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REVIEW ARTICLE

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# Diagnosis and treatment of diabetic foot ulcer complicated with lower extremity vasculopathy: Consensus recommendation from the Chinese Medical Association (CMA), Chinese Medical Doctor Association (CMDA)

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## Abstract

Diabetic foot ulcer complicated with lower extremity vasculopathy is highly prevalent, slow healing and have a poor prognosis. The final progression leads to amputation, or may even be life-threatening, seriously affecting patients' quality of life. The treatment of lower extremity vasculopathy is the focus of clinical practice and is vital to improving the healing process of diabetic foot ulcers. Recently, a number of clinical trials on diabetic foot ulcers with lower extremity vasculopathy have been reported. A joint group of Chinese Medical Association (CMA) and Chinese Medical Doctor Association (CMDA) expert representatives reviewed and reached a consensus on the guidelines for the clinical diagnosis and treatment of this kind of disease. These guidelines are based on evidence from the literature and cover the pathogenesis of diabetic foot ulcers complicated with lower extremity vasculopathy and the application of new treatment approaches. These guidelines have been put forward to guide practitioners on the best approaches for screening, diagnosing and treating diabetic foot ulcers with lower extremity vasculopathy, with

**Abbreviations:** ABI, ankle brachial index; ACC/AHA, American College of Cardiology/American Heart Association; ADA, American Diabetes Association; CMA, Chinese Medical Association; CMDA, Chinese Medical Doctor Association; CTA, computed tomography angiography; DSA, digital subtraction angiography; DVA, deep venous arterialisation; FDA, food and drug administration; IDSA, Infectious Diseases Society of America; IWGDF, the international working group on the diabetic foot; MRA, magnetic resonance angiography; NPWT, negative pressure wound therapy; PAD, peripheral arterial disease; PN, peripheral neuropathy; TASC, trans-atlantic inter-society consensus; $TcPO_2$, transcutaneous oxygen pressure; WIfI Classification, wound, ischaemia, and foot infection classification.

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the aim of providing optimal, evidence-based management for medical personnel working with diabetic foot wound repair and treatment.

KEYWORDS
bypass surgery, debridement, diabetic foot ulcer, endovascular therapy, lower extremity vasculopathy, microcirculation disturbance

## 1 | INTRODUCTION

Diabetic foot ulcer is a serious complication that patients with diabetes suffer from and is characterised by foot infections and deep tissue damage caused by vascular and nerve abnormalities. The incidence of diabetic foot ulcers among patients with diabetes is as high as 19%–34%,[1] and 20% of foot ulcers lead to varying degrees of amputation due to infection or other reasons,[2] which is also the leading cause of nontraumatic amputation of the lower extremities. Prior studies have demonstrated that the primary factors causing diabetic foot ulcers are peripheral neuropathy (PN) and peripheral arterial disease (PAD). In middle- and high-income countries, approximately half of the patients with diabetic foot ulcers have PAD.[3] However, since the clinical symptoms of lower extremity vasculopathy in most patients with diabetes are atypical before the occurrence of lower extremity ulcers and other complications, this type of vasculopathy lacks proper diagnosis and treatment.

In clinical practice at home and abroad, there are different evaluation methods for diabetic foot ulcers and lower extremity vasculopathy. For example, Wagner's classification,[4] IWGDF/IDSA grade,[5] Texas grade,[6] SINBAD classification[7] and WIfI classification[8] for diabetic foot ulcers, and ultrasound, CTA, MRA, DSA and the Trans-Atlantic Inter-Society Consensus (TASC) classification for the assessment of lower extremity vasculopathy.[9] However, considering the current emphasis on individualised treatment and multidisciplinary diagnosis and treatment, comprehensive classification and treatment suggestions are needed for diabetic foot ulcers complicated with lower extremity vasculopathy. Moreover, due to differences in protocols between medical institutions and medical groups and the advent of new knowledge, modified treatment concepts for this disease and new technological and strategic applications cannot be popularised, resulting in differences in the treatment choices and prognosis of this disease.

