initially, a thorough search was conducted in medical databases, including PubMed, Scielo, Redalyc, and Google Scholar, ensuring coverage of the available literature.

To ensure accuracy and relevance, specific keywords such as "Diabetic Foot," "Diagnosis," and "Treatment" were used. The inclusion period was from 2018 to 2023; inclusion criteria were precisely defined to ensure the compiled data were relevant and current. Case reports, review articles, and original studies in Spanish and English that provided concrete and recent data on diagnosis, disease management, epidemiology, comorbidities, treatments, and care strategies were included. Clear exclusion criteria were established, excluding articles without peer review,

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editorials, article abstracts, dissertations, in languages other than English and Spanish, as well as those that did not provide concrete data on the disease.

During the information search, the titles and abstracts of the articles found were thoroughly reviewed for selection. The full texts of these articles were then evaluated to confirm their applicability and quality, ensuring that each selected source offered significant value to the review. This rigorous and structured methodology ensured that the literature review was not only comprehensive but also up-to-date and relevant, shedding light on current innovations in diagnosis and therapeutics, providing a solid foundation for understanding and effectively managing the disease.

The search criteria included Boolean operators "AND" and "OR" using keywords and publication date. A total of 871 articles were obtained, excluding 831 that did not meet the criteria. The final total was 40 documents that met the inclusion criteria for the research.

DEVELOPMENT

Of the 40 selected articles (100 %), 2,5 % were case reports, while 85 % were review articles, and 12,5 % were original works. Similarly, regarding the origin of the studies in relation to their global distribution by continent, 55 % were conducted in the Americas, 15 % in Asia, 27,5 % in Europe, and 2,5 % in Oceania. Africa has not reported any published research in the last five years.

In this sense, the product of the compilation of the data found, taking into account the diagnosis of the disease and the epidemiology, the correspondence of 30 % of the studies, show the support of most of the research towards the subject of training, related to the UPD, where experience indicates that by having more contact with the disease, knowledge, skills and appropriate practices are acquired to treat patients with PD, as referred to by Muñoz et al,[7] summarized and grouped in table 1 below, the data being presented in ascending chronological order, that is, from the oldest to the most recent.

Table 1. Scientific articles on diagnosis and epidemiology.

Fountain	Results and conclusions
Espinoza C, et al., (2019) [8]	Of the 147 patients evaluated, 63% (n=93) were male, the most frequent age group was 50-70 years (37%; n=54), most had only primary education (69%; n=102) and came from urban areas (87%; n=125), the most frequent comorbidity was arterial hypertension (44.9%; n=66); skin and soft tissue infection was the most prevalent cause of admission (49%; n=72), while 69% (n=101) had more than 10 years with DM and suprapatellar amputation was the most used procedure (52%; n=76). There is a high frequency of patients with diabetic foot admitted to the Abel Gilbert Pontón Hospital who require amputation, the most prevalent factors being male sex, age between 50-70 years, low educational status, urban origin, coexisting arterial hypertension, infection as the most important cause of admission and time of evolution of DM greater than 10 years.
Mills J, et al., (2019) [9]	The results were limited to the English language and from 2014 to 2019. The main search retrieved 1,023 references, whose search coverages were: - Guidelines for diabetic foot infection: 25; - Diabetic foot infection: clinical trials 146; - Diabetic foot infection: cohort studies, 198. The search was conducted in components, each of which was related to a specific causal link in a formal problem structure (available upon request). The search was supplemented with very recent clinical trials known to expert panel members, specifically negative trials.

