

Practical guidelines for the prevention and management of diabetic foot disease in China

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Abstract

Diabetic foot (DF) is a prevalent and significant complication of diabetes mellitus. The primary factors that contribute to amputation and mortality in DF patients are multifaceted and include foot deformities, ulcers, ischemia, and potential concurrent infections. To further standardize DF prevention and treatment in China, improve consistency in DF diagnosis and treatment, and promote the development of a specialized tiered care system, the Chinese Burn Association, the Yangtze River Delta Integrated Diabetic Foot Alliance, and the Editorial Committee of the Chinese Journal of Burns and Wound Repair established a multidisciplinary expert team. The team identified clinical issues concerning the diagnosis, treatment, and prevention of DF via the population, interventions, comparisons, outcomes framework, assessed the quality of relevant evidence using the Grading of Recommendations Assessment, Development and Evaluation system, and ultimately formulated a consensus titled "Practical Guidelines for the Prevention and Management of Diabetic Foot Disease in China." The guidelines include 46 recommendations that address comprehensive medical assessment; internal medical treatments, including treatments related to blood glucose, blood pressure, and blood lipid control; antithrombotic and anti-infection therapy; perioperative risk assessment and management; surgical interventions, such as debridement, vascular reconstruction, and tissue repair; foot disease prevention; multidisciplinary collaboration; and the establishment of a hierarchical diagnosis and treatment system, with the objective of guiding clinical practice for managing DF in China.

Keywords: Diabetic foot; Infection; Peripheral arterial disease; Peripheral neuropathy; Wound healing

Highlights

- In recent years, the prevalence of diabetic foot has been steadily increasing. This guideline formulates a clinical practice guideline for diabetic foot suitable for Chinese patients, which is of great significance for the prevention and standardized treatment of diabetic foot.
- The members involved in the development of this guideline represent diverse clinical and academic disciplines, including endocrinology, vascular surgery, burn and wound repair, orthopedics, foot and ankle surgery, infectious diseases, cardiology, rehabilitation, and evidence-based medicine. All members had doctoral or master's degrees and had undergone systematic training in evidence-based medicine, and the guideline development process adheres to the WHO Handbook for Guideline Development (2nd Edition), which ensures a highly rigorous process for formulating the guideline.

Background

Diabetic foot (DF) includes infections, ulcers, and tissue damage occurring below the ankle in individuals with diabetes, and it is often linked to lower extremity neuropathy and peripheral arterial disease [1, 2]. The prevalence of DF is 6.3% (95% CI: 5.4%–7.3%), and the annual incidence varies between 0.1% and 11%. Approximately 55% of these ulcers are classified as neuropathic, 35% as neuroischemic, and merely 10% as purely ischemic. Research in China has shown that the incidence rate of DF is 8.1%, making it the leading cause of hospitalization for individuals with diabetes [3, 4]. The healing rate of foot ulcers after 12 weeks of treatment varies between 24% and 82%, while the recurrence rate is 31.6% within one year after healing in individuals older than 50. This condition results in decreased quality of life and elevated mortality rates, and it is the leading cause of amputation [3]. The annual incidence of amputation among patients with DF is 5.1%, resulting in an overall amputation rate of 19.03%, which includes 2.14% major amputations

and 16.88% minor amputations. The annual mortality rate is 14.4%, and the 5-year mortality rate is as high as 40% [3]. Between 2014 and 2020, the per capita total cost for treating foot ulcers in patients with diabetes varied from 15,000 to 42,000 yuan, which is double that of patients without ulcers [5]. The average hospital stay ranged from 14.29 to 31.4 days, with an average amputation rate of 9.9%. For this group, the average hospital stay extended to 33.5 days, with an average cost of 5,932 dollars [6]. By 2030, medical expenditures for diabetes treatment in China are expected to increase from the current 4.9 billion dollars to more than 7.4 billion dollars [7]. The cost of DF treatment is estimated to constitute 20% of the overall medical costs associated with diabetes, thereby imposing a considerable economic burden on society.

Patients with diabetes have a 34% risk of developing foot lesions throughout their lifetimes, which is correlated with an elevated risk of amputation and mortality [8]. It is essential to establish clinical practice guidelines for DF management to standardize prevention and treatment

Received: August 27, 2025. Revised: September 30, 2025. Accepted: October 8, 2025

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protocols. In October 2024, the Executive Committee of the Yangtze River Delta Ecological Green Integration Development Demonstration Zone, jointly overseen by the governments of Shanghai, Jiangsu, Zhejiang, and the National Development and Reform Commission, tasked the Yangtze River Delta Integration Diabetic Foot Disease Alliance (YRD-DFA) with investigating standardized medical care and the hierarchical diagnosis and treatment of complications associated with chronic diseases. A multidisciplinary expert team was established in collaboration with the Chinese Burn Association (CBA) and the Editorial Committee of the Chinese Journal of Burns and Wound Repair (Chin J Burns) to revise the Expert Consensus on Guidelines for Multidisciplinary Approaches to the Prevention and Management of Diabetic Foot Disease (2020 edition) [9]. This revision, which is based on evidence evaluation according to evidence-based medicine standards, has been renamed the Practical Guidelines for the Prevention and Management of Diabetic Foot Disease in China.

Methods

Standards and procedures for guideline development

These guidelines were established by the Yangtze River Delta Ecological Green Integration Development Demonstration Zone, collaboratively led by the CBA, YRD-DFA, and Chin J Burns, with methodological assistance from the West China Evidence-Based Nursing Center at Sichuan University. The guideline development process adheres to the WHO Handbook for Guideline Development (2nd Edition). Evidence quality is assessed, and recommendations are established using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system [10]. The guideline protocol and main text refer to the Appraisal of Guidelines for Research & Evaluation II (AGREE II) [11] and the Reporting Items for Practice Guidelines in Healthcare (RIGHT) [12]. It has been registered on the International Practice Guidelines Registration Platform (registration number: PREPARE-2024CN1219) and is intended for medical staff in institutions at all levels, targeting patients with diabetes and DF.

Establishment of the guideline project team

A guideline steering committee, guideline expert committee, and guideline secretariat were formed following the commencement of the guideline development project.

Guideline steering committee. Membership included representatives from the Yangtze River Delta Ecological Green Integration Development Demonstration Zone, CBA, YRD-DFA, and Chin J Burns. The primary responsibilities included defining the theme and scope of the guidelines, approving the guideline protocol, overseeing the guideline development process, and endorsing the recommendations and the complete text of the guidelines.

Guideline expert committee group. The committee included members from various medical centers nationwide, representing diverse professional fields, including endocrinology, vascular surgery, burn and wound repair, orthopedics, foot and ankle surgery, infectious diseases, cardiology, rehabilitation, and evidence-based methodology. The primary responsibilities included the evaluation of priority themes and

outcome indicators, the formulation of recommendations for specific issues, publication and promotion of the guidelines.

Guideline secretariat group. Members included representatives from the CBA, YRD-DFA, and 15 prominent hospitals within the Chinese healthcare sector. Their areas of expertise included endocrinology, vascular surgery, burn and wound repair, orthopedics, foot and ankle surgery, infectious diseases, cardiology, rehabilitation, and evidence-based medicine. All members had doctoral or master's degrees and had undergone systematic training in evidence-based medicine. The primary responsibilities included constructing the PICO (population, interventions, comparisons, outcomes) framework for clinical priority issues, drafting the guideline development plan, executing systematic reviews.

Drafting group. The primary responsibilities included completing the evidence summary for the guideline recommendations, preparing the initial version of the full guidelines, and documenting the entire guideline development process.

Disclosure of conflicts of interest

These guidelines are endorsed by the "2025 Special Government Fund for the Yangtze River Delta Ecological Green Integration Development Demonstration Zone (No. QZHQ[2025] 0225)". All members of the expert committee and the secretariat have accurately completed conflict of interest declaration forms, and there are no conflicts of interest pertaining to the guidelines.

Identification of key issues and outcome metrics

The Guideline Expert Committee assessed priority themes and outcome indicators; developed clinical priority issues based on pertinent guidelines, systematic reviews, and original studies; and solicited input from medical staff and patients with DF through questionnaires to identify priority issues. The committee established the PICO framework for prioritizing clinical issues in the DF clinical practice guidelines, informed by literature reviews and questionnaire findings. The content of the framework was evaluated and scored utilizing the Delphi method, resulting in the identification of 46 clinical priority issues and their corresponding key outcome indicators.

Evidence retrieval

A PICO model was developed to address clinical priority issues, facilitating the identification of Chinese and English subject terms and free words, along with the formulation of database retrieval strategies. Systematic searches for literature in Chinese and English from 2020 to 2025 were performed in CNKI, WanFang Data, CBM, PubMed, Embase, The Cochrane Library, and CINAHL, supplemented by reference tracing. Systematic reviews, randomized controlled trials (RCTs), cohort studies, case-control studies, and diagnostic studies were included. Literature management was conducted with EndNote X9. The inclusion and exclusion criteria were established according to the PICO framework, and consolidated information was extracted following deduplication and hierarchical screening.

Evidence synthesis

For each priority issue, high-quality systematic reviews published within the past 5 years were prioritized as the primary evidence source; in the absence of such reviews, evidence synthesis was performed using original studies, and systematic

Table 1. GRADE evidence quality levels

Quality level	Definition
High quality	Very confident that the true effect is close to the estimated effect.
Moderate quality	Moderate confidence in the estimated effect; the true effect is likely to be close to the estimate but may be substantially different.
Low quality	Limited confidence in the estimated effect; the true effect is likely to be substantially different from the estimate.
Very low quality	Very little confidence in the estimated effect; the true effect is likely to be substantially different from the estimate.

Table 2. GRADE recommendation strength classification

Recommendation strength	Description
Strong recommendation	The benefits of the intervention clearly outweigh the risks; it is highly credible for clinicians to implement and for the population to accept.
Weak recommendation	The benefits and risks of the intervention are roughly balanced, and it is more dependent on specific clinical situations. In general, the preferences of physicians and patients play a more important role in the decision-making process.

reviews were subsequently updated. The evaluation of various literature types was conducted using the AMSTAR 2 [13], the Cochrane Risk of Bias Tool [14], the Newcastle–Ottawa Scale [15], and the QUADAS-2 [16]. Quality evaluations of all literature were conducted independently by two researchers, and any disagreements were addressed through discussion or consultation with a third party.

Assessment of evidence quality

Following the GRADE methodology standards, the evidence for each priority issue was classified into four levels: high, moderate, low, and very low (Table 1). GRADE evidence summary tables and result summary tables were developed in accordance with the relevant evidence synthesis outcomes.

Development of recommendations

Initial recommendations were developed based on evidence classified by GRADE. In cases where guideline issues lack direct evidence or include only qualitative studies, recommendations were developed based on expert consensus through Delphi consultations and expert seminars. The final guideline recommendations were synthesized into a guideline questionnaire.

Consensus on guidelines

The Delphi method was employed to finalize the recommendations. The guideline questionnaire incorporated the results of evidence synthesis and the quality of evidence supporting each recommendation. Experts evaluated and scored the recommendations and offered revision suggestions, and the final recommendations were modified accordingly. The strength of the recommendation for evidence-based recommendations was determined according to the GRADE classification system (Table 2). Refer to the GRADE classification system to assign recommendation strengths to recommendations supported by evidence. For recommendations without direct evidence support, assign recommendation strengths based on expert consensus and set the evidence type as good practice statement (GPS).

External review of the guidelines

To gather comprehensive feedback from clinical medical personnel and evaluate the clarity and practical applicability of the guidelines, experts with associate senior titles or higher in disciplines such as endocrinology, vascular surgery, orthopedics, foot and ankle surgery, infectious diseases, cardiology, and evidence-based medicine were invited to review the guidelines after their formulation. The guideline content was revised and subsequently validated in accordance with the review findings.

Clinical questions and recommendations

Clinical question 1: diagnosis of DF

Comprehensive medical evaluation

Recommendation 1: A thorough medical evaluation of all patients with DF, including medical history acquisition, physical examination, laboratory analyses, and imaging studies, should be performed. The assessment of vital organ functions, including the heart, kidneys, and brain, along with conditions affecting the lower limbs, is crucial (recommendation grade: strong; evidence level: GPS).

Evidence summary: No relevant systematic reviews or original research evidence were identified for this recommendation.

Rationale: Approximately 50% of patients with DF also present with peripheral artery disease (PAD). Ankle artery and foot pulse palpation have a sensitivity of 71.7% and a specificity of 72.3% [8, 17]. A history of foot issues constitutes a risk factor for high-risk feet. The recurrence risks of ulcers at 1, 3, and 5 years are 42%, 58%, and 65%, respectively [8, 18]. The medical history inquiry must encompass lifestyle factors, including diet, exercise, smoking, alcohol consumption, and occupational demands, alongside cultural, psychological, and socioeconomic influences; behavioral capacity and mental state; and a history of diabetes complications and comorbidities, such as eye diseases, peripheral neuropathy, peripheral artery disease, cardiovascular and cerebrovascular diseases, chronic renal failure, and autoimmune or

Table 3. Medical history collection

Item	Content
General condition	(1) Lifestyle; (2) occupational demands, cultural, psychological, and social factors; (3) behavioral capacity and mental state; (4) Shoe-wearing habits and foot insulation practices; (5) history of exposure to mechanical or chemical irritants.
Past history of foot diseases	(1) Diabetes-related complications/comorbidities; (2) history of trauma and surgical procedures (with emphasis on foot ulcers and lower limb surgeries); (3) past lower limb diseases, including sensory symptoms, muscular symptoms, edema, structural/functional abnormalities, foot deformities (e.g., hammer toes, Charcot foot), loss of joint range of motion (e.g., ankle stiffness), abnormal plantar pressure distribution or callus formation; (4) DF treatment history.
Current condition of foot diseases	(1) Current episode (recurrence status) and healthcare utilization; (2) ulcer characteristics and perilesional tissue changes; (3) home/social barriers to ulcer healing; and (4) utilization of offloading techniques.

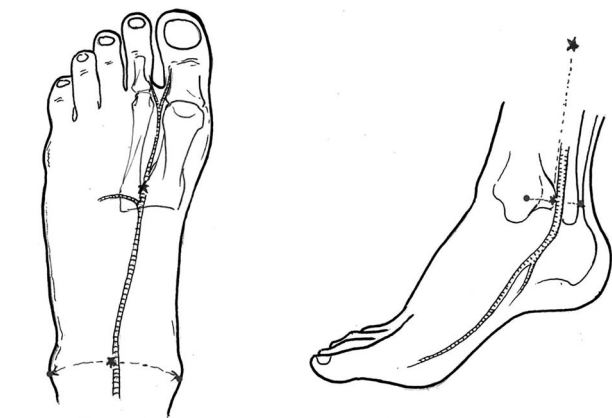


Figure 1. Superficial location of dorsalis pedis artery and posterior tibial artery

neurological disorders, including steroid use. The assessment must encompass a history of trauma and surgical interventions, particularly regarding foot ulcers and lower limb surgeries, as well as exposure to unsuitable footwear or harmful chemicals, alongside the onset and progression of the current foot condition [9] (Table 3). The physical examination must encompass routine assessments, emphasizing indicators of anemia, moist rales in both lungs, and/or jugular vein distension. Additionally, the skin, temperature, hair, foot vessels (Figure 1), and nerves of the lower limbs should be evaluated, among other factors (Table 4, and Appendix 1) [9]. Laboratory tests should include measurements of blood glucose, lipids, electrolytes, blood gases, hemoglobin, and albumin to evaluate metabolic and nutritional status; liver and renal function, myocardial enzymes, and B-type natriuretic peptide (BNP) to assess organ function; prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time (APTT), D-dimer, and fibrinogen (Fg) to analyze coagulation function; and complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), interleukin-6 (IL-6), procalcitonin (PCT), and etiological examinations to determine infection status. Special clinical examinations should include routine tests, including an electrocardiogram (ECG), chest X-ray, and B-mode ultrasound. Additional assessments may involve Holter monitoring, echocardiography, and/or coronary angiography, along with vascular, neurological, imaging, pressure, and microbiological or pathological evaluations of lower limb wounds [9].

Assessment and diagnosis of diabetic foot infection (DFI)

Recommendation 2: DF soft-tissue infection should be diagnosed clinically through the presence of local or systemic inflammatory signs and symptoms. When a DFI is clinically suspected, obtaining tissue specimens through curettage or biopsy using sterile techniques, rather than swabbing superficial exudate for culture, is recommended to identify the causative pathogen(s). Moreover, serum inflammatory biomarkers, including white blood cell count, CRP, ESR, and PCT, should be used as supplementary diagnostic tests (recommendation grade: strong; evidence level: low).

Evidence summary: The analysis included two systematic reviews. DFI is clinically diagnosed based on local or systemic inflammatory manifestations, with serum biomarkers and microbiological assessment playing significant roles. Key outcome indicators: The diagnosis and severity of DFI are significantly associated with the risks of hospitalization, amputation, and mortality [19, 20]. Currently, the ESR is recognized as the most effective biomarker for DF osteomyelitis (DFO), whereas PCT serves as the optimal blood test for differentiating DFO from non-DFO ($P=0.049$) [21]. The pooled bivariate sensitivity and specificity were 0.81 (95% CI: 0.71–0.88) and 0.90 (95% CI: 0.75–0.96), respectively. Compared with tissue sample cultures, swab cultures exhibit reduced sensitivity and specificity. The associations between specimen collection methods, sampling depth, culture positivity, therapeutic concordance, and prognosis across various grades of DF remain unclear [22, 23].