Based on the above, after consulting the evidence of clinical research on diabetic foot ulcer complicated with lower extremity vasculopathy in recent years, the “Diagnosis and treatment of diabetic foot ulcer complicated with lower extremity vasculopathy” was compiled. The CMA and CMDA set up an expert group to discuss and revise the criteria in detail, forming a relatively unified diagnosis and treatment plan for reference in clinical practice.

## 2 | METHODS

### 2.1 | Scope of the consensus

The target population of this consensus is patients with diabetic foot ulcers complicated by lower extremity vasculopathy. The content covers aspects such as evaluation, diagnosis and treatment. This consensus can be applied in medical institutions of all levels. The target implementation agencies are medical institutions and health management departments that provide health care services to the target population. The main users of the guidelines are medical workers in the departments of wound repair, burns and plastic surgery, vascular surgery, endocrinology and disease control and prevention.

### 2.2 | Data retrieval

Experts in burns, vascular surgery, and wound repair compiled these guidelines. They are based on high-quality literature on the diagnosis and treatment of diabetic foot ulcers. Each recommendation in this article is based on a consensus of the specialist committee. The keywords used to search the relevant literature were diabetic foot, diabetic ulcer, diabetic wound, lower extremity, peripheral arterial disease and PAD. Scientific databases, including PubMed, Medline, Web of Science, and CNKI, were searched. The databases were searched from their inception to 1 July 2023. References to support manual retrieval were also used for topics limited to human diseases. The types of articles that were reviewed included meta-analyses, systematic reviews, randomized controlled trials, retrospective series reviews, clinical case series and expert panel recommendations.

### 2.3 | Levels of evidence and grades of recommendation

These guidelines were subjected to the evidence grading and recommendation strength standards developed by the Oxford Centre for Evidence-Based Medicine: Levels of Evidence (March 2009). The expert group fully discussed the related problems encountered in the diagnosis and treatment of diabetic foot ulcer complicated with lower extremity vascular lesions. The group then

TABLE 1 Oxford centre for evidence-based medicine: Levels of evidence (March 2009).

| | | Definition | |
|---|---|---|---|
| Grade | Level | Diagnosis | Therapy |
| A | 1a | SR (with homogeneity) of level 1 diagnostic studies; CDR with 1b studies from different clinical centres | SR (with homogeneity) of RCTs |
| | 1b | Validating cohort study with good reference standards; or CDR tested within one clinical centre | Individual RCT (with narrow Confidence interval) |
| | 1c | Absolute SpPins and SnNouts | All or none |
| B | 2a | SR (with homogeneity) of level >2 diagnostic studies | SR (with homogeneity) of cohort studies |
| | 2b | Exploratory cohort study with good reference standards; CDR after derivation, or validated only on split-sample or databases | Individual cohort study (including low quality RCT; e.g.., <80% follow-up) |
| | 2c | | "Outcomes" research; Ecological studies |
| | 3a | SR (with homogeneity) of 3b and better studies | SR (with homogeneity) of case-control studies |
| | 3b | Non-consecutive study; or without consistently applied reference standards | Individual case-control study |
| C | 4 | Case-control study, poor or non-independent reference standard | Case-series (and poor quality cohort and case-control studies) |
| D | 5 | Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles" | Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles" |

*Note*: Definitions of different levels of evidence for diagnosis and treatment.

Abbreviations: CDR, clinical data centre; RCT, randomized controlled trial; SR, systematic review.

determined the corresponding recommendations (Table 1). Grades of recommendation were set from A to D. Grade A: consistent level 1 studies; Grade B: consistent level 2 or 3 studies or extrapolations from level 1 studies; Grade C: level 4 studies or extrapolations from level 2 or 3 studies; Grade D: level 5 evidence or troublingly inconsistent or inconclusive studies of any level.