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Pitocco D, et al., (2019) [10]	The prevalence of MRSA is high, and the incorrect use of antibacterial agents, the hospital environment, osteomyelitis, and nasal carriage of MRSA lead to MRSA infection. The pathophysiology of DFI was understood, and risk factors for DFI were quickly identified as essential. A comprehensive DFI evaluation performed by a multidisciplinary team is recommended to achieve optimal results. Accurate classification of DFI is important to guide treatment regimens, facilitate communication between healthcare professionals, and predict patient outcomes. The IDSA and UT classification provide relatively simple, objective methods for classifying DFI. Prompt recognition and treatment of DFI are mandatory to ensure maximum limb salvage.
Carro G, et al., (2020) [11]	Three types of APD have been identified (infected diabetic foot, progressive ischemic diabetic foot, and acute phase CKD), whose early treatment can improve the prognosis. However, in practice, there are cases where ischemia and infection are combined, requiring treatment of both simultaneously, making these cases potentially the most serious. Identifying these patients is the first step toward improving their care, although other measures are required, such as developing emergency department protocols with clear care pathways for those admitted with APD, rapid referral to multidisciplinary teams, avoiding bureaucratic delays in the transfer of at-risk patients, implementing referral and counter-referral systems based on severity, and others.
Calles O, et al., (2020) [12]	There was no association between marital status, educational level, psychobiological habits, nutritional status, presence of arterial hypertension or dyslipidemia, with the presentation of diabetic foot. The predominant lesion in the cases was Wagner grade 2, and according to the Texas classification it was IIB. There was a significant association of diabetic foot with poor metabolic control (p = 0.003; OR: 3.451; 95% CI: 1.517-7.852), presence of neuropathy (p = 0.0001; OR: 5.670; 95% CI: 2.144-14.997), alteration of the ankle brachial index (ABI) (p = 0.004; OR: 3.545; 05% CI: 1.487-8.454) and personal history of diabetic foot (p = 0.0001; OR: 8.609; 95% CI: 3.110-23.832). In multivariate logistic regression analysis, the presence of neuropathy, altered ABI, and personal history of PD remained as independent predictive factors.
Carro G, et al., (2021) [13]	The three cases presented here share an acute and devastating presentation that is not typically observed in patients with PD, both in clinical experience and in the literature. A history of COVID-19 in the three months prior to admission could have aggravated chronic ischemia given the increased risk of thrombosis caused by the disease, associated with the risk of vascular disease inherent to diabetes, which in these cases was poorly controlled according to glycosylated hemoglobin levels. It is noteworthy that one of the patients presented thrombosis of a gastrocnemius vein and other signs of arterial embolism. The combination of these factors (chronic ischemia due to diabetes and a prothrombotic state due to COVID-19) could have led to a torpid and rapidly evolving course that ultimately required major amputation of the affected limb.
Cascante D, et al., (2021) [14]	Enterococcus faecalis was the most frequently isolated agent (21%), followed by Staphylococcus aureus (14%), of which 70% presented a methicillin-resistant phenotype, and Escherichia coli in third place (11%). Other Gram-negative bacilli occupied fourth place, with Enterobacter cloacae (8%) and Klebsiella pneumoniae (8%) as the main isolated species; it is worth noting that the presence of 24% of strains carrying extended-spectrum β-lactamases was evident, with K. pneumoniae as the main carrier of this resistance phenotype.
Macdonald K, et al.,(2021) [15]	A total of 112 studies were included, representing 16,159 patients from whom 22,198 microbial isolates were extracted. The most frequently identified organism was Staphylococcus aureus, of which 18.0% (95% CI: 13.8–22.6%; I2 = 93.8% [93.0–94.5%]) was MRSA. Other highly prevalent organisms included Pseudomonas spp., E. coli, and Enterococcus spp. A correlation was identified between Gross National Income and the prevalence of Gram-positive or -negative organisms in diabetic foot infections.
Rubitschung K, et al.,(2021) [16]	Currently, the clinical diagnosis of diabetic foot soft tissue infection or OM relies on corroboration by multiple clinical tests, including bone probe testing, pathology, and microbiology. Many of these techniques require special training or are prone to low inter-rater reliability; while imaging modalities such as plain radiography and MRI have demonstrated reasonable agreement (62%), the area of infection is only identified after morphological alteration. In general, molecular imaging approaches have greater sensitivity and specificity and can indicate pathological changes long before morphological changes occur. Although radiotracers, such as 18F-FDG or those used in cellular carriers such as white blood cells, are useful for evaluating diabetic foot infection, the development of radiotracers that are specific to microorganisms is of great interest. This may be useful in the evaluation of complex cases or the efficacy of treatment. A new focus of interest is directly targeting osteoblasts and