Rationale: The diagnosis of DFI necessitates the presence of at least two of the following signs or symptoms: local swelling or induration, erythema extending beyond 0.5 cm, tenderness or pain, elevated skin temperature, purulent discharge, and the exclusion of alternative causes of skin inflammation. Severity must be classified in accordance with the IWGDF/IDSA guidelines. Moderate infection is characterized by the absence of a systemic inflammatory response but the presence of erythema measuring 2 cm or greater or involvement of deep structures such as tendon, muscle, joint, or bone. Severe infection is defined as a foot infection accompanied by systemic inflammatory response syndrome (SIRS). If osteomyelitis is present, the suffix “O” is appended. Leukocyte count and PCT are weakly correlated with disease severity, whereas the ESR is important for the diagnosis of DFO [19]. Following surgical debridement and prior to the administration of antibiotics, tissue from the ulcer base (rather than from a swab) should be collected, and conventional microbiological methods should be employed

Table 4. Physical examination of the lower limb

Skin examination	(1) Temperature, color, turgor/elasticity, moisture, hair growth, and fissures; (2) nail dystrophy (atrophy or hyperplasia); (3) calluses, corns (with erythematous pressure points $\pm$ hemorrhage); (4) ulcers (location, size, depth, stage) and gangrene; (5) infectious dermatoses: tinea pedis (fungal infection), paronychia (bacterial infection), excoriations (suggestive of <i>Candida</i> infection); and (6) miscellaneous conditions: microvascular changes (e.g. telangiectasia), light-brown scaly plaques (diabetic dermopathy), lipodystrophy, bullous diseases, eruptive xanthomas, sclerodactyly, disseminated granuloma annulare, allergic reactions.
Vascular examination	(1) Absence of hair growth, dystrophic toenails; (2) thinning of skin (parchment-like appearance), cyanosis/erythema, and postural color changes (limb elevation/dependent position test); (3) temperature gradient assessment (ipsilateral proximal–distal comparison and bilateral symmetry evaluation); (4) auscultation of the carotid artery, abdominal artery, femoral artery, and dorsal foot artery; (5) palpation of the femoral artery, dorsal foot artery, and posterior tibial artery; and (6) handheld Doppler ultrasound examination.
Neuromuscular and skeletal system examination	(1) Sensory and reflex testing, including vibration sensing (tested with 128 Hz tuning fork); pressure perception (10 g monofilament examination); tactile sensation testing with the cotton wool/wool fiber test (light touch), two-point discrimination (spatial sensory resolution), pain perception (blunt needle stimulation), and thermal sensation (cold/warm rod testing); and deep tendon reflex (DTR) testing; (2) foot deformities, including spontaneous muscle atrophy (neurogenic wasting without direct trauma), foot drop (dorsiflexion weakness with steppage gait), and Achilles tendon contracture/equinus deformity (plantarflexion limitation); toe deformities, including hammer toe (flexion at PIP joint), claw toe (hyperextension at MTP + flexion at DIP), and hallux rigidus/osteoarthritis of the first MTP joint; pes planus (flatfoot) <i>vs</i> pes cavus (high arch), Charcot neuroarthropathy (destructive joint disease in neuropathy), and postsurgical deformities, including amputation stump and joint fusion complications (e.g. pan-talar arthrodesis); and (3) lower limb joint restrictions.

to identify pathogens, differentiating between contaminants and true pathogens. Metagenomic next-generation sequencing (mNGS) is not advised. The accuracy of culture is contingent upon the quality of clinical and laboratory processing, including collection, transport, and incubation [19, 20].

Recommendation 3: It is essential for all DFI patients to receive plain foot X-rays to undergo an assessment for bone abnormalities, including deformities and destruction, soft tissue gas, and the presence of foreign bodies (recommendation grade: strong; evidence level: low).

Evidence summary: This recommendation includes one systematic review detailing the role of plain X-rays in the diagnosis of DFI. Key outcome indicators: The combination of plain X-rays and a probe-to-bone (PTB) test for diagnosing DFO demonstrated an accuracy comparable to that of MRI and histopathological diagnosis, which are considered the gold standards. The overall sensitivity of this combined approach was superior to that of any single method, with values of 0.94 for PTB and X-rays, 0.91 for PTB alone, and 0.76 for X-rays alone. The specificity and positive likelihood ratio (LR+) were elevated but marginally lower than those of PTB alone, with specificity values of 0.83 for PTB + X-rays and 0.86 for PTB and 0.76 for X-rays. The LR+ values were 5.684 for PTB + X-rays, 6.344 for PTB, and 1.969 for X-rays. The X-ray findings, including bone marrow involvement and periosteal reaction, were significantly associated with complications occurring within 1 year, such as infection, ulcer recurrence, amputation, and death. Specifically, 28.7% of patients exhibited imaging changes, while 73.9% experienced complications. Notably, all patients with imaging changes at initial diagnosis developed complications and had a low survival rate [24].

Rationale: Plain X-rays are characterized by cost-effectiveness, convenience, and safety. This method is capable of displaying abnormalities in soft tissue and bone and dynamically assessing progression and can be used to observe changes in the foot before and after surgery, including

neuro-osteoarthritis, bone deformities or fractures, foreign bodies, and soft tissue gases (often associated with necrotic infections), bone variants, and vascular calcification, thereby creating a “road map” for subsequent imaging examinations. The integration of X-rays and PTB is readily achievable, and the results are dependable. This assessment should be incorporated into specialized DF wards where there is a high incidence of DFO [25]. Specialized physicians with training and experience can identify abnormalities on X-ray images.

Recommendation 4: In the presence of symptoms such as “sausage” toes, deep or large ulcers, ulcers over bony prominences, or chronic nonhealing ulcers, DFO should be suspected. Further evaluation through physical examination, serum inflammatory biomarkers, and imaging studies is recommended to confirm the diagnosis (recommendation grade: strong; evidence level: high).

Evidence summary: The evidence for this recommendation includes 2 systematic reviews and meta-analyses, 1 meta-analysis, 3 retrospective diagnostic tests, and 1 prospective diagnostic test, which report on the diagnosis of DFO. Key outcome indicators: When the ulcer area exceeds 2 cm² and the ESR increases from >65 mm/h to >70 mm/h, the positive predictive value of DFO increases from 80% to 83% [26]. PTB positivity and an ESR >47 mm/h indicate a positive predictive value of 97% for DFO. Furthermore, the presence of even a single criterion can increase the positive predictive value to 78% [27]. An ulcer depth exceeding 3 mm, in conjunction with an ESR greater than 60 mm/h and a CRP above 32 mg/L, yields a positive predictive value for DFO of 73.9%–72.3% [28]. The sensitivity of X-rays in detecting acute DFO is limited. A follow-up X-ray within 2–3 weeks is typically effective if the initial X-ray is normal but there is clinical suspicion of DFO [29]. After adjusting for confounding factors and inflammatory biomarkers, its histological value has been demonstrated to exceed that of MRI [30].

Rationale: The signs of DFO include “sausage” toes, deep (>3 mm) or large (>2 cm²) ulcers situated over a bony prominence, PTB positivity (demonstrated by the use of a sterile blunt metal probe to assess the ulcer base and detect hard “bony” resistance after debridement) [27, 28, 31], and wounds that remain unhealed after 4 weeks of conventional treatment [28]. Serum inflammatory markers, including white blood cell count and CRP and PCT levels, do not effectively differentiate between soft tissue infection and DFO [28, 32, 33]. An ESR >70 mm/h holds diagnostic significance for DFO, although it should not be utilized in isolation [26–28, 31–34].

Recommendation 5: MRI should be prioritized in cases where there is a strong suspicion of soft tissue abscess or osteomyelitis in patients with DF (recommendation grade: strong; evidence level: GPS).

Evidence summary: No relevant systematic reviews or original research evidence were found for this recommendation.

Rationale: The rationale for using MRI as the preferred advanced imaging modality for diagnosing DFO includes its characteristic T1-weighted low signal and T2-weighted high signal. MRI offers several advantages, including the absence of ionizing radiation, high resolution of soft tissues, and the ability to detect lesions at an early stage. Nonetheless, the drawbacks include low specificity (ranging from 37% to 50%), interference caused by metal artifacts, and inappropriateness for patients with pacemakers. It is essential to distinguish this from bone marrow signal alterations resulting from other conditions, including fractures, tumors, inflammatory arthritis, bone infarction, and neuro-osteoarthritis. Diffusion-weighted imaging (DWI-MRI) and dynamic contrast-enhanced imaging (DCE-MRI) have sensitivities and specificities ranging from 65.0% to 100% and 56.0% to 95.0% for DWI-MRI, and from 63.6% to 100% and 66.7% to 93.3% for DCE-MRI, respectively. Inconsistent parameter settings have hindered the establishment of standardized diagnostic procedures [34]. The sensitivity of 18F-FDG PET is reported to be 83% (95% CI: 69%–94%), while its specificity is 92% (95% CI: 86%–97%). Its effectiveness is comparable to that of MRI and white blood cell scintigraphy [32]. Furthermore, the implementation of these bone scanning techniques is limited to large tertiary hospitals, resulting in inadequate availability.

Recommendation 6: The diagnosis of DFO should be based on bone tissue culture and/or pathological examination (recommendation grade: strong; evidence level: high).

Evidence summary: This recommendation comprises two systematic reviews and three meta-analyses that examine the role of bone tissue pathology and culture in the diagnosis of DFO. Key outcome indicators: The positive rate of bone culture following percutaneous bone biopsy (PBB) ranged from 56% to 99%, yet data concerning surgical safety, clinical outcomes, or antimicrobial guidance remain limited [29, 30, 33]. The safety and diagnostic accuracy of bedside percutaneous blind puncture were comparable to those of image-guided puncture. The consistency of bacterial culture results between soft tissue and bone tissue was low, ranging from 19.3% to 69.2%, with high consistency observed for *Staphylococcus aureus* and poor consistency for gram-negative bacteria [35]. Compared with traditional bone culture, molecular chemistry and 16S rRNA technology demonstrate a greater capacity for detecting various types of bacteria, particularly anaerobic bacteria, with a strong consistency observed between the two methods.

Rationale: The current diagnosis of DFO relies on bacterial culture of bone tissue or histopathological examination revealing bone necrosis, fibrosis, and infiltration of inflammatory cells. “PTB + bacteria culture” is considered the gold standard for diagnosing DFO. The procedure must be conducted by surgeons, radiologists, or trained endocrinologists, adhering to the principles of sterility and noncontact. The needle should be inserted from clean skin, and repeated punctures should be avoided. Notably, PBB is not appropriate for moderate to severe ischemic wounds. Negative culture cannot entirely eliminate DFO, as it may be influenced by sampling errors, contamination, or antibiotic use. A unified standard for histopathology is lacking, leading to potential variations in interpretation. Molecular biology methods, including 16S RNA and whole-gene sequencing, have specific effects; however, these methods cannot be used to determine bacterial activity and pathogenicity and are not suitable for routine application [29].

Recommendation 7: DFI can coexist with cellulitis, necrotizing fasciitis, or gas gangrene and may be easily mistaken for erysipelas, acute lymphangitis, thrombophlebitis, and Charcot foot. Differentiation is essential to prevent misdiagnosis or overlooked diagnoses (recommendation grade: strong; evidence level: moderate).

Evidence summary: This recommendation comprises one meta-analysis, which detail the differential diagnosis of DFI, indicating a high risk of bias. Key outcome indicators: The LRINEC score demonstrated a sensitivity of 36%–77% and a specificity of 72%–93% in the diagnosis of necrotizing fasciitis in the limbs. The accuracy rate was 77.95% when the score was equal to or ≥6 points [36]. The systemic immune inflammation index (SII), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and procalcitonin (PCT) are effective at distinguishing DFO from cellulitis. In the osteomyelitis group, the SII, ESR, CRP, and PCT were significantly elevated ($P < 0.05$), with the ESR (AUC 0.722) and SII (AUC 0.687) demonstrating superior diagnostic value. The SII cutoff value was 2.182, demonstrating a sensitivity of 39.8% and a specificity of 79.8%. This value may serve as an auxiliary biomarker for predicting DFO [37]. Gas-producing foot infections, including those caused by *Clostridium* and non-*Clostridium* species, are characterized primarily by multiple microbial infections. Sepsis occurs in more than half of cases, with a 64% amputation rate; however, the mortality rate remains low. Surgical exploration is essential [38].

Rationale: The primary pathophysiological factors contributing to foot infection in patients with diabetes are neuropathy, ischemia, and nutritional dysfunction [39]. Impaired circulatory systems and immune responses can lead to the rapid development and dissemination of skin infections to adjacent tissues. Table 5 presents specific identification points [19, 37, 38,40–42].

Assessment and diagnosis of peripheral artery disease (PAD)

Recommendation 8: For individuals with diabetes aged 40 years or older, it is advisable to conduct annual assessments of the lower extremity arteries. This should include a review of medical history, pulse palpation, and measurement of the ankle-brachial index (ABI). For individuals at elevated risk for PAD, such as those aged 50 years or older, with foot ulcers, cardiovascular disease (CVD), or a history of lower extremity vascular abnormalities or surgeries, it is advisable to perform

Table 5. Differential diagnosis of DFI

Disease	Common causes	Key points of clinical differentiation	Treatment
Cellulitis	<i>Streptococcus</i> spp., <i>Staphylococcus aureus</i>	Local redness, swelling, heat, pain, and unclear boundaries; no invasion of the deep fascia layer, slow progression, and no skin necrosis	Local treatment + antibiotics
Necrotizing fasciitis	Multiple bacterial infection (Group A streptococcus, <i>Escherichia coli</i> , anaerobic bacteria, etc.)	The severe pain is disproportionate to the physical signs, often accompanied by shock, and involves the fascial layer. In severe cases, the skin may be pale or purplish black, with blisters and twisting sounds, and progress rapidly	Emergency surgery + antibiotics
Gas gangrene	<i>Clostridium</i> genus (<i>Clostridium perfringens</i>)	Muscle necrosis, severe pain, twisting sounds, foul-smelling secretions, sepsis	Emergency surgery + antibiotics
Acute lymphangitis	<i>Streptococcus</i> spp., <i>Staphylococcus</i> spp.	A “red line” extends proximally from the primary lesion, accompanied by tenderness, local lymph node swelling, or fever	Antibiotics
Thrombophlebitis	Vascular injury, bed rest, hypercoagulability, etc.	Swelling, pain, redness, or cyanosis may indicate pulmonary embolism; D-dimer elevation; ultrasound shows venous thrombosis	Anticoagulation or thrombolysis
Charcot foot	Sensory loss and joint instability caused by DPN	Painless swelling, deformation, gait abnormalities; X-ray shows bone destruction or dislocation	Offloading (TCC, etc.); surgery if necessary

PAD evaluations every 1–3 months. In patients who exhibit signs of foot ischemia and foot ulcers, it is advisable to assess the ABI to determine the presence of PAD (recommendation grade: strong; evidence level: GPS).

Evidence summary: No relevant systematic reviews or original research evidence were found for this recommendation.

Rationale: The presence of diminished or absent lower extremity pulses indicates the likelihood of lower extremity arterial disease (LEAD). In a cohort exceeding 1.92 million individuals, the prevalence of LEAD was notably low prior to the age of 40, regardless of diabetes status [43]. Individuals aged 50 to 65 years with diabetes, hypertension, chronic kidney disease, or a family history of PAD are recognized as having an increased risk for LEAD [44]. Approximately 50% of patients with DF also present with concurrent PAD [45]. The IWGDF/ESVS/SVS guidelines recommend annual screening of PAD in all individuals with diabetes who do not have foot ulcers [46]; however, universal screening prior to age 40 is not cost-effective because of the low prevalence of LEAD in this population. The current guidelines recommend annual screening starting at age 40, with an increased frequency (every 1–3 months) for high-risk individuals, and immediate screening upon the emergence of foot ischemia or ulcer symptoms. PAD can be classified into three clinical subsets based on severity. Asymptomatic PAD is characterized by the absence of claudication or atypical symptoms. Diagnosis can be established through the presence of abnormal pulses or imaging tests, as well as an abnormal ABI or toe–brachial index (TBI). Symptomatic PAD is characterized by intermittent claudication, atypical symptoms, or a foot ulcer/gangrene lasting for 2 weeks or more, accompanied by abnormal ABI or TBI results. Critical limb ischemia (CLI) is characterized by pain at rest, nonhealing ulcers, or gangrene and is accompanied by an ankle pressure below 50 mmHg, toe pressure below 30 mmHg, or transcutaneous oxygen tension (TcPO₂) below 30 mmHg [47]. Considering convenience and cost, along with medical history, pulse palpation serves as a crucial bedside tool for identifying LEAD. Consideration

should be given to additional hemodynamic tests, including ABI, TBI, and TcPO₂.

Recommendation 9: Determination of the resting ABI is the preferred initial approach for evaluating the vascular system of the lower extremities. Combining ankle pressure, toe pressure, the TBI, and color duplex ultrasonography with the ABI is a rational approach to enhance the diagnostic accuracy for LEAD. In patients being evaluated for revascularization, it is essential to assess the complete lower extremity arterial circulation using CTA, MRA, or digital subtraction angiography (DSA) (recommendation grade: strong; evidence level: GPS).

Evidence summary: No relevant systematic reviews or original studies were identified for this recommendation.

Rationale: An ABI of <0.9 is associated with an increased probability of LEAD, as indicated by a positive likelihood ratio ranging from 1.7 to 19.9. Conversely, an ABI >0.9 does not completely rule out this condition, as evidenced by a negative likelihood ratio between 0.0 and 0.84. Toe pressure has moderate diagnostic value, with a positive likelihood ratio ranging from 1.43 to 17.55. A TBI of <0.7 demonstrates a sensitivity of 71.25% and a specificity of 90.76% [44]. Integrating the ABI and TBI with pedal Doppler waveform analysis enhances the evaluation of lower extremity arterial disease. No universally accepted diagnostic or exclusion criteria currently exist. When the ABI is between 0.90 and 1.30, the TBI is ≥0.7, and when triphasic or biphasic pedal Doppler waveforms are observed, the likelihood of LEAD is low [47].