## 3 | RESULTS

### 3.1 | Clinical epidemiology of diabetic foot ulcer with lower extremity vasculopathy

According to statistics reported by the Global Burden of Disease study,[10] approximately 529 million people worldwide had diabetes in 2021, and nearly a quarter of them will have at least one diabetic foot ulcer in their lifetime. In addition, diabetes is the primary cause of nontraumatic lower extremity amputation worldwide. Data reveal that low distal amputation related to diabetes accounts for approximately 60% of all amputations in developed countries, 85% of which occur as a means to eradicate diabetic foot ulcers.[11,12]

As mentioned above, nearly half of the patients with diabetic foot ulcers in middle- and high-income countries have PAD, of which lower extremity arterial disease is directly related.[3] Diabetic PAD is not only a high-risk factor for diabetic foot but also an independent risk factor for amputation.[5,13] In the same age group, the incidence of PAD in patients with diabetes is twice as high as that in nondiabetic patients, and the incidence of PAD in hospitalised patients with diabetes can be as high as 19.47%–23.80%.[14] Another multicenter investigation indicated that the morbidity of diabetic PAD in China was as high as 21.2%, and the proportions of diabetic macrovascular and microvascular complications were 55.6% and 62.1%, respectively. Moreover, it was found that approximately half of the patients with diabetic PAD had missed diagnoses, resulting in a large number of missed opportunities for optimal treatment in the early stage of the disease.[15] Therefore, the timely diagnosis and treatment of diabetic foot ulcer with lower extremity vasculopathy is of great significance to reduce the disability and mortality rates of patients with diabetes.

### 3.2 | Evaluation of diabetic foot ulcer complicated with lower extremity vasculopathy

It is critical to master simple and effective evaluation methods for screening and treating diabetic foot ulcer complicated with lower extremity vasculopathy. Considering the implementation of national graded diagnosis and treatment policies, community outpatient service is generally the initial choice for patients with a diabetic foot. Therefore, it is worth standardising the screening method and recommending a graded diagnosis and treatment plan for patients with diabetic foot ulcer complicated with lower extremity vasculopathy according to these guidelines. The emergence and development of new theories and methods also allow for optimizations in the diagnosis of diabetic foot ulcer with abnormal macrovasculature or microcirculation (Figure 1).

(1) **Symptoms and signs**: Diabetic lower extremity vasculopathy often develops without any signs or symptoms, and patients often ignore routine physical examinations that screen for lower extremity vasculopathy before the diabetic foot ulcer even