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	osteoclasts, which can be infected by microorganisms. As a result, changes in the production of proteins for immune modulation, bone resorption, and intracellular signaling have been observed.
Wang Y, et al., (2021) [17]	Research on biomarkers for systemic diseases continues to develop rapidly in many fields. For example, some valuable physical biomarkers have been considered for diagnosis, risk stratification, or monitoring of DFU. Ideally, combining markers with clinical observations and comparing these results with better routine tests, such as current clinical benchmarks, and even with quantitative methods can be used to validate the correlation between these potential new markers and DFU clinical observations, avoiding exaggeration of the value of the new platform. To the extent that DFU is based on complex systemic diseases, multiple factors related to clinical potential become relevant for the collaboration, validation, and consistency of clinical evidence considered for studies. Ultimately, the study of biomarkers in DFU is still in its early stages, and continued efforts in this field will help reveal insights into DFU management and improve prevention and treatment outcomes.
Muñoz L, et al., (2022) [7]	There were 148 participants. Overall, knowledge about risk assessment and stratification is low. 16.9% of participants knew how to perform the monofilament test, and 22.3% knew how to interpret it. There is also a lack of awareness about risk factors for amputation; only 20.9% of respondents demonstrated knowledge on the topic. The study concludes that the level of knowledge about diabetic foot, its diagnosis, and risk stratification is low among the study participants. This indicates that final-year medical students at the University of Antioquia have only superficial information on the topic, which can lead to delays in diagnosis and implementation of timely treatment.
Du F, et al., (2022) [18]	A total of 63 articles on DFI and antibiotic susceptibility testing in diabetics with patients in China were included. There were 11,483 patients with a mean age of 60.2 ± 10.1 years and a median age of 10.6 ± 5.0 years between 2010 and 2019, covering most geographical regions in China. The prevalence of Gram-positive (GP) bacteria (43.4%) was lower than that of Gram-negative (GN) bacteria (52.4%). The most frequently isolated pathogens were Staphylococcus aureus (17.7%), Escherichia coli (10.9%), Pseudomonas aeruginosa (10.5%), Klebsiella pneumoniae (6.2%), Staphylococcus epidermidis (5.3%), Enterococcus faecalis (4.9%), and fungi (3.7%). The prevalence of polymicrobial infection was 22.8%. GP bacteria were susceptible to linezolid, vancomycin, and teicoplanin. More than 50% of GN bacteria were resistant to third-generation cephalosporins, while resistance rates to piperacillin/tazobactam, amikacin, meropenem, and imipenem were relatively low. Among the 6017 strains of isolated organisms, 20% had multidrug resistance (MDR). Staphylococcus aureus (30.4%) was the most predominant MDR bacterium, followed by extended-spectrum β-lactamase (ESBL) (19.1%).

Likewise, regarding table 2 relating to applicable treatments and care strategies, they correspond to 70 % of the studies found where it is evident that interventions by clinical care procedures, types of treatments, medications, teaching-learning strategies for both the patient and their caregivers, care therapies for patient care, are amplified according to the types of PD, degree and level of the disease, frequency of exposure to interventions, cure rates, among others, as stated by Vásquez et al.,[19] when they affirm that the care staff (Doctors and Nurses) must maintain their performance according to their academic trajectory, expertise, roles, directing their efforts even towards the family that accompanies the patient with PD.

Table 2. Scientific articles on treatments and care strategies.

Fountain	Results / Conclusions
Boulton A, et al., (2018) [5]	Efforts designed to identify pre-ulcer inflammation through previous-generation home monitors have now culminated in devices that can alert patients up to several weeks before a complication develops. Similarly, smart insoles combined with smartwatches may be able to identify potentially damaging pressure, which over time can cause blisters or calluses and tissue loss.
González J, et al., (2019) [20]	Foot care education is essential to prevent this complication. It was concluded that diabetic foot is a serious cause of morbidity, disability, and poor quality of life for patients; a program with prevention strategies, education, treatment of foot complications, and monitoring has proven effective in reducing the frequency of amputations.
Coffey L, et al., (2019) [21]	The findings were synthesized using a meta-ethnographic approach in 42 selected articles. The synthesis resulted in the development of five overarching themes: personal understanding of diabetic foot ulceration; diabetic foot ulceration prevention: knowledge,