No single test has been demonstrated to be optimal for diagnosing PAD. The resting ABI serves as the primary screening and diagnostic instrument recommended for initial evaluation. It is straightforward, noninvasive, cost effective, and comparatively objective. The normal range is 0.91–1.40; values ≤0.9 indicate arterial stenosis, whereas values >1.4 suggest arterial calcification [44, 47]. Approximately 25% of patients with CLI exhibit a “normal” ABI due to medial arterial calcification. In these instances, determination of the postexercise ABI (ankle systolic pressure decrease >30 mmHg

or ABI reduction >20%) or TBI testing is recommended [47]. The TBI provides a more accurate representation of actual tissue perfusion because of the reduced susceptibility of digital arteries to calcification. A TBI of <0.7 is deemed abnormal. Toe pressure <30 mmHg indicates CLI. Lower extremity color duplex ultrasonography serves as the preferred confirmatory test. It is noninvasive, devoid of radiation, widely accessible, and efficient in terms of resource utilization [44]. When endovascular intervention through a femoral approach is considered, evaluating the iliac-femoral arteries using duplex ultrasonography is essential [47]. Revascularization may involve the use of CTA, MRA or contrast-enhanced MRA, and digital subtraction angiography (DSA) to delineate the complete lower extremity arterial tree. CTA is the preferred modality for planning interventions in the aortoiliac and femoropopliteal segments. It is constrained by calcification and contrast-induced nephropathy (CIN). Contrast-enhanced MRA serves as a tool for evaluating blood flow both prior to and following surgical procedures. MRA provides superior visualization of below-knee and pedal vessels; however, it is unable to evaluate calcification and may underestimate the complexity of procedures. DSA is a definitive imaging modality utilized for patients preparing for endovascular procedures, although it is associated with inherent risks associated with puncture [48, 49].

Assessment and diagnosis of diabetic peripheral neuropathy (DPN)

Recommendation 10: A thorough evaluation of the monofilament test, 128 Hz tuning fork vibration perception, pinprick pain sensation, temperature sensation, Ipswich Touch Test (IPTT), and tendon reflexes is essential for the assessment of DPN. An abnormal nerve conduction velocity (NCV) should be considered the definitive diagnostic standard (recommendation grade: strong; evidence level: moderate).

Evidence summary: An umbrella review including seven systematic reviews ($n = 19\,531$) was included to assess the efficacy of various DPN screening tests for this issue. Key outcome indicators: The monofilament test demonstrated variable sensitivity (53%–93%) and specificity (64%–100%), accompanied by significant variability in its application. The IPTT demonstrated sufficient diagnostic accuracy, with a sensitivity of 77%, specificity of 96%, and a diagnostic odds ratio of 75.24; however, no control study comparing it to the gold-standard test was found. An abnormal nerve conduction velocity serves as the definitive criterion for diagnosing DPN. Vibration perception threshold (VPT, see the supplementary file) testing exhibits markedly enhanced diagnostic efficiency relative to that of the 128 Hz tuning fork vibration perception test [50].

Rationale: The rationale is that various straightforward and effective screening tools, such as the 10 g monofilament, 128 Hz tuning fork, pin, cold/hot rod or TipTherm, and Buck reflex hammer, are advised for a thorough evaluation of DPN in accordance with the IWGDF/IDSA guidelines. This integrated strategy demonstrates significant clinical utility, especially in primary care health units and resource-constrained areas [9, 19]. The operational procedures and interpretation of the results for each test are delineated by multidisciplinary guidelines (refer to the Appendix 1) [9]. Electromyography is considered the gold standard for diagnosing diabetic peripheral neuropathy through the measurement of nerve conduction velocity. Nonetheless, limitations such as the need for

operator expertise, availability issues (including cost or equipment shortages), and testing duration hinder their routine recommendation. Electromyography is indicated in patients who present atypical symptoms that necessitate differential diagnosis. SUDOSCAN or corneal confocal microscopy (CCM) may be utilized by adequately equipped institutions.

Recommendation 11: Immediate initiation of knee-high offloading devices is recommended for patients with suspected diabetes and active Charcot foot. Subsequent confirmation of the diagnosis requires the use of plain X-rays and MRI (recommendation grade: strong; evidence level: moderate).

Evidence summary: Three systematic reviews reporting on the diagnosis of Charcot foot were included in this recommendation. Key outcome indicators: A delay in diagnosis was observed in 53.2% of cases of Charcot osteoarthropathy (95% CI: 28.9%–77.4%). The diagnostic delay was 86.9 days (95% CI: 10.5–162.1) [51, 52]. No evidence was found regarding the diagnostic accuracy of a temperature difference >2°C between the feet in patients suspected of having active Charcot neuro-osteoarthropathy (CNO). Evidence indicates that MRI has adequate diagnostic accuracy for CNO in patients with intact skin, supporting both its inclusion and exclusion in diagnostic considerations. Active CNO with intact skin may present with normal MRI findings [1–3].

Rationale: Delayed diagnosis is common in clinical practice for suspected active CNO with intact skin in patients with diabetes. Early identification is critical for preventing joint collapse. Inspecting the foot for signs (localized redness, swelling, deformity, or ulceration) and measuring skin temperature (a difference >2°C between feet warrants attention) are necessary. Once active CNO is suspected, a knee-high offloading device should be initiated immediately. Plain X-rays and MRI should be performed to confirm active CNO. Nuclear imaging can also be used to detect active CNO with high sensitivity but low specificity. ESR, CRP, or (bone-specific) alkaline phosphatase determination is not recommended for the diagnosis or exclusion of active CNO [53, 54].

Perform diagnostic and differential diagnostic procedures

Recommendation 12: In patients with DF, a comprehensive evaluation should precede the diagnosis, etiology classification, and severity grading, all of which should be conducted according to established criteria to inform individualized management and prognostic assessment (recommendation grade: strong; evidence level: low).

Evidence summary: This recommendation includes one systematic review, which address the diagnosis, classification, and grading of DF. Key outcome indicators: The Meggitt–Wagner system, Texas classification system, Wound, ischemia, and foot infection (WIFI) classification system, and SINBAD classification system have shown clinical utility in assessing wound healing rates, healing durations, lower limb amputation rates, and associated costs. Higher classification grades correlate with decreased wound healing rates, extended healing durations, significantly elevated amputation rates and costs, and increased in-hospital mortality rates, especially when assessed using the Wagner system [55].

Rationale: Diagnostic criteria for DF: Meets the diagnostic criteria for diabetes mellitus. Exhibits features indicative of DF, comprising a history of previous ulcers, amputations, or current treatment, including revascularization; neuropathy of the distal lower extremities; peripheral arterial disease

Table 6. Clinical manifestations of lower limb ulcers by etiology

Category	Etiology	Preferred site	Ulcer characteristics
Venous ulcers	Chronic venous insufficiency (venous hypertension)	Medial malleolar, pretibial, and lower third leg regions	Superficial, with irregular edges, granulation tissue or fibrin at the base, accompanied by edema, pigmentation, and scleroderma.
Arterial ulcers	Atherosclerosis and thrombosis	Acral and lateral foot regions	Deep, with well-defined/punched-out edges, pale/necrotic base, and severe pain (at rest).
Neuropathic ulcers	Ulcers associated with diabetes, spinal cord injury, and leprosy	Pressure-induced	Deep, painless, with frequent LOPS and callus-covered ulcers.
Neoplastic Ulcers	Ulcers associated with primary or metastatic cutaneous tumors	Leg, dorsal foot, periungual or subungual areas	Irregular edges, necrotic base prone to bleeding, rapid progression, and refractory to conventional treatment
Drug-induced ulcers	Drug-induced ulcers (e.g. hydroxyurea, warfarin, chemotherapeutics)	Ankle and foot	Dry necrosis with well-demarcated borders (e.g. vasoconstrictor or warfarin-induced); erythema, exudation, and irregular edges (e.g. immune-related ulcers).
Metabolic ulcers	Gout-related, malnutrition-associated, and calciphylaxis ulcers	Periarticular regions and distal anterior leg	Irregular edges with a base of white tophi, white exudate, or dry gangrene.
Hematologic ulcers	Ulcers associated with sickle cell anemia and thrombotic thrombocytopenic purpura (TTP)	Distal lower limb, ankle, and dorsal foot	Prone to recurrence, accompanied by anemia, bone pain, ecchymosis, and microangiopathic hemolysis.
Autoimmune disease-associated ulcers	Ulcers associated with vasculitis, lupus erythematosus, pyoderma gangrenosum, antiphospholipid syndrome, and Behçet's disease	Distal calf and ankle region	Painful, refractory, and recurrent deep irregular ulcers.

presenting with varying degrees of severity; and foot infection, ulceration, and deep tissue destruction. Exclusion of alternative etiologies for foot ulcers in diabetic patients [56]. Classification and grading systems: The SINBAD system provides benefits, including simplicity and the absence of specialized equipment, rendering it appropriate for communication among healthcare providers at various levels during consultations, referrals, or tiered medical care. The IDSA classification is extensively utilized in the IWGDF guidelines and other frameworks for evaluating infection severity. The WifI classification has been validated for predicting amputation risk in patients with chronic limb-threatening ischemia (CLTI) and is relevant for perfusion assessment and revascularization planning.

Recommendation 13: In cases where diabetic patients exhibit foot ulcers with unusual anatomical distributions, atypical morphological characteristics, or inadequate responses to standard treatment, a differential diagnosis is essential (recommendation grade: strong; evidence level: low).

Evidence summary: This recommendation is based on one meta-analysis reporting various etiologies of lower limb ulcers. Key outcome indicators: Seventy percent of lower limb ulcers were of vasculogenic origin, comprising venous ulcers (46.7%), arterial ulcers (14.5%, which increased to 15%–20% after the age of 70), and mixed arteriovenous ulcers (17.6%). The remaining 30% were linked to rare diseases, such as vasculitis (5.1%), external factors (e.g. trauma, 3.8%), pyoderma gangrenosum (3.0%), infection (1.4%), neoplasms (1.1%), calciphylaxis (1.1%), and drug-induced ulcers (1.1%), etc. [57] (Table 6).

Rationale: The etiologies of lower limb ulcers in diabetic patients are varied and include venous, arterial, hypertensive-arterial, neuropathic, neoplastic, drug-induced, metabolic, hematologic, autoimmune, and other categories, such as

mixed arteriovenous ulcers, nonhealing ulcers, and necrobiosis lipoidica [57–63]. The differential diagnosis may be conducted utilizing the ABCDE rule: A (Anamnesis): Detailed collection of medical history; B (Bacteria): Assessment of infections and microbiological analysis; C (Clinical examination): Physical evaluation including neurological and vascular assessments; D (Dynamics of perfusion): Hemodynamic evaluation (e.g. ABI, TcPO₂); and E (Extended investigations). Additional diagnostic tests, with tissue biopsy and pathological examination as the most critical diagnostic methods [59].

Clinical question 2: treatment of DF

Internal medicine treatment

Maintain vital signs and internal environment stability and protect the function of vital organs.

Recommendation 14: Maintaining the stability of vital signs, the internal environment and nutritional status and protecting major organ functions are the foundations for the treatment of DF (recommendation grade: strong; evidence level: moderate).

Evidence summary: One systematic review and meta-analysis ($n = 801\,985$) was included for this recommendation, detailing the internal environmental status of patients with DF, and two meta-analyses were analyzed for the relationship between cerebrovascular diseases and DF. Key outcome indicators: Patients with DF were typically elderly, had a prolonged duration of diabetes, and presented with multiple comorbidities, indicating a strong association between internal environmental disorders and the development of foot ulcers. Additionally, ulcers were notably prevalent in individuals with type 2 diabetes mellitus who exhibited poor glycemic control. A history of smoking (29.1% compared

with 17.4%) was linked to microcirculatory disorders and tissue hypoxia. A low BMI (23.8 ± 1.7 vs 24.4 ± 1.7) might indicate malnutrition or metabolic imbalance. There were notable regional disparities, with a high prevalence in North America potentially linked to the increased incidence of metabolic syndrome, while a significant burden in Africa is likely attributable to inadequate medical resources [4]. Cerebrovascular disease could significantly increase the risk of developing DF (OR = 1.79, 95% CI: 1.06–3.03, $I^2 = 83\%$, but there was high heterogeneity among the three included studies) [64], as well as the risk of major amputation [65].

Rationale: Comprehensive management of patients requires a multifaceted approach: first, close monitoring of vital signs and strict maintenance of fluid, electrolyte, and acid–base balance are essential to ensure physiological stability. Second, intensified glycemic control, smoking cessation, and nutritional status optimization should be implemented. This includes the intake of high-quality carbohydrates, 1.0–1.5 g/kg/day of high-biological-value protein, and a balanced fatty acid profile with a 1:1:1 ratio of saturated, monounsaturated, and polyunsaturated fats. Short-term supplementation with ω -3 fatty acids, vitamins, and iron may be beneficial, while critically ill patients may require enteral or parenteral nutritional support [66, 67]. Third, efficient allocation of intervention-related resources—such as personnel, technology, medications, and time—should be optimized to enhance treatment efficacy and clinical outcomes. Fourth, neurological assessments should integrate clinical manifestations with cranial imaging findings to evaluate cerebral status; maintaining adequate cerebral perfusion is crucial for stroke prevention, and antithrombotic and vasodilatory therapies should be rationally adjusted based on individual patient conditions.

Recommendation 15: Assess cardiac function in patients with DF and administer treatments as needed, including oxygen inhalation, sedation, vasodilation, and diuresis. Patients should be referred to the cardiology department or intensive care unit (ICU) (recommendation grade: strong; evidence level: moderate).

Evidence summary: This recommendation includes two systematic reviews and meta-analyses ($n > 613\,925$ cases) examining the risk of heart failure (HF) and its management in patients with diabetes-related foot disease [68, 69]. Key outcome indicators: Between 23% and 64% of individuals with diabetes also have HF. The risk of HF increases by 23% for each 20 mg/dl increase in fasting blood glucose, demonstrating a J-shaped relationship, particularly with an increased risk associated with type 1 diabetes. Coexisting conditions such as coronary heart disease and hypertension increase the risk of HF (pooled RR = 1.69, 95% CI: 1.57–1.81). Approximately 20%–30% of hospitalized patients with DF exhibit microvascular and macrovascular complications, while 64.3% of patients with DF also present with concurrent HF [68, 69].

Rationale: The primary symptoms of HF include exertional dyspnea and paroxysmal nocturnal dyspnea. Additionally, pulmonary edema or pitting edema in the lower extremities may occur and is frequently associated with jugular vein distension and a positive hepatojugular reflux sign. Risk stratification must be conducted utilizing electrocardiography, echocardiography, BNP/NT-proBNP level assessments, and the NYHA classification criteria, in addition to determination of the left ventricular ejection fraction (LVEF). HF and DF conditions exhibit a reciprocal relationship. Eliminating

factors that induce or exacerbate HF, such as infection and anemia, is essential. The use of vasoactive drugs such as nitroglycerin is contraindicated when the patient's systolic blood pressure is <90 mmHg. Additionally, controlling the volume and rate of fluid replacement can help prevent HF. Conversely, managing HF and increasing cardiac stroke volume can improve blood flow to the foot. During HF treatment, oxygen should be administered through a face mask or ventilator-assisted ventilation, particularly for patients with ischemic ulcers. Additionally, morphine may be used to alleviate pain and anxiety, in addition to medications such as nitroglycerin and diuretics [70], while managing arrhythmias and enhancing myocardial remodeling. Patients should be referred to the cardiology department or ICU if necessary [71]. The criteria for coronary artery intervention should be carefully assessed to prevent unnecessary coronary angiography and interventions in patients with DF who lack appropriate or have overly broad indications.

Recommendation 16: Assess the renal function of patients with DF, refrain from using medications that may exacerbate renal burden, and improve monitoring while ensuring adequate fluid replacement (recommendation grade: strong; evidence level: GPS).

Evidence summary: No relevant systematic reviews or original research evidence were found for this recommendation.

Rationale: The prevalence of CIN is $\sim 21\%$. The baseline estimated glomerular filtration rate (eGFR) serves as an independent predictor of CIN. Estimation formulas for the eGFR, including the CKD-EPI formula, are highly accurate and applicable for assessing CKD stages 1–5. Fluid replacement can notably decrease the risk of CIN to 11% (RR: 0.69, 95% CI: 0.53–0.89). The type of fluid, including isotonic saline and half-isotonic saline, as well as the fluid replacement rate and duration, significantly affect preventive efficacy. The risk of CIN is similar for isosmolar contrast agents (iodixanol) and low-osmolar contrast agents (RR: 0.72, 95% CI: 0.49–1.04; $P = 0.08$), both of which are associated with a lower risk than iohexol is [72, 73]. Persistent hypertension, an anemic appearance, oliguria or anuria, proteinuria, and hematuria are significant indicators of abnormal renal function [74]. Medications that may worsen renal insufficiency, including contrast agents and aminoglycoside antibiotics, should be avoided. For patients with DF, injection with nonionic low-osmolar contrast agents, such as iopamidol, should be chosen over injection with iohexol. Additionally, these patients should receive enhanced fluid replacement, with individualized plans for those with eGFRs of 30–60 ml/min and intensified renal function monitoring for patients with eGFRs <30 ml/min [75]. In patients with concurrent uremia, the dialysis regimen must be modified based on the status of foot surgery, and the monitoring of vital signs and the management of the internal environment should be enhanced [76].

Management of blood glucose levels, blood pressure, lipid levels, and antithrombotic therapy in patients with DF.

Recommendation 17: Developing an individualized glucose-lowering plan and effective glycemic control, characterized by the prevention of hypoglycemia and minimization of glycemic variability, facilitates the healing of DF and decreases the likelihood of amputation in patients (recommendation grade: strong; evidence level: moderate).