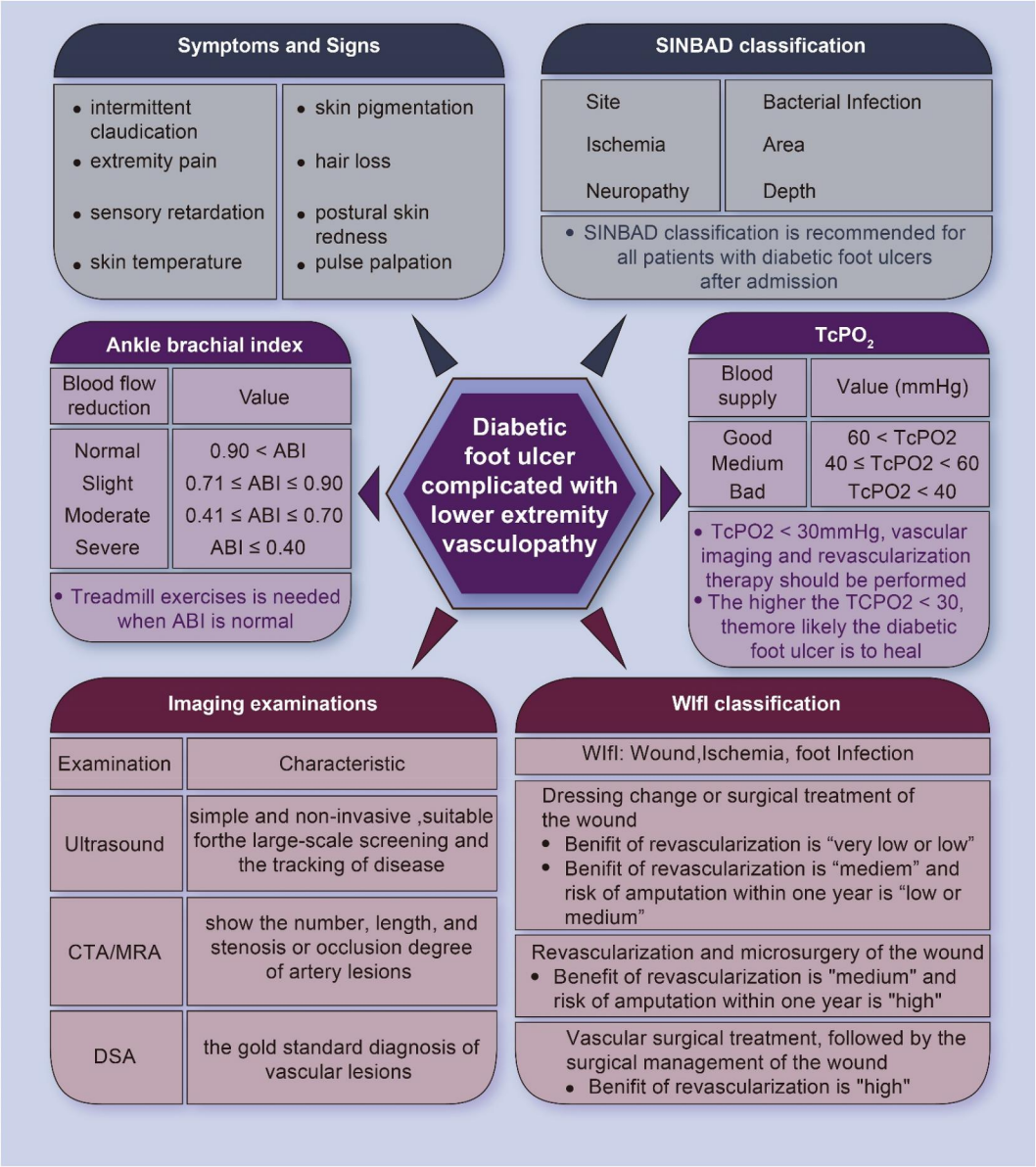


**FIGURE 1** Evaluation and grading method of diabetic foot ulcer combined with lower limb vasculopathy.

occurs.[16] Therefore, patients with diabetes, especially those with foot ulcers, should be asked about a possible history of intermittent claudication, extremity pain, or sensory retardation.[17,18] Some studies have also pointed out that the resting pain, claudication and other symptoms may not be obvious because patients with diabetes often have peripheral neuropathy and other complications.[16] In the physical examination of patients at presentation to the clinic, careful attention should be given to the skin temperature below the knee joint, skin pigmentation, hair loss, and postural skin redness.[19] In addition, it is vital to palpate the pulses of the anterior and posterior tibial arteries and auscultate the murmur of the femoral artery.[20,21] According to recent statistics, the rate of accurate diagnosis of lower extremity artery lesions in the physical examination can reach over 90%.[22] However, it is worth noting that patients with a negative physical examination cannot be diagnosed with PAD, considering possible arteriovenous short circuit and bypass vascular compensation; thus, a more objective evaluation is required.[23]