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	attitudes, and behaviors; perspectives on healthcare experiences; progression of diabetic foot ulceration and actions taken; and the broader impact of diabetic foot ulceration. The findings highlight several barriers for foot care providers, who experienced that people with diabetes demonstrate significant consequences of ulcers on their physical, social, and psychological well-being. The insights provided inform the development of interventions that effectively promote foot care and provide appropriate support to those living with ulceration.
Pérez A, et al., (2019) [22]	Twelve articles were selected after reviewing the inclusion criteria and performing a quality assessment. A summary and classification of recommendations were completed. They concluded that the heterogeneity of the levels of evidence and degrees of recommendation of the included CPGs regarding the management, approach, and treatment of FD makes their interpretation and adoption in clinical practice difficult, as is the selection of the appropriate procedure. Despite this, and based on a detailed review of the included guidelines, it was concluded that the highly recommended interventions for the management of FD are debridement (very high level of evidence and recommended), foot assessment (moderate level of evidence and highly recommended), and therapeutic footwear (high level of evidence and highly recommended).
Pérez A, et al., (2019) [23]	Therapeutic footwear reduces ulcer recurrence, although few studies have evaluated its efficacy and the prevention of initial ulceration. Various methods of debridement (including the use of maggots) and revascularization have been used to improve the healing process of ischemic ulcers. They have been shown to be effective in reducing pain and increasing arterial flow to the ischemic limb, as well as reducing the risk of amputation. However, further studies are needed to determine the patient populations for whom these therapies are useful, as well as their cost-benefit ratios. AMPs are potent agents against a broad spectrum of pathogens, including viruses, fungi, and antibiotic-resistant bacteria, and have antitumor activity, representing an alternative treatment to conventional antibiotic therapy.
Meneses J, et al., (2020) [24]	Four clinical trials and two cohorts were included. Mean plantar pressure in individuals exposed to felt was reduced by 10.77 kilopascals (95% CI -14.92, -6.62; p<0.001). They concluded that greater reductions in plantar pressure were associated with the development of new felt models. Relief orthoses with felted foam for plantar pressure are recommended, along with further clinical research to clarify the associated outcomes.
Oliveira D, et al., (2021) [25]	Twelve educational strategies were implemented to prevent foot ulcers in people with diabetes: health education, educational programs with pamphlets, follow-up and PowerPoint presentations for seminars, informational brochures, diabetic foot screening with self-care guidelines, motivational interviewing, motivational videos, educational interventions, workshops/educational workshops, small message services, educational groups, individualized education, and an educational brochure.
Mateus L, et al., (2021) (26)	Twenty-nine articles were selected, and the strategies were organized into three themes, by prevention level: 1) promotion, prevention, and harm mitigation; 2) identification, diagnosis, and treatment; and 3) rehabilitation. Conclusions: Periodic evaluation of diabetic foot is vitally important and should be performed by an interdisciplinary team.
Vásquez S, et al., (2021) [19]	Six of the eight included articles were classified as having a high risk of bias. The two interventions that demonstrated improved cost-effectiveness compared with the control group were beta-glucan gel (compared to placebo) and negative pressure therapy (compared to advanced moist wound therapy). National and international guidelines for the nursing management of diabetic foot ulcers propose at least 15 different interventions. However, the limited availability of high-quality cost-effectiveness studies makes selection difficult and leads to greater variability in nursing practices. They conclude that cost-effectiveness studies in direct comparisons of nursing interventions for the management of diabetic foot ulcers are needed.
Boulton A. (2021) [1]	The most important thing in managing diabetic foot disease is to provide appropriate treatment to patients if possible while they are safe at home, but if not, to do so, when indicated, in outpatient centers and hospital services for the most severely affected.
Chen L, et al., (2021) [27]	Initially, 363 articles were reviewed, and finally, 9 literatures were included, involving a total of 943 patients. The pooled analysis using the fixed-effect model showed that the cure rate of the NPWT group was significantly lower than that of the standard group [odds ratio (OR) = 3.60, 95% confidence interval (CI): 2.38 to 5.45, P < 0.001]. The granulation tissue formation time of the NPWT group was significantly shorter than that of the standard group [mean difference (MD) = -8.95, 95% CI: -10.26 to -7.64, P < 0.001]. The adverse event rate of both groups showed no significant difference (OR = 0.49, 95% CI: 0.10 to 2.42, P = 0.38). The amputation rate of both groups did not show statistical significance (OR = 0.33, 95% CI: 0.09 to 1.26, P = 0.10)