Evidence summary: This recommendation is based on two systematic reviews and one meta-analysis that examine the

relationship between glycemic control and DF. Key outcome indicators: Increased glycemic variability is associated with a higher incidence of DPN [77]. Intensive glycemic control markedly decreases the risk of DPN in patients with both type 1 and type 2 diabetes, as evidenced by annualized risk differences (RDs) of -1.84% (95% CI: $-2.56, -1.11$) and -0.58% (95% CI: $-1.17, 0.01$), respectively [78]. The recommended HbA1c target for diabetic patients with PAD is typically $<8\%$, although it may be adjusted to be higher for individuals at risk of hypoglycemia [46]. Intensive glycemic control is linked to the healing of DF, with an HbA1c level of $\geq 7\%$ serving as a significant predictor for nonhealing ulcers [11], while levels $\geq 8\%$ increase the risk of amputation [79]. GLP-1 drugs (GLP-1 receptor agonists, GIP/GLP-1 and GCG/GLP-1 dual receptor agonists) can improve cardiovascular and renal outcomes, thereby changing the treatment landscape for patients with type 2 diabetes, specifically in multiple aspects related to the “cardio–renal–metabolic–foot” connection [80]; that is, based on enteroinsulin therapy, the incidence of DF can be reduced, and the prognosis can be improved [81]. Although early RCTs (such as the CANVAS study) suggested that the sodium–glucose cotransporter-2 inhibitor (sodium–glucose cotransporter-2 inhibitor, SGLT-2) canagliflozin might increase the risk of amputation [82], real-world data do not support this conclusion. For example, the risk of major amputation in PAD patients treated with SGLT-2 inhibitors is not greater than that in patients treated with GLP-1RA (HR = 1.29, $P = .095$) but is greater than that in patients treated with sulfonylurea drugs (the risk is more than doubled) [83]. A retrospective case–control study that included eight studies based on propensity score matching (improving the credibility) also revealed that SGLT-2 inhibitors do not increase the risk of major amputation [84].

Rationale: Intensive glycemic control with minimal glycemic variability should be adopted to decrease the risks of DPN, facilitate the healing of DF, and lower the likelihood of amputation (low). Patients at risk of hypoglycemia, including the elderly or individuals with a prolonged history of diabetes or severe complications/comorbidities (e.g. CVD, HF, and lower extremity arterial disease), should have their glycemic control targets adjusted to a less stringent level (HbA1c $< 8\%$) to mitigate the occurrence of hypoglycemic events. For patients with DF who have abdominal obesity and fatty liver, new hypoglycemic drugs such as GLP-1 receptor agonists, GIP/GLP-1 and GCG/GLP-1 dual receptor agonists, and SGLT-2 inhibitors can be selected to achieve weight loss, adjust metabolism, and improve cardiovascular and renal outcomes.

Recommendation 18: Antihypertensive agents should be selected on an individual basis for DF patients with hypertension. Blood pressure control should be defined by a target of $<130/80$ mmHg or a less stringent target of $<140/90$ mmHg for geriatric or critically ill patients (recommendation grade: weak; evidence level: GPS).

Evidence summary: No relevant systematic reviews or original research evidence were found for this recommendation.

Rationale: Hypertension is correlated with amputation (OR = 0.58, 95% CI: 0.40, 0.84) [85]; elevated systolic blood pressure (SBP ≥ 140 mmHg) is a risk factor for foot deformities in diabetic patients [86] and amputation in individuals with type 1 diabetes [87]. The IWGDF/ESVS/SVS guidelines suggest a blood pressure target of $<140/90$ mmHg for patients with diabetes and PAD, although this may be

adjusted considering the risk of orthostatic hypotension and other negative effects. For patients under 65 years of age with a low risk of adverse effects, a stricter blood pressure control target of $<130/80$ mmHg is recommended [46]. For elderly patients with DF and multiple complications or comorbidities, a blood pressure target of $<140/90$ mmHg is advised.

Recommendation 19: Patients with DF and hyperlipidemia should be advised to implement suitable dietary and exercise modifications, and moderate- or high-intensity statin therapy should be commenced under medical supervision. The combination with additional lipid-lowering agents may yield beneficial outcomes (recommendation grade: strong; evidence level: moderate).

Evidence summary: This recommendation included eight RCTs reporting on hyperlipidemia control and targets in DF patients. Key outcome indicators: Dietary intervention significantly decreases triglyceride (TG) and TG-rich lipoprotein levels in patients with type 2 diabetes [88]. Fenofibrate lowers the risk of major amputation (HR 0.64, 95% CI: [0.44–0.94], $P = 0.02$) [89]. PCSK9 inhibitors reduce LDL levels by -18.57% ($-27.30\%, -9.84\%$) at 12/24 weeks [90, 91]. The combination of statins and ezetimibe reduces the 7-year Kaplan–Meier major endpoint event rate (cardiovascular death, major coronary events, stroke) by 5.5% (HR 0.85; 95% CI: [0.78–0.94]) in diabetic patients [92]. *Post hoc* analysis indicated that in patients with baseline LDL-C levels <70 mg/dl, the combination of statins and ezetimibe further decreased the risk of cardiovascular events following acute coronary syndrome (ACS) [93, 94].

Rationale: The relationship between lipid-lowering therapy and the healing of DF remains debated; however, it is evident that reducing LDL levels significantly decreases the risk of cardiovascular events. The 2013 ACC/AHA guidelines recommend the use of moderate- to high-intensity statins for diabetic patients [95]. In 2018, guidelines advised the administration of moderate-intensity statins for diabetic individuals aged 40–75 years with LDL-C levels of 1.8 mmol/L or higher. High-intensity statins are recommended for high-risk diabetic patients, particularly those with multiple risk factors or those aged 50–75 years, to achieve a $>50\%$ reduction in LDL-C levels [96]. In 2024, guidelines endorsed statin use to decrease macrovascular events and amputation risk in patients with DF [44].

Recommendation 20: For patients with DF and coronary heart disease or PAD, initiating an appropriate antithrombotic regimen as soon as possible following a bleeding risk assessment is recommended (recommendation grade: strong; evidence level: GPS).

Evidence summary: No relevant systematic reviews or original research evidence were found for this recommendation.

Rationale: Compared with aspirin monotherapy, “ticagrelor + aspirin” therapy is associated with a lower incidence of ischemic cardiovascular events (7.7% vs 8.5% , $P = 0.04$) [97]. However, this combination therapy also increases the risk of major bleeding (2.2% vs 1.0% ; $P < 0.001$) [97] and decreases the occurrence of limb events and revascularization [98]. A 1-month treatment course demonstrates effects comparable to those of the standard 3-month regimen but results in fewer bleeding events [99]. The “rivaroxaban + aspirin” regimen is associated with a reduced risk of macrovascular diseases and major limb events; however, it is associated with an increased risk of bleeding events (2.7% vs 1.0% , $P = 0.001$), while the risk of all-cause

mortality remains comparable [100, 101]. There is no difference between ticagrelor and clopidogrel regarding the prevention of macrovascular events and the risk of bleeding [102]. Hyperglycemia is linked to increased risks of both arterial/venous thrombosis and bleeding, making it essential to balance these thrombotic and bleeding risks [103]. Numerous guidelines recommend long-term antiplatelet therapy in patients with DF, including monotherapy options such as aspirin (75–325 mg/day), clopidogrel (75 mg/day), or ticagrelor (90 mg twice daily). The duration of treatment (1–3 months) for patients necessitating dual antiplatelet therapy (DAPT, such as ticagrelor and aspirin) following intervention should be determined by the associated bleeding risk. Patients identified as having a low risk for bleeding may choose a regimen consisting of a single antiplatelet agent combined with an anticoagulant (e.g. aspirin plus rivaroxaban 2.5 mg administered twice daily) [46, 101].

Treatment of diabetic peripheral neuropathy.

Recommendation 21: The management of patients with diabetic peripheral neuropathy should emphasize both resolving the underlying causes and relieving symptoms; anticonvulsants and/or antidepressants are preferred for pain alleviation. Opioid medications are not advised as first-line or second-line treatments; local pain-relieving drugs have effects similar to those of first-line painkillers and can be used as adjunctive treatments in clinical practice (recommendation grade: strong; evidence level: high).

Evidence summary: This recommendation included 10 meta-analyses and 8 RCTs reporting the etiological treatment and pain relief of DPN. Key outcome indicators: The administration of acetyl levocarnitine (1500 mg/day) for 24 weeks resulted in a significant improvement in the neurological lesion score, with a change of -6.9 ± 5.3 points compared with -4.7 ± 5.2 points ($P < 0.001$) [104]. Compared with monotherapy or dual-drug combinations, combination therapy with lipoic acid, epastat, and mecobalamin resulted in superior improvements in the nerve conduction velocity and vibration perception threshold (OR 3.74, 95% CI: [2.57, 5.45]) [105]. Pregabalin in conjunction with antidepressants may reduce pain (MD -0.39 , 95% CI: $[-0.67, -0.12]$) [106]. Duloxetine (60–120 mg) monotherapy demonstrated efficacy [107]. Additionally, various treatments, including vitamins, traditional Chinese medicines, stem cells, pulsed electromagnetic waves, and foot training, have been shown to have therapeutic effects [108–111]. The 8% capsaicin patch is not inferior to and is even superior to pregabalin in alleviating abnormal dynamic mechanical pain (with a faster onset, a median of 7.5 days *vs* 36 days), and it has a better analgesic effect than the 5% lidocaine patch ($P < 0.01$) [112–115].

Rationale: Antioxidants and aldose reductase inhibitors, including prostaglandin E1 and pancreatic kininogenase, which increase microcirculation and alleviate symptoms, exert therapeutic effects on the etiology of DPN [116]. Mecobalamin facilitates nerve repair, whereas traditional Chinese medicines have demonstrated potential in alleviating symptoms. These studies have several limitations, including inadequate evidence and unverified long-term efficacy. Anticonvulsants such as pregabalin and gabapentin, along with antidepressants such as duloxetine, amitriptyline, promethazine, and cetirizine, are considered first-line medications for pain management. Opioid medications, including tramadol and hydrocodone, are not advised as first-line or second-line

treatments because of their associated adverse effects and potential for addiction [117, 118]. Alternative treatments, such as electromagnetic waves, lasers, and exercise, may demonstrate efficacy; however, the supporting evidence remains inadequate. Local drug therapy is also effective for treating painful neuropathy. For instance, an 8% capsaicin patch, as a topical medication, achieves pain relief by depleting substance P in sensory nerve endings. In recent years, it has been considered a promising alternative or complementary treatment option that can be used alone or in combination with other pain-relieving drugs.

Recommendation 22: Spinal cord stimulation (SCS) is indicated for the treatment of refractory painful diabetic neuropathy, necessitating an evaluation of individual preferences, surgical conditions, and economic feasibility (Recommendation grade: Weak; Evidence level: High). SCS is contraindicated for the treatment of DF or other related foot conditions with identifiable and reversible underlying causes (recommendation grade: strong; evidence level: low).

Evidence summary: This recommendation includes two RCTs and two cohort studies that examine the efficacy of spinal cord stimulation for pain relief. Key outcome indicators: High-frequency SCS at 10 kHz has been shown to alleviate chronic pain, enhance neurological function, and sustain satisfactory outcomes for 24 months after treatment, with effects observed to extend up to 4.1 years after implantation, along with ongoing improvements in weight and HbA1c levels [119, 120]. SCS has the potential to enhance lower limb hemodynamic parameters, significantly decreasing the risk of ischemic DF amputation, particularly at the 12-month mark. However, this study solely utilized the amputation rate as an endpoint and did not evaluate wound healing, in addition to experiencing a high patient dropout rate [121]. The efficacy of CSC treatment for foot ulcers surpasses that of debridement alone within a 2-week period; however, this effect typically diminishes after 6 weeks [122].

Rationale: SCS is a minimally invasive technique that involves the use of implanted electrodes to deliver weak electrical currents to targeted spinal cord segments, thereby modulating nerve signal transmission. High-frequency SCS at 10 kHz is an effective intervention for refractory painful diabetic neuropathy, as supported by RCTs and real-world studies, which have demonstrated significant pain relief within 1 year. Nonetheless, it presents disadvantages, including elevated costs and possible complications [47, 123]. At present, high-quality RCTs supporting the application of spinal cord stimulation for the management of DF or other associated foot conditions with identifiable reversible causes are lacking. Additional assessments are needed regarding mechanisms, the optimization of personalized parameters, and health economics.

Recommendation 23: In patients with diabetic CNO, non-surgical treatment should focus on foot offloading using appropriately fitted devices to prevent the onset and progression of foot ulcers (recommendation grade: weak; evidence level: GPS).

Evidence summary: No relevant systematic reviews or original research evidence were found for this recommendation.

Rationale: Diabetic CNO is a degenerative condition that affects the bone structure of the foot and results from significant peripheral neuropathy, increasing the risk of ulceration and amputation. Compared with a removable cast walker (RCW), a nonremovable device (nonremovable RCW,

N-RCW) demonstrated superior ulcer-healing rates (80–90% *vs* 60–75%, $P < 0.05$), with outcomes closely linked to device adherence, weight-bearing status, and activity level [124, 125]. The use of a total contact splint (TCS) and RCW with felted-foam modifications produced ulcer-healing times similar to those of a total contact cast (TCC) [126]. In patients with midfoot osteomyelitis, the application of an external fixator (Exfix) significantly reduced the wound healing time (68 days *vs* 102 days, $P < 0.05$) [127]. No significant differences were observed in major amputation rates among offloading devices, which ranged from 7% to 8% [128]. After TCC application, the recurrence rate of ulcers was between 5% and 13%, whereas following RCW use, the recurrence rate for ulcers in the contralateral foot increased to 20% [129]. The primary goals of offloading intervention in Charcot foot include stabilizing structural alignment, limiting further osseous destruction, and preventing secondary ulceration [53]. During the active phase, first-line management involves a nonremovable knee-high offloading device (N-RCW), which includes options such as a TCC, TCS, or a knee-high removable walker made nonremovable (commonly referred to as an “instant TCC”) [53, 129]. In cases where N-RCW is not tolerated or resources are constrained, an RCW with felted-foam modifications may be utilized. In the remission or stable phase, it is advisable to prescribe custom therapeutic footwear, a Charcot restraint orthotic walker, or ankle–foot orthoses to ensure proper alignment and redistribute plantar pressure.

Antimicrobial treatment

Recommendation 24: The antimicrobial regimen for DFIs should be determined through a thorough evaluation of infection severity, microbiological results, and the patient’s overall health status (recommendation grade: strong; evidence level: high).

Evidence summary: The analysis for this recommendation included two meta-analyses, one RCT, and two cohort studies. Key outcome indicators: *S. aureus* is the predominant pathogen, accounting for 5073 of 5670 isolates, with 18.0% classified as methicillin resistant (MRSA). This is followed by *Pseudomonas* spp., *Escherichia coli*, and *Enterococcus* spp. [130]. In China, gram-negative bacteria constitute 52.4% of the bacterial population, surpassing gram-positive bacteria, at 43.4%. Among these, 20% are multidrug resistant, with *S. aureus* accounting for 30.4% of the multidrug-resistant cases [131]. Gram-positive isolates exhibit sensitivity to linezolid, vancomycin, and teicoplanin. More than 50% of gram-negative isolates are resistant to third-generation cephalosporins, while resistance rates to piperacillin-tazobactam, amikacin, meropenem, and imipenem remain relatively low. The failure rate associated with broad-spectrum agents is ~30% [131, 132]. Following debridement, the clinical failure rate is 17%, regardless of whether antibiotics are administered for 7 days or discontinued immediately [133]. A 10-day course is not inferior to a 20-day course, with comparable clinical cure rates (77% *vs* 71%), adverse event rates (40% *vs* 35.5%), and rates of new osteomyelitis (23% *vs* 16%) [134].

Rationale: Selection of narrow-spectrum, short-course agents that exhibit minimal adverse effects, are cost-effective, and demonstrate high safety profiles whenever feasible. There is no universally superior regimen; the selection should consider the pathogen profile, extent of infection, antibiotic

usage in the preceding 3 months, presence of osteomyelitis, and individual factors such as allergies, immune status, hepatic or renal function, peripheral arterial disease, and the risk of multidrug-resistant organisms [46, 135]. Mild infections may not necessitate antibiotics or may only require a brief course aimed at gram-positive organisms. Early empirical therapy is essential for moderate to severe or deep infections, with coverage for MRSA or *Pseudomonas* as indicated. De-escalation should follow based on susceptibility results, and antianaerobic or antifungal agents should be added when necessary. Treatment should be initiated intravenously and transitioned to oral therapy at the earliest opportunity. The duration of treatment should be determined by infection control protocols, typically not exceeding 10 days; however, it should extend to at least 3 weeks if residual bone infection persists following debridement (≥ 6 weeks if osteomyelitis remains unaddressed). Reasons for treatment failure include sampling error, delayed or false-negative cultures, drug allergies that restrict options, and the presence of multidrug-resistant organisms, such as ESBL-producing Enterobacterales and carbapenem-resistant strains [136]. Topical antibiotics or antibiotic-impregnated materials, such as sponges, creams, and cement, are not recommended because of insufficient high-quality evidence and the risk of increased resistance [46, 137]. The IWGDF guidelines do not support the use of hyperbaric oxygen as an exclusive adjunct for DFIs. Cold atmospheric plasma significantly decreases the bacterial load ($P = 0.01$ *vs* control) [138], whereas infrared therapy has been noted for its antimicrobial properties; however, both interventions are supported by limited high-quality evidence.

Perioperative risk management

Recommendation 25: Assess the perioperative risk of patients with DF and implement appropriate preventive measures based on the results of risk stratification (recommendation grade: strong; evidence level: GPS).

Evidence summary: No relevant systematic reviews or original research evidence was found for this recommendation.

Rationale: The association between diabetes and venous thromboembolism (VTE) is characterized by an increased risk of recurrence, bleeding, and mortality [139]. VTE is associated with foot and ankle surgery, with a 90-day thrombus incidence and mortality rate of 0.87% and 0.03%, respectively [140]. A Caprini score of 3–4 or higher signifies a high risk of VTE, necessitating a combination of pharmacological interventions—preferably low-molecular-weight heparin or Xa factor inhibitors over aspirin alone—and mechanical methods [9, 141]. Bleeding risk increases in patients receiving rivaroxaban in combination with aspirin (5.94% *vs* 4.06%, HR 1.42) [142], as well as in individuals undergoing peripheral vascular interventions, where the major bleeding rate is ~4.1% [143]. The use of medications and surgical procedures should be standardized to mitigate the risk of VTE [144]. An OAC3 PAD score of 3 or higher signifies a significant bleeding risk, requiring necessary modifications to anticoagulant therapy (aspirin need not be discontinued prior to surgery, whereas clopidogrel should be stopped 7 days in advance). Additional medications, including nonsteroidal anti-inflammatory drugs and corticosteroids, should be optimized in conjunction with the interventional surgical procedure. The femoral artery puncture site is located 2 cm below the skin crease in the inguinal area; in obese patients, retrograde puncture may be considered. The risk of hospital-acquired pressure ulcers

(HAPUs) is linked to five primary factors: CVD, respiratory system diseases, diabetes, anemia, and extended surgery or ICU stays [144]. Locally purified membrane lipid agents, alternating-pressure mattresses, foam mattresses, and five-layer silicone resin sacral foam are effective at preventing HAPUs, reducing the incidence from 50% to 2% [145]. A Braden score of 10–12 or lower signifies a high HAPU risk, necessitating improved nutrition, positional adjustments, and the application of topical agents and foam dressings [9,140]. Risks of anesthesia are linked to diabetes in conjunction with CVD, diabetic neuropathy, and foot–ankle surgery [146]. Compared with alternative anesthesia techniques, peripheral nerve block (PNB) is favored because of the reduced associated occurrence of hypotension and transfusion events, along with its effective analgesic properties [147]. ASA PS system level III and higher are classified as high risk for anesthesia-related incidents, necessitating the avoidance of both epidural and general anesthesia risks. An ASA PS system rating of III or higher signifies a significant risk of anesthesia-related incidents. The risks linked to epidural anesthesia, including the challenges of puncture, bleeding, nerve injury, hypotension, and cardiovascular incidents, as well as those associated with general anesthesia, such as intraoperative hypotension, cardiovascular events, and postoperative pulmonary complications, should be mitigated. Ultrasound-guided PNB is recommended as the primary treatment option [147, 148].

Surgical treatment

Debridement and bone reconstruction surgery

Principles of debridement.

Recommendation 26: The debridement plan for diabetic patients must be tailored to the specific characteristics of foot ulcers and individual baseline conditions while also considering technical or equipment factors (recommendation grade: strong; evidence level: moderate).

Evidence summary: This recommendation included seven meta-analyses and systematic reviews, along with two RCTs that address the debridement of DF. Key outcome indicators: Sharp debridement facilitates the healing of nonischemic wounds, with no significant difference in effectiveness between weekly and biweekly applications [149]; however, the evidence remains insufficient [46]. Improved surgical training has been shown to decrease the likelihood of repeat surgeries by a factor of five ($P=0.003$) and to shorten hospital stays from a median of 36–21.5 days ($P=0.02$) [150]. There was no difference in ulcer changes following laser debridement; however, the pain score ($P=0.003$) and bacterial load decreased, with 52.9% of patients expressing a preference for this treatment option [151]. Ultrasound debridement markedly enhanced wound healing ($P<0.001$) [46, 152]. Larval debridement does not enhance ulcer healing; however, it may decrease amputation rates ($P=0.02$) [153]. Autolytic debridement and enzyme agents, such as P1G10 and kiwi extract, promote ulcer healing; however, the overall quality of evidence remains low, and the results are typically unstable [72, 154]. The frequency and number of debridements correlate with infection control, repeat debridement rates, admission rates, length of hospital stay, and associated costs [149, 155].

Rationale: The purpose of debridement is to incise, drain, and remove necrotic tissue and foreign matter to promote tissue growth. Multiple debridement methods exist, each characterized by distinct mechanisms along with specific advantages and disadvantages. Mechanical debridement

includes sharp debridement, surgical debridement, wet-to-dry debridement, ultrasound debridement, hydrosurgery, and biological debridement. Mechanical debridement is typically rapid and highly specific; however, it can result in pain, wound expansion, or significant costs. Nonmechanical debridement includes autolytic debridement, which utilizes hydrogels, hydrocolloid, or alginate dressings, and enzymatic debridement, exemplified by collagenase. Nonmechanical debridement is straightforward to perform, highly selective, and generally well tolerated by patients. Nonetheless, the progress of debridement is relatively slow, and certain methods are constrained by the risks of infection or allergic reactions [149, 153] (Table 7).

Soft tissue debridement.

Recommendation 27: In cases of moderate to severe infections of DF, particularly when abscesses, wet (gas) gangrene, or necrotizing fasciitis are present, urgent debridement is indicated. In instances of severe ischemia, initial incision and drainage should be performed to eliminate necrotic tissue (without an extensive incision), followed by comprehensive debridement after lower limb perfusion is restored (recommendation grade: strong; evidence level: moderate).

Evidence summary: This recommendation incorporates five RCTs and two systematic reviews reporting on debridement strategies for DFIs. Key outcome indicators: Compared with patients who received a combination of antibacterial drugs and debridement surgery, patients who received only antibacterial drug treatment had a higher amputation rate (27.6% *vs* 13%, $P<0.01$) and an extended hospital stay (6 days) [156]. The amputation rate for patients who received timely debridement (within 6–8 h) was 0%, whereas for those who received delayed debridement (average delay of 6.2 ± 7.5 days), the rate increased to 7.9%. Additionally, each day of delay correlated with a 1.6-fold increase in the risk of Chopart or above-ankle amputation ($P=0.015$) [157]. Compared with patients who underwent surgical debridement, patients who received conservative treatment had a higher mortality rate (23.1% *vs* 0%), a lower wound healing rate (46.2% *vs* 88.9%), and a longer duration of antibiotic use (median 55 days *vs* 17 days), with 61.5% ultimately requiring amputation [158]. Delayed referrals markedly increase the risk of major amputation in patients with moderate to severe infections [159]. Early vascular reconstruction (within 48 h) combined with broad-spectrum antibiotic therapy is both safe and effective for wounds characterized by ischemia and infection. This approach does not increase the risk of graft or ulcer infection, enhances tissue perfusion, decreases hospital stay and costs, and improves limb salvage rates [160].

Rationale: The surgical debridement of DF should be performed with the patient under anesthesia or in a calm state by a qualified surgeon. Indications include moderate to severe infections, including abscesses, wet or gas gangrene, and necrotizing fasciitis; chronic or hard-to-heal ulcers lasting 6 weeks or more, characterized by fibrosis or devitalized tissue; and osteomyelitis with exposed bone. Relative indications include infected ischemic ulcers with a viable perfusion status, which may necessitate combined revascularization [9]. Contraindications include a significantly unstable overall health status, particularly in cases of unstable respiratory and circulatory conditions, advanced age, and multiple comorbidities. Additionally, palliative treatment or treatment near the end of life, with an expected survival time of

Table 7. Advantages and disadvantages of different debridement methods

Method	Explanation	Advantages	Disadvantages
1. Mechanical debridement			
Sharp debridement	Use a sharp tool to incise and drain, as well as remove dead tissue	Quick, less costly, specific	Painful, large injury
Surgical debridement	Similar to sharp debridement, performed in an operating room	Clear thoroughly, available for biopsy, beneficial for wound bed preparation	High technical requirements, painful, large injury, expensive
Wet-to-dry debridement	Moisten, then remove dead tissue after it dries	Less costly, easy	Nonspecific, easily damages other tissue, painful
Ultrasound debridement	Use the energy generated by ultrasound to remove dead tissue	Quick, specific	Painful, expensive
Hydrosurgery	Use high-pressure water to remove dead tissue	Quick, nonspecific	Infection spreading, painful, expensive
Maggot debridement	Direct engulfment, enzyme-containing secretions/excretions	Quick, effective, specific	Difficulty accessing maggots, painful, patients may resist for psychological reasons, contraindicated for wound next to great vessels or suspected cancerous wound
2. Nonmechanical debridement			
Autolytic debridement	Use enzymes and body fluids of the wound itself to soften and remove necrotic tissue	Convenient, minimal discomfort, less costly, specific	Slow process, increased infection risk
Enzymatic debridement	Use exogenous enzyme agents to directly degrade necrotic tissue	Convenient, fast, specific	Slow process, expensive, may cause allergic reactions or other discomfort, not ideal for heavily infected wounds

<3 months, and uncorrected severe coagulopathy (INR > 3.0) are also considered contraindications. Severe lower extremity arterial disease (ABI < 0.4 and not revascularized) constitutes a relative contraindication [161, 162]. Perioperative management primarily includes the following aspects: Nonthreatening limb infections must be differentiated from threatening limb infections. Timely surgical intervention can decrease the incidence of amputations. Moderate and severe infections, particularly those complicated by abscesses, wet (gas) gangrene, or necrotizing fasciitis, necessitate emergency debridement within 24–48 h [19]. In cases of CLI in the lower limbs, it is essential to individually analyze the timing, method, and extent of debridement. The IWGDF/ESVS/SVS guidelines highlight the need for the concurrent management of infection and ischemia [19]. During the ischemic period, blind sharp debridement should be avoided to prevent microvascular thrombosis and worsening of the wound. Immediate debridement is necessary after restoration of the blood supply to prevent delayed management from exacerbating the infection. It is essential to recognize that in cases of suspected unstable necrotic tissue, including necrotic tissue or abscess, immediate incision and drainage are warranted. Antimicrobial drugs cannot be substituted for debridement, and any delay in surgical intervention is not permissible [159].

Osseous debridement and reconstruction

Recommendation 28: For severe osteodestructive lesions of the foot refractory to conservative management, the extent of bone resection should be determined based on the local tissue

destruction, vascular supply, soft tissue integrity, and systemic conditions. Subsequent reconstruction should adhere to foot biomechanical principles (recommendation grade: strong; evidence level: GPS).

Evidence summary: No relevant systematic reviews or original research evidence were found for this recommendation.

Rationale: Comprehensive preoperative radiographic evaluation and thorough neurovascular assessment indicate that surgical debridement effectively reduces the risk of major amputation in DF patients. In instances of severe osteodestructive lesions that do not respond to conservative treatments, the degree of osseous resection must be tailored to the level of local tissue damage, vascular perfusion status, soft tissue viability, and systemic patient considerations. The primary surgical objective in managing osteomyelitis is the complete elimination of infected tissue in conjunction with targeted antibiotic therapy. Current evidence indicates no significant difference in clinical outcomes between a combined approach of surgical debridement with 10 days of antibiotic therapy and extended 90-day antibiotic treatment alone [163]. Comparative analyses revealed similar efficacy between 3-week and 6-week postoperative antibiotic regimens after surgical intervention [164]. The use of antibiotic-impregnated bone substitutes has resulted in ulcer resolution in 66% of cases [165]; however, the current evidence supporting their routine application is limited. After effective infection control, reconstructive procedures should aim to restore the stable, plantigrade architecture of the foot. In cases of noninfected ulcerations resulting from structural

deformities, such as CNO and hallux valgus, direct corrective osteotomy accompanied by soft tissue reconstruction may be considered after a thorough risk–benefit analysis, such as triple arthrodesis [166]. In cases of osteomyelitic bone defects, initial management should include antimicrobial void-filling strategies alongside targeted antibiotic therapy. Subsequent reconstruction should utilize a staged surgical approach, incorporating increasingly advanced techniques to maximize functional recovery and reduce surgical morbidity [167]. This treatment algorithm highlights the need for a thorough evaluation of surgical indications, weighing them against possible complications and analyses of cost-effectiveness.

Recommendation 29: Treatment selection for forefoot osteolytic lesions, including flexor tenotomy, joint arthrodesis, partial metatarsal head resection, or amputation, should be determined by the lesion's location and severity (recommendation grade: weak; evidence level: GPS).

Evidence summary: No relevant systematic reviews or original research evidence were found for this recommendation.

Rationale: Surgical intervention alongside antimicrobial therapy in patients with forefoot DFO includes a reduction in antibiotic duration, an increase in wound healing, and a decrease in ulcer recurrence [168]. In the case of plantar metatarsal head ulcers, metatarsal head resection and osteotomy have similar efficacy, with comparable 1-year ulcer recurrence rates [169]. However, inadequate resection (<25% of the metatarsal length) may increase the risk of recurrence beyond 6 months [170]. In limited osteotomy, preoperative imaging must accurately delineate bone involvement to guarantee thorough intraoperative resection of infected bone and prevent insufficient debridement [171–173]. No standardized surgical protocol for evaluating forefoot osteolytic lesions currently exists. In accordance with the literature and expert consensus, postdebridement management involves the following steps: In cases of toe deformities such as mallet toe, hammer toe, and claw toe, isolated flexor tenotomy is the preferred intervention for ulceration. If ulceration persists, partial or total phalangeal resection should be considered, ensuring the preservation of toe length. Recent guidelines from the IWGDF recommend the use of antimicrobial monotherapy in cases of nonulcerated DFO [19]. In cases of destruction of the first metatarsophalangeal joint (MTPJ), the Keller (Figure 2) procedure may be utilized in severe cases, whereas the Chevron (Figure 3) osteotomy is indicated for hallux valgus correction. Bone grafting is still considered investigational for postinfection reconstruction. For lesser metatarsophalangeal joint (second to fifth) involvement, options include condylectomy, single metatarsal head resection, or Weil (Figure 4) osteotomy, and arthrodesis is utilized as necessary. In instances of significant soft tissue loss or persistent ulceration, partial phalangeal or metatarsal resection is recommended to optimize residual limb length while reducing the loss of weight-bearing surfaces. When appropriate, multiple metatarsal head resection (MMHR) (Figure 5) or transmetatarsal amputation (TMA) may be considered.

Recommendation 30: For lesions of the midfoot and hindfoot involving bone and joints, combined reconstruction of osseous and soft tissue following comprehensive debridement is advised. If reconstruction is not feasible, amputation at different levels may be considered (recommendation grade: weak; evidence level: GPS).

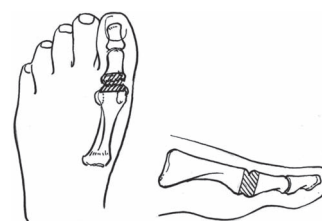


Figure 2. Keller procedure

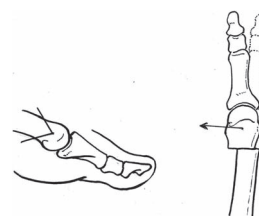


Figure 3. Chevron procedure

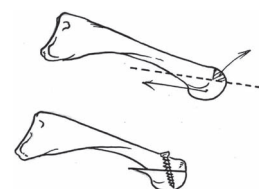


Figure 4. Weil procedure

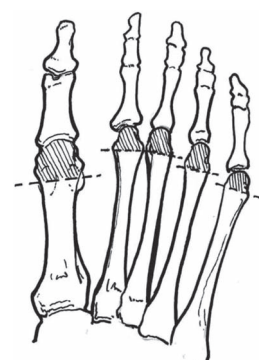


Figure 5. Multiple metatarsal head joint resection

Evidence summary: No relevant systematic reviews or original research evidence were found for this recommendation.

Rationale: Midfoot DFO often arises from proximal extension due to forefoot infection, and major amputation rates surpass 20.9%, which is considerably higher than the 6.1% rate recorded for the forefoot [174]. Transtarsal amputation (TA) is recommended for patients who are not candidates for TMA or for those who experience nonhealing ulcers related to TMA, with >70% attaining functional ambulation after the procedure [175]. Partial or complete calcaneal resection accompanied by biocomposite void filling results in a 90% rate of ulcer healing, with minimal complications reported [176, 177]. Charcot foot deformities leading to plantar ulceration can be treated with circular external fixation, hindfoot arthrodesis, and internal fixation to restore biomechanical stability [178, 179]; the fusion success rate is 84.2%, with 15.8% of cases necessitating amputation because of ongoing osteomyelitis [180]. Current surgical protocols for midfoot and hindfoot lesions lack standardization.

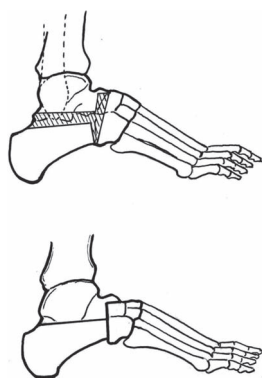


Figure 6. Triple arthrodesis

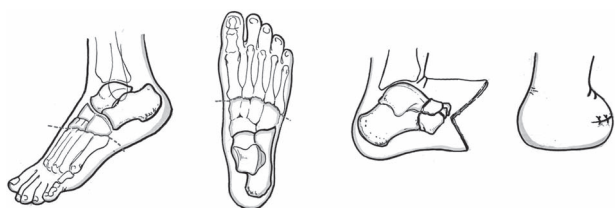


Figure 7. Lisfranc amputation

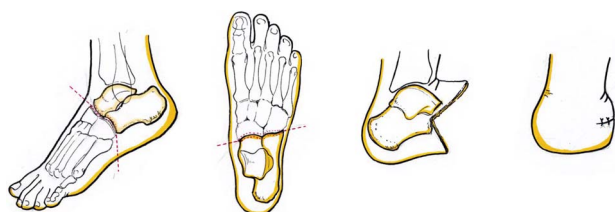


Figure 8. Chopart amputation

Management strategies, as indicated by the literature and expert consensus, include the following: radical debridement to eliminate osteomyelitis and external fixation for offloading [181], potentially augmented by midfoot arthrodesis, triple arthrodesis (Figure 6), pantalar fusion, or peritalar fusion to rectify the deformity and preserve plantigrade alignment. In certain instances, bone grafting (usually from the iliac crest) with free flap coverage may be considered, although the supporting evidence is limited, and these high-risk procedures should be conducted exclusively at specialized centers [182–184]. In cases of extensive destruction that prevents reconstruction, options such as TA, Lisfranc amputation (Figure 7), Chopart amputation (Figure 8), or major amputation may be considered as final interventions.