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Edwards J, et al., (2021) [28]	DFU has serious consequences for the individual patient, their family, the healthcare system, and society as a whole. Patients who experience amputations and severe infections, along with associated impairment and disability, result in financial hardship and loss of productivity. The patient faces a reduced quality of life along with increased 5-year mortality. The costs of care presented in this review illustrate the impact of this disease process on the patient and society.
Dayya D, et al., (2021) [29]	Among 93 enrolled patients (18% women; median age 65 years), 44 were randomized to the 3-week arm and 49 to the 6-week arm. The median number of surgical débridements was 1 (range, 0–2 interventions). In the intention-to-treat (ITT) population, remission occurred in 37 (84%) patients in the 3-week arm compared with 36 (73%) in the 6-week arm ($p = 0.21$). The number of AEs was similar in the two studies (17/44 vs. 16/49; $p = 0.51$), as were the incidences of remission in the per-protocol (PP) population (33/39 vs. 32/43; $p = 0.26$). In multivariate analysis, treatment with the shortest course of antibiotics was not significantly associated with remission (for the ITT population, hazard ratio 1.1, 95% CI 0.6-1.7; for the PP population hazard ratio 0.8, 95% CI 0.5-1.4)
Gariani K, et al.,(2021) [30]	Major amputations were once common for DFO, but with improved surgical and diagnostic techniques, conservative surgery (foot spacing, resecting only infected and necrotic bone) is becoming more common, especially for forefoot infections. Traditional antibiotic therapy, administered predominantly intravenously and often for several months, can often be replaced by appropriately selected oral antibiotic regimens after brief (or even no) parenteral therapy, administered for no more than 6 weeks. Based on ongoing studies, the recommended duration of treatment may be even shorter, especially for cases where a substantial portion of infected bone has been resected. The use of culture results (preferably from bone samples) and antimicrobial stewardship principles allows clinicians to select evidence-based antibiotic regimens, often for a narrow spectrum of pathogens.
Liu Y, et al., (2021) [31]	Overall, experiments have shown that multiple FGFs mentioned above are closely related to diabetic wound healing. However, the limitations of FGFs have greatly hampered their application. For FGFs to be a potential option for the treatment of DFU, improved carriers must be developed with other methods, such as novel dressings, as well as the combination of tissue-engineered skin substitutes with FGFs for DFU. Furthermore, the single, long-term use of FGFs to treat diabetic ulcers remains to be further studied due to other systemic side effects.
Miranda C, et al., (2021) [32]	Foot ulcers are a preventable complication of diabetes. Understanding the factors that place patients with diabetes mellitus at high risk for ulceration, along with strict glycemic control and early treatment of risk factors, as well as ongoing patient and caregiver education, is essential for the prevention and management of diabetic foot complications.
Tran M, et al., (2021) [33]	Three randomized controlled trials (139 participants) were included in the review. All studies incorporated a form of non-weight-bearing exercise as an intervention over a 12-week period. One study conducted the intervention in a supervised setting, while two studies conducted the intervention in an unsupervised setting. Two studies found greater improvement in the percentage of wound size reduction in the intervention group compared with the control group; one of these studies achieved statistically significant results ($p < 0.05$). The results of the third study demonstrated statistically significant findings for total wound size reduction ($p < 0.05$); however, the results were analyzed within each treatment group and not between groups.
Castro N. (2022) [3]	Eleven articles were found that met the established inclusion criteria. Nine articles effectively evaluated the use of ozone therapy as a treatment for chronic diabetic foot wounds, demonstrating beneficial effects such as pain reduction, accelerated tissue granulation time, reduced hospital stay, and control of parameters indicative of infectious processes. One article found no significant differences between the use of ozone therapy and conventional treatments such as antibiotics; another found adverse effects after its application.
Delabra, et al., (2022) [4]	Foot care education with support from materials was the most widely used and evaluated intervention strategy for self-care behavior and neuropathy symptoms. They concluded that the most effective interventions for preventing diabetic foot disease in older adults with diabetes included foot care education and knowledge; telephone follow-up; printed materials; and foot care materials. Based on the quality criteria of the reviewed studies, it was not possible to determine the optimal intervention.
Bardill J, et al., (2022) [2]	Topical gel treatments for DFUs have been extensively studied in research settings, but few have been tested in the clinical setting, with only one topical gel (Regranex®) currently FDA-approved specifically for DFU treatments. DFUs will continue to be a major threat to diabetic patients and the healthcare system, as diabetes is expected to increase dramatically in the coming decades. The combined lack of available topical treatments for patients with DFUs