Management of peripheral artery disease

Recommendation 31: In individuals with DF, if the wound exhibits no signs of healing after 4 weeks of standard care, analyzing factors that may be hindering the healing process is essential. Reassessment of the lower extremity arteries is recommended, followed by direct lower extremity angiography and/or revascularization if indicated (recommendation grade: strong; evidence level: GPS).

Evidence summary: No relevant systematic reviews or original research evidence were found for this recommendation.

Rationale: A reduction exceeding 50% in the ulcer area within 4 weeks serves as a reliable predictor of eventual healing [185]. A failure to meet this threshold suggests a diminished likelihood of full recovery [186]. Following optimal antimicrobial therapy, glycemic control, local wound care, and offloading, any wound that fails to show significant improvement (defined as <50% area reduction within 4 weeks) or worsens should lead to a consultation with a vascular specialist and a repeat vascular evaluation to assess the potential for revascularization [46, 47, 186]. Revascularization must focus on the artery that directly supplies the anatomical region of the ulcer, referred to as direct revascularization. In cases where direct revascularization is not technically feasible, indirect revascularization should be considered. This approach aims to re-establish in-line flow to a vessel that supplies collateral circulation to the target artery, ultimately restoring perfusion to the ulcer area [47, 187]. The microcirculation status and other potential barriers to healing, including immune system disorders or malignancy, should be systematically identified and addressed.

Recommendation 32: The objective of lower extremity revascularization is to re-establish blood flow in at least one artery from below the knee to the foot, ideally targeting an artery that directly supplies the ulcerated region (recommendation grade: strong; evidence level: moderate).

Evidence summary: This recommendation is derived from six systematic reviews and meta-analyses that examined the objectives and outcomes of lower extremity revascularization in the management of DF [188–190]. Key outcome indicators: Compared with indirect revascularization (IR), direct revascularization (DR) is associated with enhanced wound healing (OR 2.45; $P = 0.001$) and improved limb salvage rates (OR 0.48; $P < 0.00001$). The 1-year and 2-year limb salvage rates for DR are 86.2% and 84.9%, respectively, demonstrating superiority over IR. Comparable benefits were noted for wounds resulting from infrapopliteal vessel occlusion; however, the quality of evidence was assessed as “low” or “very low” [191]. No differences in overall mortality were observed among the DR, IR, and IR with collateral (IRc) approaches. No differences in reoperation rates were observed between DR and IR [192].

Rationale: In patients with severe wounds, particularly those classified as having a WIfI of grade 3 or 4 and affecting the midfoot or hindfoot, it is advisable to consider vascular territory-oriented revascularization on the basis of the “angiosome” principle, provided that a suitable target vessel territory exists [192]. In diabetic patients with PAD and foot ulcers or gangrene, revascularization surgery should focus on restoring antegrade blood flow in a minimum of one foot artery. When possible, the target artery supplying the anatomical region of the ulcer should be identified using digital subtraction angiography (DSA) [193] (Figure 9). Before performing lower extremity vascular surgery, it is essential to comprehensively assess and balance the benefits and risks of the procedure. A detailed surgical plan should be developed and effectively communicated to the patient and their family. Decisions must be tailored to the individual, considering anatomical factors, technical feasibility, and additional comorbidities.

Recommendation 33: Choose a suitable revascularization strategy for each patient, considering their overall health status, characteristics of the vascular lesion (such as location, severity, and extent), and technical feasibility (recommendation grade: strong; evidence level: high).



Figure 9. Lower extremity vascular map. 1: Perfusion area of the anterior tibial artery. 2–3: Perfusion area of the peroneal artery. 4–6: Perfusion area of the posterior tibial artery

Evidence summary: This recommendation is substantiated by one meta-analysis and four RCTs that evaluated the outcomes of lower extremity bypass surgery (BSX) versus percutaneous vascular intervention (PVI). Key outcome indicators: Compared with the BSX group, the PVI group had a lower 30-day mortality rate, fewer major adverse cardiovascular and cerebrovascular events (MACCEs), and lower surgical site infection risk but greater risk of primary and secondary patency failure and all-cause mortality. Limb salvage and survival rates were comparable between the two methods, although BSX was associated with higher costs [194]. PVI is correlated with improved amputation-free survival and reduced mortality rates (~53% compared with 63%) and is recommended for infrainguinal arterial lesions [194]. In parallel cohort studies—one involving patients with a single-segment of the great saphenous vein available (cohort 1) and the other with patients requiring bypass grafts (prosthetic grafts) (cohort 2)—follow-up at 2.7 years indicated that, relative to the intervention group, cohort 1 exhibited a lower incidence of major adverse limb events (42.6% *vs* 57.4%, $P < 0.001$). Conversely, cohort 2 demonstrated no significant difference (42.8% *vs* 47.7%, $P = 0.12$) and no notable variation in adverse event rates [195]. In a cohort of CLI patients receiving femoropopliteal PVI (with or without infrapopliteal arteries), the incidence of major amputation or mortality was 66% in the plain balloon angioplasty (PBA) + bare metal stent (BMS) group, 60% in the drug-coated balloon angioplasty (DCBA) + BMS group, and 58% in the drug-eluting stent (DES) group. Drug-coated stents or balloons showed no benefits in terms of amputation-free survival or a reduction in severe adverse events [196].

Rationale: Due to the complexity of managing lower extremity arterial occlusive disease, which is characterized by multiple treatment options and significant restenosis rates, adhering strictly to the indications for surgical intervention is crucial. Fontaine stage IIb or Rutherford grade III, characterized by a claudication distance of <200 m, is generally considered a relative indication. In contrast, manifestations of critical limb ischemia (CLI), including pain at rest and tissue necrosis, are classified as absolute indications [197]. Regarding the selection of surgical methods, PVI decreases the risks of perioperative MACCEs and surgical site infections; however, PVI is associated with poor long-term patency. This option is favored for elderly patients who present with multiple comorbidities and femoropopliteal occlusions. BSX demonstrates superior long-term patency and markedly reduced rates of major adverse limb events and mortality compared with PVI; however, it is associated with a risk of incision infection and nonhealing, which are particularly prevalent in infrapopliteal surgeries and exacerbated in patients with diabetes or renal failure [198].

This approach is appropriate for younger patients who present with complex lesions. Hybrid procedures can be utilized for lesions located in specific areas, such as the femoral bifurcation, or when endovascular techniques are inadequate. Treatment strategies differ according to the specific lesion segment involved. After recanalization of common or external iliac artery lesions, the direct implantation of bare metal or covered stents may be considered; other new technologies are still being validated. For femoropopliteal lesions, drug-eluting therapy is the preferred approach, with balloon angioplasty and stenting or BSX as alternative options. In contrast, for infrapopliteal lesions, PVI is favored, with plain balloon angioplasty recommended solely for the distal tibiofibular trunk and anterior tibial, posterior tibial, or peroneal arteries; the use of drug-eluting balloons or stents is not indicated [47]. In instances where reperfusion is unfeasible, deep vein transvenous arterialization may be considered [47].

Recommendation 34: For patients with DF who have previously undergone lower extremity revascularization, an immediate assessment for revascularization and/or surgical intervention is warranted if surgical outcomes are unsatisfactory or if signs of recurrent ischemia are present, irrespective of the duration since the last procedure (recommendation grade: strong; evidence level: moderate).

Evidence summary: This recommendation is derived from two meta-analyses and one RCT that examined additional management strategies for patients experiencing poor outcomes or recurrent ischemia after lower extremity revascularization. Key outcome indicators: Interventional therapy is the primary approach for femoropopliteal in-stent restenosis. Drug-coated balloons (DCBs) demonstrate benefits in terms of the risk of target lesion revascularization, the rate of restenosis, and clinical outcomes at 6 and 12 months following the procedure [199]. Excimer laser atherectomy (ELA) in conjunction with DCBs demonstrates notable efficacy, whereas covered stents (CSs) are considered the preferred option [200]. For infrapopliteal restenosis, intervention is the primary approach; however, BSX remains a viable alternative. Both methods yield similar rates of 30-day mortality, amputation, and reintervention. Nevertheless, the BSX group exhibited elevated rates of cardiovascular events (2.2% compared with 5.8%) and infection (7.7%) [201–203]. In cases where intervention is unsuccessful and conversion to BSX occurs, the revascularization success rate may reach 92%, accompanied by positive long-term patency and limb salvage rates. If BSX fails and an attempt is made to convert to intervention, the success rate is merely 66% [204].

Rationale: In patients with DF who have undergone lower extremity revascularization, any indication of surgical failure or recurrent ischemia—irrespective of the time elapsed since the last intervention—should prompt a re-evaluation of the vascular status and modification of the treatment strategy in accordance with current evidence [205, 206]. Recurrent ischemia is characterized by symptoms such as worsening intermittent claudication, a decline in the ABI of ≥ 0.15 , deterioration of ulcers, or the emergence of new-onset pain at rest. In cases where these issues affect quality of life and do not respond to medication (e.g. recurrence of CLTI, emergence of new ulcers or gangrene), selective surgical intervention may be warranted. Secondary revascularization strategies include PVI and autologous or synthetic graft BSX. Drug-coated balloons and stents demonstrate greater efficacy than conventional balloons do in the treatment of restenosis, with the exception

of infrapopliteal segments. BSX or hybrid procedures, which integrate proximal stenting with distal PVI, present certain advantages; nonetheless, evaluating the risks associated with perioperative cardiovascular events and surgical site infections is crucial. In cases of limbs with significant tissue necrosis and infection or those deemed unsuitable for revascularization, amputation should be considered a viable option. In patients deemed unsuitable for surgical intervention, adjustments may be made solely to antithrombotic and vasodilator medications [101]. Future research should focus on conducting additional RCTs to address ongoing controversies. Key areas include comparing outcomes of “immediate reintervention” versus “selective intervention after close monitoring” in failed revascularization cases, assessing the long-term effects of endovascular versus open surgery on patency and limb salvage rates, and producing further clinical evidence regarding novel endovascular devices and techniques.

Wound repair surgery

Preparation of DF wounds

Preparation of DF wounds requires an assessment of the various causes and conditions leading to these wounds, followed by appropriate measures to establish an infection-free and well-perfused wound bed. This approach facilitates endogenous wound healing and provides a foundation for subsequent wound repair.

Recommendation 35: Evaluate the dimensions and advancement of DF every 1–4 weeks, and manage the wound in accordance with the TIME principle/TIME-H principle (recommendation grade: strong; evidence level: GPS).

Evidence summary: No relevant systematic reviews or original research evidence was found for this recommendation.

Rationale: Chronic wounds present significant healing challenges attributed to factors such as tissue necrosis, inflammatory imbalance, abnormal exudation, and impaired epithelialization, leading to increased treatment costs. The concept of wound preparation was introduced in 2000, highlighting that the patient’s overall condition is fundamental for effective local wound treatment. The “TIME (tissue, infection/inflammation, moisture balance, edge advancement)” principle, introduced by Falanga in 2000 and Schultz *et al.* in 2003, offers a systematic framework for managing chronic wounds, achieving significant recognition and application in the field [207, 208]. If the wound remains unhealed after 60 days, the tissue, infection/inflammation, moisture balance, edge advancement, host (TIME-H) principle should be utilized to evaluate and address the factors obstructing the healing process [209]. DF exhibit a dynamic trend of change. A decrease in the area of 10%–15% within 1 week, or a reduction exceeding 50% within 4 weeks, correlates with a low probability of ulcer reinfection and amputation. The percentage reduction in the ulcer area over time serves as an early predictor of treatment efficacy [210, 211]. Compared with biweekly debridement, weekly debridement promotes more rapid wound healing [212–215], decreases the risk of infection, and decreases hospitalization requirements [149].

Recommendation 36: Employ appropriate dressings and wound management techniques to maintain moisture, regulate exudate, and foster an environment conducive to epithelial growth (recommendation grade: strong; evidence level: moderate).

Evidence summary: This recommendation is supported by eleven RCTs, and four systematic reviews that examined the

effectiveness of dressings, oxygen therapy, and negative pressure in the treatment of DF. Key outcome indicators: Regarding dressings: (1) Autologous leukocyte, platelet, or fibrin patches can significantly increase the wound healing rate ($P=0.0235$) and shorten the median healing time ($P=0.0343$) [212]. Among these, 11 reviews and 2 randomized controlled trials (RCTs) on autologous platelet-rich plasma (PRP) gel indicate that both its injection and topical application are effective for DF. However, they all have limitations such as high research heterogeneity (differences in PRP preparation, administration methods, combined treatments, and follow-up durations), limited sample sizes, and low methodological quality [213–215]. (2) There are 7 and 4 randomized controlled trials (RCTs) respectively on platelet-derived growth factor (PDGF) dressings and epidermal growth factor (EGF) dressings, among which only 1 RCT for each type shows positive results. The 3 RCTs on granulocyte colony-stimulating factor (G-CSF) dressings focus on infection treatment and are ineffective for wound growth. The 2 small-scale RCTs on fibroblast growth factor (FGF) dressings indicate that FGF dressings have no significant advantages in terms of wound healing rate or healing time, and the only reported positive result (reduction in ulcer area) has methodological flaws [18]. (3) Sucrose octasulfate dressings increase wound healing rates (48% compared with 30%, $P=0.002$), decrease the average healing time to 60 days, and offer cost-effectiveness benefits [216, 217]. (4) Dehydrated amniotic and chorionic membrane grafts, cryopreserved placental membranes, dehydrated human umbilical cords, powdered dehydrated amniotic membranes, and other placenta-derived products have been shown to increase wound healing rates [218]. (5) Silver-containing dressings, as demonstrated by four RCTs, displayed short-term antimicrobial effects and facilitated growth. Methodological flaws were frequently identified across the studies [219–222]. (6) Collagen or alginate. Twelve randomized controlled trials demonstrated a moderate to high risk of bias, necessitating cautious interpretation of positive outcomes [18]. (7) Hydrogels were evaluated in one randomized controlled trial ($n = 31$), which indicated a higher complete healing rate after 16 weeks [223]. (8) A single RCT and a post-analysis study demonstrate that, relative to hydrophilic fiber dressings, ON101 offers superior overall healing rates for DF, particularly among patients with high-risk factors such as elevated HbA1c, obesity, and a prolonged disease duration (60.7% *vs* 35.1%, $P<0.001$), while maintaining a favorable safety profile [224, 225]. Regarding technology: (1) Both transcutaneous oxygen therapy (TWO2) and hyperbaric oxygen therapy enhanced wound healing, resulting in a 12-month ulcer healing rate of 52%, surpassing the rate of 29% in the control group. Several study conclusions exhibit contradictions, with one study being prematurely terminated because of baseline imbalance [222, 226–231]. (2) Negative-pressure wound therapy (NPWT), recognized for its advantages in postoperative wound healing, demonstrates ambiguity concerning its effectiveness in the treatment of nonsurgical ulcers [153]. (3) Tibial transverse transport (TTT), as evidenced by six cohort studies and one self-controlled study, has been demonstrated to enhance the healing of DF and decrease the risk of amputation. Compared with endovascular therapy alone, the combination of TTT and endovascular intervention yields superior limb salvage outcomes. Nonetheless, the studies examined exhibit design flaws, including nonrandomized controlled trial (non-RCT) designs, inadequate sample sizes,

limited follow-up durations, and a lack of control groups, among other methodological limitations [232–234]. (4) For the local application of antibiotic-loaded bone cement, 2 systematic reviews and 2 randomized controlled trials (RCTs) show that it can increase the cure rate of infected DF, shorten the healing time, reduce the risk of amputation, and has good safety. However, the included studies also have obvious methodological flaws (such as insufficient randomization, allocation concealment, and blinding) [235, 236].

Rationale: The provision of an appropriate and moist healing environment can enhance epithelial migration by 40%. Compared with traditional dressings such as gauze, contemporary dressings offer benefits by facilitating an optimal healing environment [153]. Autologous white blood cells, plasma, and fibrin adhesive patches serve as auxiliary therapy for DF that do not respond to standard treatment. Their application necessitates access to resources and technical expertise for repeated venipuncture, with a moderate level of evidence supporting this approach [237]. Growth factor-based agents, which exhibit variable efficacy and safety issues, are not advised for standard application in the management of DF disease. Sucrose octasulfate dressings are indicated for noninfectious neuroischemic DFUs that have not improved with standard treatment for a duration of at least two weeks [153]. Placenta-derived products are recommended by guidelines for patients who do not respond to standard treatment; however, the supporting evidence comes mainly from single-center studies, and their long-term safety and cost-effectiveness remain unclear, necessitating cautious application [153]. Silver-containing dressings. Current evidence does not support the routine use of this intervention for promoting wound healing. For infected wounds, silver ions combined with EDTA can inhibit bacterial biofilms and potentially disrupt bacterial structures by binding to cell walls and enzymes, thereby presenting a viable option. Additional high-quality randomized controlled trials (RCTs) are needed for future validation [238, 239]. Hydrogels are effective only in comparison with saline gauze, with insufficient comparative data available regarding other advanced dressings [240]. ON101 cream, which includes extracts from *Coleus strobilifer* and asiaticoside, was examined in an open-label study involving a limited number of participants, indicating a low level of evidence. Its high-cost results in a weak recommendation for the treatment of DF. TWO2 is appropriate for domestic use because of its affordability. Hyperbaric oxygen therapy is applicable for patients with neuroischemic or ischemic DF who have not responded to standard treatment. However, it is contraindicated in individuals with severe complications, such as uremia or hypoglycemia, as well as those with comorbidities such as HF or claustrophobia. The evidence indicating a low risk of bias for this technology is limited, and the conclusions are inconsistent. NPWT is appropriate for nonischemic DF following comprehensive debridement surgery. It is essential to avoid excessive negative-pressure settings or inadequate coverage that could lead to local tissue compression-induced ischemia. The application of NPWT is contraindicated for inadequately debrided wounds to avoid exacerbating infection [241, 242]. TTT is a limb-preserving technique that employs minimally invasive osteotomy and lateral displacement of the tibial cortex block to promote angiogenesis in microvessels. A deficiency of high-quality RCTs exists. Its clinical application is restricted to patients with an adequate blood supply at the

osteotomy site, those with distal limb circulation disorders (including severe atherosclerosis, calcific defense disease, or autoimmune diseases), and patients for whom vascular reconstruction surgery is either not feasible or ineffective. Strict adherence to indications and contraindications is essential to prevent inappropriate expanded applications. Antibiotic-loaded bone cement is a type of local sustained-release material made by mixing antibiotics with bone cement. It is only used as an adjuvant to the standard treatment for osteomyelitis, and contraindications such as allergies, tumors, and special infections must be excluded.