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	and the rising incidence of DFUs should incentivize researchers to develop topical gels capable of treating DFUs.
Yang L, et al., (2022) (34)	The current situation is that the detection rate and follow-up rate of DFUs are low, the incidence rate and amputation rate are high, and many treatment methods are available, but the effect is unsatisfactory. However, with the development of the information age, public understanding of diabetes and DFUs has gradually improved, and various new technologies have been continuously developed, providing opportunities for their management. In the future, comprehensive prevention and treatment management of DFUs are necessary to prevent their onset, effectively shorten the cure time, improve the clinical cure rate, reduce the amputation rate, improve patients' standard of living, and reduce the social burden. This task may be complex, enormous, and requires significant projects.
Yu Q, et al., (2022) (35)	Stem cell-based therapies hold promise in the field of regenerative medicine, and their mechanisms include promoting angiogenesis, ameliorating neuroischemia and inflammation, and promoting collagen deposition. However, little is known about their specific molecular mechanisms and biological properties. Although stem cell application has entered the clinical practice stage, discussion about their safety remains an integral part of research. MSCs promote wound healing in a dose-dependent manner, but at the same time, they also promote tumor growth. Currently, there are no clear standards regarding the dosage for MSC application.
Ballesteros A, et al., (2023) (36)	The educational interventions reviewed by the 10 CPGs were compiled, which are considered most effective in preventing the onset of PD in primary care. These recommendations have been included as activities in the Nursing Interventions Classification (NIC) related to the topic.
Lira J, et al., (2023) (37)	The predominant educational technologies were training and verbal guidance, with soft-hard technologies being the most prevalent. Compared with usual care, educational technologies were shown to be a protective factor in preventing the incidence of diabetic ulcers (RR=0.40; 95% CI=0.18-0.90; p=0.03), and the certainty of the evidence was low. Educational technologies were also shown to be a protective factor in preventing the incidence of lower-limb amputations (RR=0.53; 95% CI=0.31-0.90; p=0.02), and the certainty of the evidence was very low.
López M, et al., (2023) (38)	Specific training in diabetic foot is required, integrating recognition of the risk factors of diabetic patients, updating in the correct assessment of the foot and risk stratification, correct vascular examination using Doppler and interpretation of Doppler curves and calculation of the ankle-brachial index, updating in DFU treatment, updating in the use of felt offloading, correct management of the follow-up of patients with ulcerated foot risk, knowledge of the criteria for referral to different professionals and their prioritization, and health education for injury prevention.
Moreno F, et al., (2023) (6)	Properly treating diabetic foot is a challenge for physicians, healthcare workers, and hospitals, but the high prevalence of the disease both globally and in Latin America makes the study of updated diagnostic and management techniques extremely important. In this regard, the article suggests and presents the development of best clinical practices and current multidisciplinary approaches to optimize the management of this disease and provide the quality care patients require, seeking to safeguard their physical and mental health, as well as their quality of life.
Masmiquel M et al.,(2023) (39)	Gentamicin is shown to eradicate infectious microorganisms, is well tolerated by patients, decreases healing time, and is active against several microorganisms such as Psedomonas aeruginosa, E. coli, Enterobacter, and Staphylococcus, including methicillin-resistant Staphylococcus. They concluded that topically applied gentamicin appears to have a positive therapeutic effect on infected diabetic foot ulcers, although they cannot conclude that gentamicin is the most appropriate treatment, as many lines of research in this area are lacking.
McDermott K, et al.,(2023) (40)	Major efforts are needed to develop health system-wide improvements in DFU prevention and early diagnosis, especially in disadvantaged populations. Funding should be prioritized for high-quality population-based registries to track incidence, prevalence, outcomes, and process measures. Initiatives should expand the use of effective home-based screening modalities, allocating resources for more frequent foot examinations of patients in regions

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	with high major amputation rates, with the potential to reduce the incidence of DFUs, whose morbidity is highest among patients.