Recommendation 37: The selection of soft tissue repair techniques for patients with DF should be determined by the characteristics of the foot tissue defect, alongside a thorough assessment of the patient's overall health, mobility requirements, and additional relevant factors (recommendation grade: strong; evidence level: high).

Evidence summary: This recommendation is supported by four RCTs and two systematic reviews and meta-analyses that examined the selection of soft tissue repair techniques for DF. Key outcome indicators: Skin grafting and tissue replacement have been shown to enhance the healing of foot ulcers (RR 1.55, 95% CI: 1.30–1.85) while decreasing the likelihood of amputation and infection [243]. Cellular, acellular, and matrix-like products significantly increase the healing rate of ulcers [244]. Local intrinsic muscle flaps demonstrate positive outcomes in ankle reconstruction for DF; however, further high-quality studies are needed to confirm the long-term effects [245]. Soft tissue reconstruction, including flap transplantation, in conjunction with joint fusion surgery, is effective for treating CNO in midfoot ulcers. Free tissue transplantation for chronic ulcers in diabetic lower limbs demonstrated a flap survival rate of 91.9% and a limb preservation rate of 83.4%. This approach is effective for treating refractory DF, but it necessitates careful patient selection and enhanced perioperative management [246, 247].

Rationale: Soft tissue repair techniques include a spectrum from simple to complex methods, including primary closure, secondary closure, negative-pressure wound therapy, skin grafting, dermal matrix grafting, local or distant flap transplantation, tissue expansion, and various forms of local fascial or myofascial flap, island flap, and free tissue transplantation (Figure 10) [7]. The success of flap transplantation is determined by the blood supply at the base of the flap rather than the length-to-width ratio [248]. Research has indicated that local plantar flaps can be constructed to incorporate nerves and blood vessels without necessitating subcutaneous flap division [249]. The incision line for the flap must be aligned with the relaxed skin tension lines (RSTLs) (Figure 11) to minimize lateral force on the skin. An effective flap is characterized by its ability to move unidirectionally, without lateral or rotational displacement, unless concurrent bone surgery is being conducted, in which case this factor may be disregarded. Flap transplantation failure is primarily attributed to infections, particularly those induced by *S. aureus*, *Pseudomonas aeruginosa*, and beta-hemolytic streptococci. Furthermore, complications, including elevated mechanical shear force, an inadequate blood supply, seroma formation, and hematoma occurrence, are prevalent.

Repairing DF wounds requires a thorough assessment of the stability and integrity of the underlying bone structure, particularly to determine whether all infected bone has been excised. This evaluation is crucial for determining the necessity and

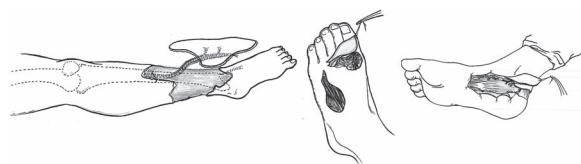


Figure 10. Schematic diagram of flap surgery. From left to right, they are free anterior tibial flap, dorsalis pedis island flap and medial pedal island flap

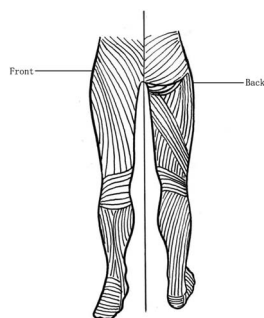


Figure 11. Relaxed skin tension lines

appropriateness of soft tissue reconstruction, as well as the specific reconstruction method to be employed [250]. Various soft tissue reconstruction techniques are employed clinically, depending on the characteristics of the ulcer, including its location, depth, and vascular supply. Skin grafting is suitable for ulcers with adequately prepared wound beds located in relatively superficial and non-weight-bearing or low-weight-bearing areas. It is contraindicated for wounds that exhibit severe uncorrected ischemia and those with exposed deep tissues. Flap transplantation is appropriate for addressing deep defects or ulcers in weight-bearing regions; however, a thorough evaluation of the patient's tolerance is essential. It is not recommended for patients with severe uncorrected ischemia and those in poor overall condition who are unable to tolerate prolonged anesthesia. The efficacy of skin grafting and flap surgery is contingent upon infection management, enhancement of the wound bed (ensuring an adequate blood supply and absence of necrosis), and the patient's overall condition, which includes addressing biomechanical abnormalities, ischemia, and glycemic control.

Offloading of DF

Recommendation 38: The most suitable offloading device for plantar forefoot or midfoot ulcers should be chosen, considering the ulcer location, available resources, and specific circumstances of the patient (recommendation grade: weak; evidence level: moderate).

Evidence summary: Eleven studies (five RCTs and six cohort studies) reported on device selection for the treatment of foot ulcers by offloading among people with diabetes. Key outcome indicators: Nonremovable knee-high offloading devices, such as TCCs, have been shown to significantly increase ulcer healing rates, reduce the time to healing, and lower recurrence rates. Comparative analyses indicated that the TCC group achieved a healing rate of 93.2%, compared with 83.5% for the RCW/shoe group, and demonstrated lower rates of major amputation (4.0% *vs* 7.3%). Additionally, TCCs exhibited advantages in terms of adherence, cost-effectiveness, and reduced infection rates. Knee-high removable offloading

devices (RODs) and ankle-high RODs did not affect ulcer healing [251], whereas another study similarly reported the efficacy of TCCs in promoting healing [252]. Both RCWs and TCCs reduced whole-foot plantar pressure, with RCWs demonstrating a greater reduction in midfoot peak plantar pressure (77% *vs* 63%, $P=0.036$), although TCCs achieved higher healing rates. Felted foam in conjunction with properly fitted therapeutic footwear is appropriate for resource-limited settings or when a TCC is contraindicated, showing modest efficacy that surpasses conventional shoes or standard therapeutic footwear [253, 254]. A recent study revealed that allowing weight-bearing during TCC therapy in patients with CNO did not negatively impact healing [129]. Multiple studies lacked clear documentation of randomization procedures, and control interventions exhibited variability, which introduced potential bias; however, the overall effect direction remained consistent across the studies.

Rationale: The IWGDF 2023 guidelines indicate that the optimal offloading treatment for neuropathic plantar forefoot or midfoot ulcers is a nonremovable knee-high offloading device to promote healing. In cases where a nonremovable knee-high offloading device is contraindicated or poorly tolerated by the patient, a removable knee-high or ankle-high offloading device should be considered. In the absence of alternative biomechanical relief methods, the use of felted foam may be considered, provided that it is paired with suitable footwear. In cases where a metatarsal head ulcer does not respond to nonsurgical offloading treatment, options such as Achilles tendon lengthening, metatarsal head resection, arthroplasty, or metatarsal osteotomy should be considered. For plantar or apical toe ulcers resulting from flexible toe deformity, digital flexor tenotomy is advised [237, 251]. Several precautions are identified: The use of half shoes (forefoot offloading shoes) is contentious. While Chantelau *et al.* (1993) reported potential benefits and the 2016 IWGDF guidelines provided a related recommendation, high-quality evidence remains scarce. When considering the selection of shoes to avoid weight-bearing walking without any decompression measures, it is necessary to carefully choose the target population and indications and take all measures to prevent falls. Furthermore, the guidelines do not endorse routine use. Current evidence does not support specific offloading recommendations for hindfoot ulcers. Additionally, the application of other physical modalities in DF should be approached with caution.

Amputation surgery

Recommendation 39: Clinicians should evaluate the therapeutic risks and benefits when choosing between limb salvage and amputation for patients with severe DF disease. It is essential to engage in comprehensive discussions and honor patients' preferences to ensure a transparent decision-making process (recommendation grade: weak; evidence level: GPS).

Evidence summary: No relevant systematic reviews or original studies were identified for this recommendation.

Rationale: In clinical practice, certain severely affected patients may still qualify for limb salvage. However, they must also consider the risks associated with multiple surgeries, including revascularization, debridement, and reconstructive procedures, which may ultimately lead to amputation. A judicious choice between salvage and amputation is thus crucial. Amputation is defined as the removal of a portion of a limb via bone or joint division. It is categorized into major

types (e.g. transtibial, knee disarticulation, transfemoral) and minor types (e.g. toe amputation, transphalangeal amputation, transmetatarsal amputation). Major amputation is indicated in cases of uncontrollable severe infection, irreversible ischemia with nonviable tissue and unsuccessful revascularization, incurable ulceration, malignant tumor involvement in the limb, irreparable traumatic injury, and recurrent neuro-osteoarthropathy that significantly impacts quality of life. Contraindications include reversible diseases that can be managed nonsurgically, as well as any systemic conditions that significantly increase surgical risk [19]. Approximately 17% of patients with DF eventually require amputation [19]. Advanced foot lesions, peripheral vascular disease, and hypertension represent significant risk factors (all $P < 0.01$). Compared with nonamputees, amputees exhibit a longer duration of diabetes; elevated HbA1c levels, leukocyte counts, and CRP levels ($P < 0.05$); and reduced hemoglobin and serum albumin levels ($P < 0.01$) [255]. A study involving 41 below-knee amputees—comprising 24 primary amputations and 17 salvage attempts with multiple procedures—revealed that 94.1% of patients in the salvage-attempt group would choose repeated salvage, in contrast to only 37.5% of patients in the primary-amputation group who would select limb salvage if the option was given again ($P = 0.001$) [256]. Preamputation assessments should involve vascular surgery, orthopedics, and rehabilitative medicine, particularly in younger patients, to ensure surgical success and facilitate postoperative rehabilitation and prosthetic fitting. Indications for limb salvage include early interventions such as debridement, offloading, and revascularization; successful vascular reconstruction; infection management; effective treatment of Charcot foot; and a multidisciplinary, individualized treatment approach. Contraindications include irreversible tissue necrosis, life-threatening infections, and systemic comorbidities that greatly increase the risk of complex salvage procedures [19, 257]. Current evidence suggests that personalized decision-making should be grounded in a risk-benefit analysis, emphasizing limb preservation whenever possible. Internal pedal amputation, with TMA as a significant example, represents a crucial limb-sparing method [258].

Recommendation 40: For patients undergoing amputation, a rehabilitation plan should be developed that includes care for the residual limb, personalized prosthetic fitting, and progressive training. Psychological support should be provided throughout the entire process (recommendation grade: weak; evidence level: GPS).

Evidence summary: No relevant systematic reviews or original studies were identified for this recommendation.

Rationale: For patients undergoing DF amputation, compared with patients in the routine care group, those in the combined rehabilitation or psychological care group experienced lower complication rates, lower Hamilton Anxiety Rating Scale scores, and higher Diabetes-Specific Quality of Life Scale scores ($P < 0.05$) [259, 260]. However, owing to the low quality of evidence, the clinical validity of these findings remains to be confirmed. Multidisciplinary guidelines on lower limb amputation have indicated that during prosthetic fitting, one-on-one training by physical therapists, group training between trainees and instructors, and modern training methods using virtual or augmented reality can improve walking speed and support surfaces, although the evidence quality is still low [261]. For first-time prosthesis users, a progressive rehabilitation training plan

aimed at enhancing walking ability should be customized based on the patient's preferences and goals, including setting training goals, content, intensity, and duration. In summary, rehabilitation after DF amputation requires the integration of precise prosthetic technology, phased training, and interdisciplinary management. The primary goal is to reduce secondary ulcers and improve quality of life.

Clinical question 3: prevention of DF

Risk assessment and stratification of diabetic foot

Recommendation 41: At the time of initial diagnosis or first visit for diabetic patients, an assessment of the risk for foot disease is warranted. A comprehensive evaluation of the patient's foot condition, including neurological and vascular status, should be performed annually based on the risk stratification results (recommendation grade: strong; evidence level: GPS).

Evidence summary: No relevant systematic reviews or original research evidence were found for this recommendation.

Rationale: The application of internationally recognized risk classification systems, such as IWGDF, for assessing and stratifying foot disease risk in diabetic patients (Table 8) can enhance foot care behaviors ($P < 0.05$) [262], demonstrate cost-effectiveness, and accurately identify high-risk patients, consequently decreasing the incidence of new foot ulcers (28.6% in high-risk patients versus 3.2% in low- to moderate-risk patients) [263, 264]. Five cross-sectional studies highlighted that employing a DF risk stratification system or screening tools effectively identifies high-risk patients [265–269]. Additionally, screening must be conducted by trained healthcare professionals, with methods and evidence detailed in the sections on peripheral neuropathy and peripheral arterial disease [18]. Presently, the majority of pertinent studies are observational and characterized by a scarcity of evidence from RCTs and a predominance of low-quality evidence. The advantages of early identification and prevention of foot diseases require further validation through additional research.

Health education

Recommendation 42: Structured health education is effective in preventing the occurrence and progression of foot ulcers in patients with high-risk DF (recommendation grade: strong; evidence level: moderate).

Evidence summary: Eleven randomized controlled trials that examined the effects of structured health education interventions on patients with diabetes were included in this analysis. Key outcome indicators: Education influenced the occurrence of foot ulcers [RR 0.62, 95% CI: (0.37, 1.03), $P < 0.05$] and amputation [RR 0.51, 95% CI: (0.27, 0.96), $P < 0.05$]; however, education did not affect the overall mortality rate or the incidence of foot deformity. The results of secondary outcome indicators indicated that education can increase glycated hemoglobin levels and self-care efficacy, particularly through significant improvements in foot care knowledge and behavior [270–280].

Rationale: Structured health education enhances self-care efficacy and knowledge among patients with high-risk DF, promotes positive foot care behaviors, decreases amputation rates, and is cost-effective with minimal operational complexity. Structured educational content includes the enhancement of foot protection for diabetic patients susceptible to foot ulcers (IWGDF grades 1–3). Key recommendations include avoiding barefoot walking, refraining from wearing thin-soled slippers or shoes without socks, daily washing and

Table 8. IWGDF risk stratification system and corresponding foot screening frequency

Category	Ulcer risk	Characteristics	Frequency
0	Very low	No signs of LOPS and no signs of PAD	Once a year
1	Low	Presence of LOPS or PAD	Once every 6–12 months
2	Moderate	Presence of LOPS + PAD, or LOPS + foot deformity, or PAD + foot deformity	Once every 3–6 months
3	High	Presence of LOPS or PAD, along with one or more of the following medical histories: foot ulcer; lower extremity amputation (minor or major); end-stage renal disease	Once every 1–3 months

thorough drying of feet, the use of moisturizers to maintain skin hydration, and proper toenail trimming. Patients classified as moderate to high risk (IWGDF grades 2–3) should have the skin temperature of both feet monitored on a daily basis. If the temperature difference exceeds 2.2°C (4.0°F) over two consecutive days, it is advisable to reduce activity and seek professional guidance [18]. The importance of the rational use of offloading devices in preventing high-risk feet is highlighted.

Recommendation 43: In individuals with diabetes and high-risk factors, such as established foot ulcers and a history of lower extremity amputation or foot deformity, the use of offloading therapeutic footwear is advised to prevent the occurrence and recurrence of foot ulcers. Conversely, for low-risk patients without structural deformities or those capable of wearing standard footwear, this recommendation is less stringent (recommendation grade: strong; evidence level: moderate).

Evidence summary: Five retrospective cohort studies and four systematic reviews investigated footwear selection in both low- and high-risk populations with diabetes. Key outcome indicators: In individuals at low risk for DF, standard footwear does not significantly increase the risk of developing ulcers, and there is no evidence that offloading footwear is more effective than regular shoes in preventing ulcers [281]. In high-risk populations, such as those with a history of foot ulcers, partial amputation, and foot deformities, compared with ordinary shoes or conventional therapeutic shoes, offloading therapeutic footwear significantly decreases the incidence of ulcers (RR 0.49; 95% CI: 0.28–0.84), with no indication of publication bias ($P=0.69$). Furthermore, the effectiveness of footwear is inversely related to the duration of the intervention (coefficient = 0.085; $P < 0.05$) [282]. Additional prospective cohort studies support these findings. The overall methodological quality was moderate; several studies inadequately reported blinding procedures, and the control interventions lacked uniformity.

Rationale: Individuals at high risk of DF, including those with a history of foot ulcers, partial amputation, or Charcot foot deformity, should utilize therapeutic offloading footwear, such as custom-molded insoles and rocker-sole shoes. This method diminishes the likelihood of new ulcers and can decrease recurrence by more than 50%. Standard footwear is recommended for low-risk patients lacking structural foot deformity or peripheral neuropathy. It is advisable to select well-fitting, closed, and sufficiently cushioned athletic shoes while avoiding slippers, high heels, or other poorly fitting footwear. Numerous studies indicate favorable safety and acceptability for this strategy [237]. This approach is applicable at all levels of care and, considering China's significant

burden of DF disease, holds considerable public health value for broader implementation.

Management of precursor foot ulcer lesions

Recommendation 44: Patients with diabetes should actively manage precursor lesions that can lead to foot ulcers, including plantar calluses, corns, ingrown nails, tinea pedis, blisters, and cracks, to effectively prevent the onset and recurrence of foot ulcers (recommendation grade: strong; evidence level: GPS).

Evidence Summary: No relevant systematic reviews or original research evidence were found for this recommendation.