Diagnosis

According to Miranda C,[1] the International Working Group on the Diabetic Foot (IWGDF) has published guidelines as rapid pathways for the care of diabetic foot ulceration, which have been advocated as simple tools for primary care physicians treating DFUs. These guidelines suggest that patients should be rapidly classified into three potential levels of severity and need for care:
(a) uncomplicated diabetic foot ulcers;
(b) complicated, defined as potentially ischemic or infected with osteomyelitis; and
(c) Severely complicated DFUs, defined as gangrene, abscess, among others; providing a useful algorithm that can be appropriately adapted and used worldwide.[13]

Likewise, Moreno et al.,[6] report that diabetic patients should have a routine foot examination by a general practitioner or specialist, especially those with active ulcers or infections, whose evaluation should be performed with adequate history, looking for pain, paresthesia and loss of sensitivity, performing the appropriate physical examination of the skin, sensory and arterial tissues that allows starting treatment to prevent progression, and if necessary, refer the patient. To do this, the following should be performed:
a) cutaneous and inflammatory examination;
b) sensory exploration;
c) Arterial exploration;
d) triphasic Doppler and Doppler ultrasound;
e) radiology;
f) thermography;
g) magnetic resonance;

According to Carro et al.,[11] in cases of infected DFU, immediate hospitalization and surgical intervention are required, with exploration and removal of sloughed tissue, drainage of collections, taking samples for culture, and rapid initiation of treatment with broad-spectrum antibiotics intravenously, with coverage of Gram-positive, Gram-negative and anaerobes. Other acceptable methods for diagnosis are: fine needle puncture of collections, tissue biopsy and surgical biopsy during toilette, as well as biopsy of remaining bone in the case of bone excision, which is generally applied to phalanges and distal metatarsus.

Epidemiology

According to Moreno et al.,[6] patients with DM reflect loss of sensitivity in the extremities, which is why they are seven times more likely to develop ulcer diseases, with prevalence of peripheral neuropathies in 30 % of type 1 diabetic patients, while in type 2 diabetic patients it is 42 %. In this sense, the peak incidence is found in elderly people or older adults, where 50 % are affected by diabetic neuropathy in the course of their life as reported by González et al.[19]

In this regard, Espinoza et al.,[8] state that patients suffering from PD experience frequent relapses, with 40 % of these patients experiencing complications in the affected area; therefore, once an active ulcer has formed, it presents a risk of sepsis in 50 % of diabetic patients, and studies show that 85 % of patients with a history of recurrent ulcer disease undergo amputation within five years of the diagnosis of the active ulcer.[6]

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The above indicates that, in accordance with what was defended by Calles et al.,[12] the strong association between PD and poor metabolic control, being directly proportional to the structural alterations of the foot, relative to the high incident rate in patients with DM, which generally result in amputations. Therefore, as Mateus L et al.,[25] assure, among the most important predisposing factors that can cause an amputation in patients with UPD are those who have an underlying pathology such as: hypertension, peripheral neuropathy, smoking habit, alcohol consumption, with a family history of diabetes, overweight, physical inactivity, poor healing process, foot deformities, dyslipidemias and decreased perfusion; however, there are other factors that are not related to the health status of people, proving that the use of inadequate footwear can generate ulcers, as well as walking barefoot and lack of foot hygiene.

Treatments

Regarding the use of antibiotics for the treatment of PD, Masmiquel and Ovejero,[40] state that the effect of local gentamicin on different types of microorganisms, including those resistant to methicillin (MRSA), are highly effective, given recent publications of case-control and prospective observational studies without comparator, which show that they have effects on isolated strains of different microorganisms such as Staphylococcus aureus, even those resistant to methicillin, Proteus spp., Enterobacter spp., Escherichia coli, Pseudomonas spp. and Citrobacter sp. The authors mentioned above assure that these results support the concept that locally applied gentamicin may be a useful and safe treatment for DFUs caused by microorganisms resistant to commonly used antibiotics.