Rationale: Numerous clinical studies have shown that examined the effects of eliminating or not eliminating precursor foot ulcer lesions in diabetic patients were included in this analysis. Key outcome indicators: In one study, 40.6% of individuals with type 1 diabetes and 39.5% of those with type 2 diabetes exhibited precursor lesions indicative of foot ulcers. The corresponding prevalence of calluses, ingrown nails, and fungal infections reached 16.8% and 10.5%, 15.8% and 18.5%, and 21.9% and 24.7%, respectively [283]. Heel cracks and corns were also linked to foot ulcers [267]. Callus removal was shown to decrease total plantar pressure and impulse, as well as local pressure and impulse, while improving patients' scores across disease, physical, psychological, and social dimensions, with Wagner grades showing improvement postsurgery [284]. Following podiatrist guidance on lifestyle and intervention for ulcer precursors, the incidence of foot ulcers significantly decreased after one year (20.7% *vs* 6.7%, $P < 0.001$), and the number of interventions was inversely correlated with ulcer occurrence (Spearman correlation coefficient: -0.496 , $P < 0.001$). For patients with a history of ulcers, the recurrence rate also significantly decreased (89.7% *vs* 27.9%, $P < 0.001$) [285].

Rationale: Toe deformities, including hallux valgus and elongated second metatarsals, are present in nearly 50% of diabetic patients. These conditions can result in abnormal plantar pressure areas and calluses, frequently without pain, contributing to additional plantar weight-bearing of ~18 600 kg per day [286]. Tight interdigital spaces, along with unsuitable footwear, can lead to the formation of corns in nonweight-bearing regions, resulting in pain. Initially, calluses and corns provide a protective effect on the local skin; however, as they develop, the excessively thick and rigid skin may act as a foreign body, causing subcutaneous hemorrhage and ulceration, particularly in areas of bony prominence, potentially involving bone. Furthermore, ingrown nails, tinea pedis, blisters, and cracks frequently serve as common precursors to foot ulcers. The removal of calluses and corns using a scalpel is acknowledged as an effective strategy for preventing

foot ulcers. The frequency of trimming should be modified in response to variations in dynamic plantar pressure within the shoes rather than solely relying on the thickness of the calluses [287]. Patients with ingrown nails, fungal infections, or blisters should promptly seek medical attention for treatments, including partial nail extraction, localized antifungal therapy, and blister drainage. The use of acid-containing ointments or topical treatments in isolation is not advisable.

Surgical intervention

Recommendation 45: For patients at high risk of DF, if preulcerative lesions are challenging to manage or do not respond to conservative treatment, surgical interventions should be considered after a thorough medical evaluation (Recommendation grade: Strong; Evidence level: Moderate).

Evidence summary: This recommendation is based on one RCT and six systematic reviews, detailing the use of surgical interventions for the prevention of DF complications. Key outcome indicators: Flexor tenotomy significantly reduces plantar pressure (mean difference [MD] -398 kPa; $P < 0.00001$) and decreases the risk of ulcer recurrence (0%–20% recurrence at 11–36 months). Additionally, it improves conditions such as toe tip callus, hammer toe, and nail hypertrophy by alleviating pressure and reducing the incidence of ulcers [288]. Plantar fascia release for forefoot ulcers and flexor hallucis longus transfer for heel ulcers result in a 0% recurrence rate of ulcers within 24 months [289]. Achilles tendon lengthening (ATL) is associated with a reduction in forefoot plantar pressure (MD -218 kPa; $P = 0.03$), a decrease in ulcer recurrence (0%–20% at 17–48 months), and an improvement in healing rates ($P = 0.006$) [251]. Metatarsal head resection significantly decreases plantar pressure (MD -511 kPa; $P < 0.00001$) and decreases the 1-year ulcer recurrence rate (15.2% compared with 39.1%; $P = 0.02$) [290,291]. Osteotomy with arthrodesis significantly decreases ulcer recurrence and amputation rates (7.5% compared with 35.5%; $P = 0.0013$). Patients who underwent the first MTPJ arthroplasty had significantly reduced ulcer incidence rates at the 6-month follow-up. The combination of Keller's arthroplasty with interphalangeal joint resection and arthroplasty for hallux valgus demonstrated improved outcomes. The weighted healing rate was 94%, the mean healing time was 3.1 ± 0.4 weeks, the ulcer recurrence rate was 6%, and the ulcer transfer rate was 4.5% [292]. Medial column intramedullary screw fusion and multilevel external fixation are first-line surgical options for patients with ulcer-free Charcot foot that is refractory to conservative therapy [293].

Rationale: DF have significant incidence and recurrence rates, with up to 40% occurring within four months and 60% occurring within 3 years. The 2023 IWGDF guidelines offer definitive recommendations regarding the efficacy and safety of surgical interventions aimed at preventing DF. Surgery significantly mitigates ulcer risk in high-risk feet, primarily by alleviating localized high pressure resulting from bony prominences. Preventive surgical approaches: Percutaneous flexor tenotomy (PFT) (Figure 12) is a safe and effective surgical intervention for flexible toe deformities and achieves therapeutic outcomes through the release of flexor tendons to rectify digital malformations. This intervention is important for reducing plantar pressure and preventing ulceration in the management of DF. Achilles tendon lengthening (ATL) (Figure 13) is indicated for patients who exhibit restricted ankle dorsiflexion or who experience healing complications after TMA or toe amputation (TA),

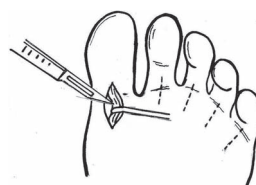


Figure 12. Percutaneous flexor tenotomy

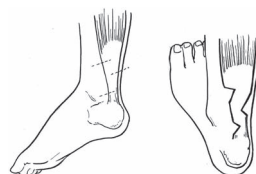


Figure 13. Achilles tendon lengthening

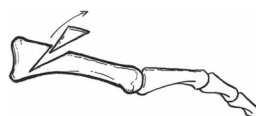


Figure 14. Dorsiflexion metatarsal osteotomy

and it effectively alleviates forefoot pressure. Dorsiflexion metatarsal osteotomy (Figure 14) is a surgical intervention aimed at preventing chronic or recurrent neuropathic forefoot ulcers. This procedure realigns the metatarsal bones to diminish plantar pressure concentrations via bony correction. Distal metatarsal metaphyseal osteotomy (DMMO) and distal metatarsal diaphyseal osteotomy (DMDO) (Figure 15) are indicated for the prevention of metatarsal head pressure ulcers. These procedures achieve precise bony decompression through minimally invasive techniques involving metatarsal shortening and realignment. Modified Keller resection arthroplasty is intended to prevent plantar hallux ulcers through the excision of the proximal phalanx base and reconstruction of the first metatarsophalangeal joint, facilitating permanent pressure redistribution. Hallux valgus correction requires procedure selection based on the severity of the deformity: silver bunionectomy (Figure 16) for mild cases, Chevron osteotomy (Figure 4) for moderate cases, and proximal metatarsal osteotomy with the Akin procedure (Figure 17) for severe cases, with similar surgical principles applied to fifth toe varus correction (Figure 18). Surgical interventions for Charcot foot deformity include exostectomy, medial column arthrodesis (Figure 19), multiplanar realignment, and midfoot/hindfoot arthrodesis, such as triple arthrodesis (Figure 7). The development and recurrence of DF are linked primarily to localized high pressure. Although surgical decompression has been shown to be effective in several studies, few high-quality RCTs exist, and a thorough clinical risk–benefit analysis for each surgical decision is needed.

Clinical question 4: establish multidisciplinary teams and implement a tiered healthcare delivery system

Recommendation 46: Establish a multidisciplinary limb salvage team and promptly refer patients to advanced DF centers to decrease amputation rates and mortality (recommendation grade: strong; evidence level: moderate).

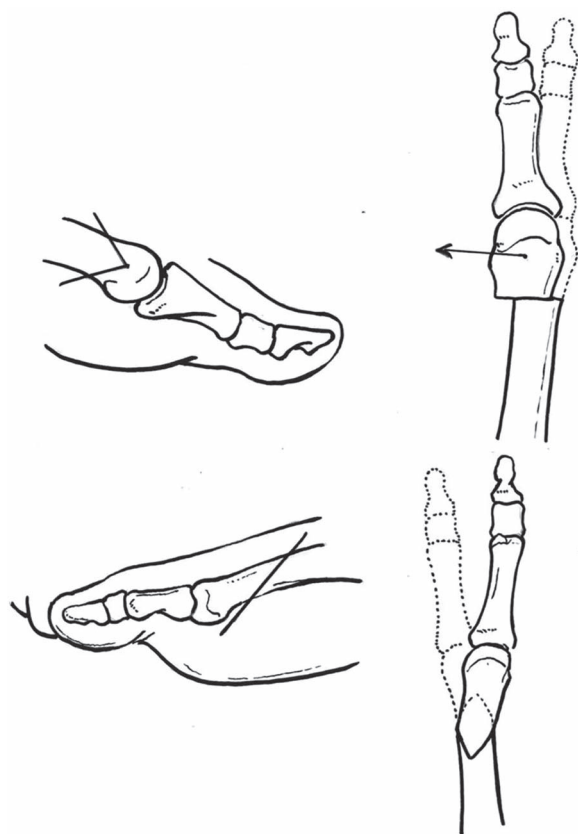


Figure 15. Distal metatarsal metaphyseal osteotomy and distal metatarsal diaphyseal osteotomy

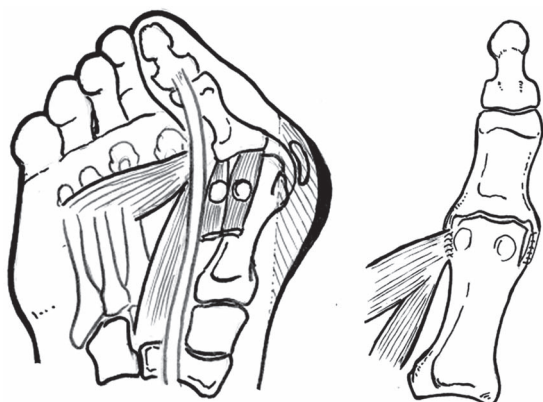


Figure 16. Silver bunionectomy

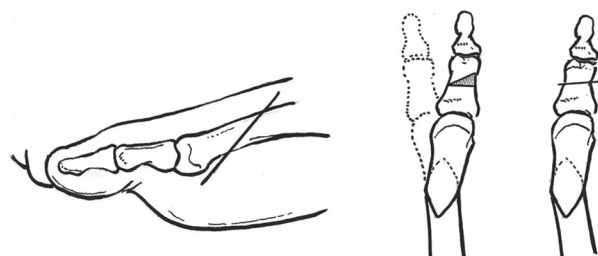


Figure 17. Proximal metatarsal osteotomy with the akin procedure

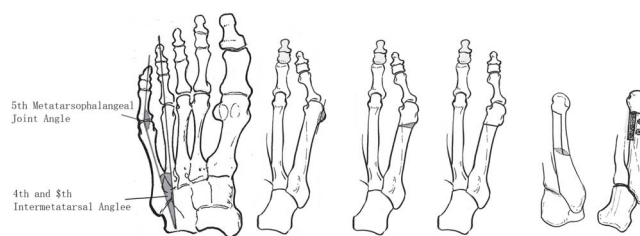


Figure 18. Varus deformity of the 5th toe and its corrective surgery

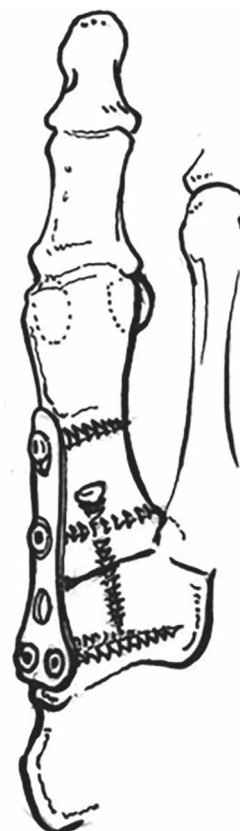


Figure 19. Medial column arthrodesis

Evidence summary: This recommendation is supported by three systematic reviews and two observational studies detailing the effects of multidisciplinary treatment and timely referral on clinical outcomes in patients with DF complications. Key outcome indicators: After multidisciplinary therapy with consultation and referral collaboration was implemented, notable enhancements in various clinical parameters were observed. Major amputation rates fell below 5%, indicating a 24% reduction in amputation risk [294]. Mortality risk decreased by 69%, with a corresponding reduction in all-cause mortality (OR 0.31 [95% CI: 0.18–0.53]) [295]. Wound healing time demonstrated a significant reduction (inverse variance –46) [294]. Systemic healthcare delivery metrics significantly improved, characterized by a notable decrease in the mean referral-to-first visit interval (38.6 days *vs* 9.5 days, $P < 0.001$), reduced bloodstream infection rates (2% *vs* 13%, $P = 0.04$), increased vascular intervention rates (18% *vs* 1%, $P < 0.01$), and enhanced outpatient follow-up compliance (33% *vs* 76%, $P < 0.001$) [296, 297].

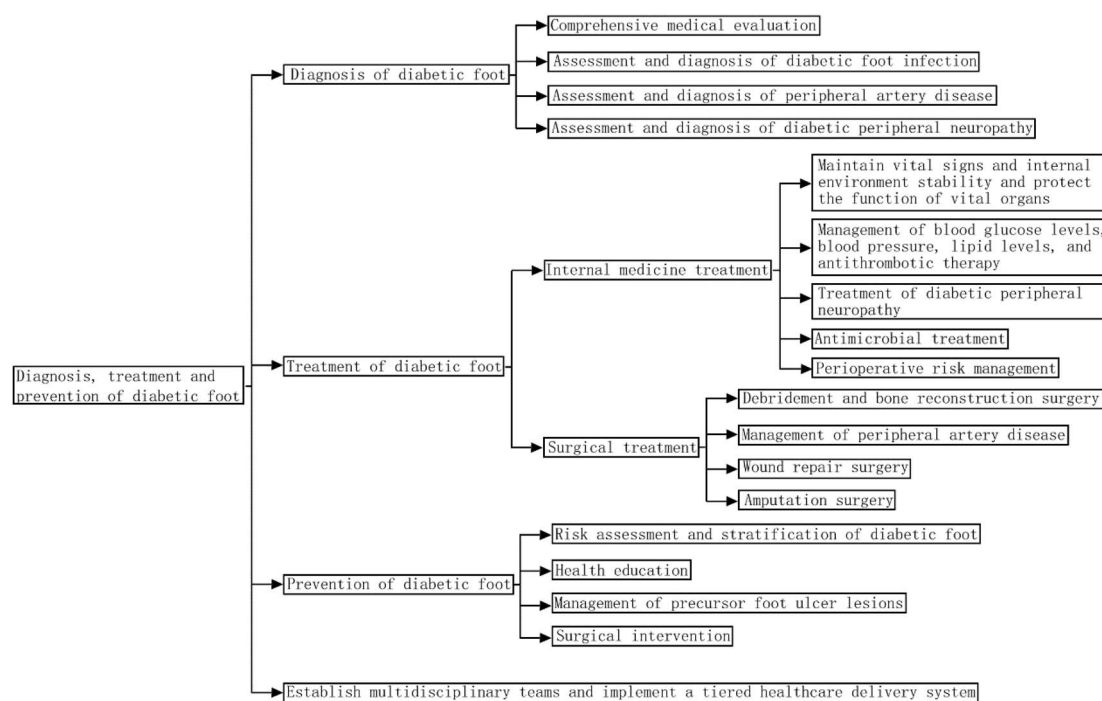


Figure 20. Flow chart

Rationale: Patients with diabetes who present with any of the following conditions necessitate prompt surgical consultation and urgent referral to specialized treatment centers: Emergent conditions (transfer within 24 h): Acute changes in limb coloration (erythema or pallor), abrupt temperature variations (hypothermia or hyperthermia), escalating pain, unexplained increased edema, sepsis (including shock or altered consciousness), disseminated cellulitis, necrotizing fasciitis, or gas gangrene. High-risk foot lesions, including new deep ulcers, superficial ulcers that progress to osteoarticular involvement, exacerbation of chronic osteomyelitis, and recurrent ulcers associated with severe foot deformities [56]. It is advisable for DF centers with multidisciplinary teams to establish clear diagnostic and management protocols for DF and to implement expedited emergency referral pathways.

At present, there is no unified standard for the hierarchical diagnosis and treatment of diabetic foot in China. Taking the Yangtze River Delta region (with demonstration zones as the core) as an example, the “Yangtze River Delta Five-Level Collaborative Management Model” has been adopted. This model establishes a five-level disease-specific prevention and treatment organizational system consisting of regional centers, provincial, municipal, and county-level centers, as well as primary-level institutions (such as community service centers). Patients are classified according to the SINBAD system, and hospitals’ diagnosis and treatment capabilities are evaluated based on the Wifl classification system. Automatic classification and hierarchical management are realized through an information system, and this model has now been incorporated into the Clinical Pathway for the Diagnosis and Treatment of Diabetic Foot in China (2023 Version) [56, 298].

In summary, this guideline has formulated a set of clinically practical recommendations and drawn a flow chart, aiming to provide a decision-making basis for standardizing the prevention and treatment of diabetic foot (Figure 20).

Conclusions

In conclusion, based on the PICO and GRADE methods, this guideline puts forward 46 recommendations for the prevention and treatment of diabetic foot. It emphasizes conducting a comprehensive assessment through medical history, physical examination, and auxiliary examinations, and formulating individualized plans according to the severity of infection, vascular status, and neurological conditions. In terms of treatment, it covers the management of blood glucose, blood pressure, and blood lipids, anti-infection, debridement, revascularization, and wound repair. Meanwhile, it recommends decompression, health education, and surgical intervention to prevent ulcers, and advocates hierarchical diagnosis and treatment, thereby providing systematic guidance for clinical practice.

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Supplementary data

Supplementary data is available at *Burns & Trauma Journal* online.

Funding

These guidelines are endorsed by the “2025 Special Government Fund for the Yangtze River Delta Ecological Green Integration Development Demonstration Zone (No. QZHQ[2025] 0225)”.

Conflict of interest statement

All members have accurately completed conflict of interest declaration forms, and there are no conflicts of interest pertaining to the guidelines.

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