However, Carro et al.,[11] believe that antibiotic treatment should be started intravenously as soon as possible, providing broad spectrum coverage for Gram-negative, Gram-positive and anaerobic bacteria, while the patient is hospitalized. However, the recommendations for the initial regimen for moderate to severe infections include different antibiotics such as: levofloxacin (low coverage for Staphylococcus aureus), cefoxitin, ceftriaxone, ampicillin sulbactam (low coverage for Gram-negative bacteria), moxifloxacin, ertapenem, ciprofloxacin with clindamycin (low evidence for severe S. aureus infections), among others. This aspect is also supported by Cascante et al.[14]

In the opinion of Bardill et al,[2] contrary to the increased prevalence and morbidity associated with DFUs, effective treatment options are limited, with surgical debridement being the standard conventional treatment for DFUs, the process of which removes necrotic and inflammatory tissue from the wound to promote the acute wound healing process. Forms of debridement include mechanical, enzymatic, autolytic, biological and surgical; and may vary from wet to dry gauze dressing changes, pulse lavage, hydrotherapy and low frequency ultrasound.

Other common techniques are pressure relief to relieve pressure on wounds located at the base of the feet, reduction of edema to improve perfusion and hyperbaric oxygen to increase arterial oxygen pressure, ozone therapy emerging as a therapeutic alternative for the treatment of chronic wounds, an aspect defended by Castro,[3] as a benefit and advantage over conventional treatments, given the bactericidal, germicidal, analgesic and anti-inflammatory power or stimulation of tissue regeneration of the diabetic foot.

Likewise, as suggested by Boulton et al.,[5] skin grafts are an effective option for larger wounds, providing complete epidermal or dermal treatments; however, with limitations, including limited donor site availability for autologous grafts and immunological rejection of allografts. On the other hand, bioengineered skin substitutes have been developed, utilizing extracellular matrix (ECM) and/or cell-based strategies to provide protection and prevent further mechanical stresses on the wound, as well as moisture retention, promotion of cell growth, and management of

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wound exudates. Although these substitutes have great potential, many have limited application in patients with DFUs in the clinical setting.

Topical treatments are advantageous due to the ease of application as suggested by Meneses L et al.,(23) Regarding this, they indicate that gels also provide moisture retention in the wound area, which is a critical component to promote keratinocyte migration, collagen formation, angiogenesis and reduction of scar formation in both acute and chronic wounds; while felts reduce plantar pressure and provide quality of life models for the patient.

Care strategies

According to the criteria set forth by Ballesteros et al.,[36] patients with diabetes at risk of developing foot ulcers are recommended to inspect both feet daily (with the help of a mirror) as well as the inside of the shoes they are going to use, in case there are foreign objects, small animals, nails, torn parts of the lining or areas with wrinkles; they should also wear suitable socks, made of absorbent material and that do not squeeze; they should wash their feet daily with warm water, using mild soap, and dry them thoroughly with soft cloths, particularly between the toes.

Similarly, the same authors suggest using emollients to moisturize dry skin; cutting fingernails straight along the contour of the finger and filing sharp edges with a nail file; and avoiding the use of abrasive chemicals or any other technique to remove calluses or corns.[36]

On the other hand, Lira et al.,[37] indicate that educational technologies facilitate the management of PD care, classified into soft, soft-hard and hard technologies, where the first ones consist of relationships, such as welcoming, creating bonds and promoting patient autonomy, through open dialogue, qualified listening and group dynamics; while the second ones correspond to structured knowledge, such as educational portfolios, educational videos, brochures and posters; finally, the third ones include material resources, such as technological equipment and registration forms. These resources allow the prevention of the incidence of DFUs and their complications in diabetic patients, as well as the medical and nursing staff to guide clinical practice, improve the quality of care, comprehensiveness of care, self-management, quality of life and patient satisfaction.[24]

CONCLUSIONS

Diagnosis of PD requires routine checkups at each visit, especially in patients with ulcers or active infections, who should be monitored weekly, assessing symptoms such as pain, paresthesias, and loss of sensation, along with skin, sensory, and arterial examinations to prevent complications and reduce the risk of amputations associated with poor metabolic control. Factors such as hypertension, peripheral neuropathy, harmful habits, foot deformities, and poor hygiene predispose to complications. Treatment includes antibiotics, debridement, topical therapies, pressure offloading, hyperbaric oxygen, and, in extreme cases, skin grafting. Preventive care includes daily foot and footwear inspection, meticulous hygiene, adequate hydration, and patient education to encourage self-management and prevent complications through technological resources and ongoing support.

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