(2) **Ankle brachial index**: The ankle brachial index (ABI) is a recognized index that can reliably predict lower extremity arteriosclerosis.[24] ABI measures the systolic pressures of the posterior or anterior tibial artery at the ankle and the brachial artery. The ratio between the pressure of the ankle artery and the brachial artery is obtained. According to the American College of Cardiology/American Heart Association (ACC/AHA) guidelines published in early 2006, an ABI≤0.9 is recommended as the standard for diagnosing PAD.[25] An ABI≤0.9 has 95% sensitivity and 99% specificity for diagnosing PAD in the lower extremity and is considered the best noninvasive index for diagnosing PAD in the lower extremity.[26] An ABI value in the range of 0.71–0.90

indicates a slight reduction in blood flow, an ABI value in the range of 0.41–0.70 indicates a moderate reduction in blood flow, and an ABI≤0.40 indicates a severe reduction in the blood flow of the lower extremity arteries.[27] However, these values may lead to a false-negative results in some patients with a normal ABI. ABI can be detected after treadmill exercises, and lower extremity artery lesions should be considered when the ABI is 15%–20% lower than before.[28]

(3) **$TcPO_2$**: Transcutaneous oxygen pressure ($TcPO_2$) is obtained via noninvasive, repeatable techniques and is used to detect vascular lesions. It can not only directly detect the actual oxygen supply of skin tissue but can also reflect the overall blood supply of the extremity.[29] Therefore, it is often used to determine whether vascular intervention and other operations are needed, evaluate the perfusion function of tissue microcirculation, and predict the therapeutic effect of vascular lesions and skin ulcers.[29] For normal individuals, $TcPO_2$ should be higher than 60 mmHg. According to American Diabetes Association (ADA) standards, emergency angiography and revascularisation should be considered when $TcPO_2$ is less than 25 mmHg.[30]

(4) **Colour-flow Doppler ultrasound**: Colour-flow Doppler ultrasound is simple and noninvasive for vascular examination and can quickly specify the status of atherosclerotic plaques and whether there is arterial stenosis or occlusion.[31] Prior studies have focused on diagnosing pathological changes in diabetic foot arteries using colour-flow Doppler ultrasound. Compared with digital subtraction angiography (DSA), the gold standard for diagnosing vascular diseases, colour-flow Doppler ultrasound has a diagnostic accuracy of over 95%.[32] However, a colour-flow Doppler ultrasound examination also has many shortcomings. For example, the distal blood flow velocity of multisegment stenosis in some patients is slow, and the condition may be misdiagnosed as vascular occlusion on ultrasound examination. In addition, an ultrasound examination is easily affected by the operator's experience, as it does not require extensive training and may therefore lead to misjudgement.[33] In terms of diagnosing difficult cases, contrast-enhanced ultrasonography can obtain much more diagnostic information than colour-flow Doppler ultrasound.

(5) **CTA/MRA and DSA**: Computed tomography angiography/magnetic resonance angiography (CTA/MRA) provides clear images that can show the number, length, and stenosis or occlusion degree of lower extremity artery lesions. Prior studies have reported that the sensitivity, specificity and accuracy of CTA and MRA in the assessment of arterial occlusion of the lower extremities can reach over 90%.[34,35] In terms of CTA and MRA, the former is more sensitive in detecting calcification than the latter and has a better spatial resolution.[36] DSA remains the "gold standard" for diagnosing lower extremity vascular lesions.[37] For all this, DSA is typically employed when noninvasive tests indicate that interventional treatment may be necessary for lower extremity arterial disease. At the same time, interventional therapy needs to be done under the guidance of DSA. It can accurately reveal the status of clogged arteries and the situation of collateral circulation establishment as well as assist in interventional treatment selection.

(6) **Assessment methods for diabetic foot complicated with lower extremity vasculopathy**: To facilitate the adoption of a classification system among health care practitioners involved in the management of patients with diabetic foot ulcer, it is imperative that the implementation of said system is quick and simple and that the system does not require specialised equipment. The SINBAD and WIfI classifications have been broadly and externally validated for application in measuring wound healing and predicting the need for amputation in patients with diabetic foot ulcers.

The SINBAD classification (Table 2) is a commonly used clinical evaluation method for diabetic foot ulcers that is applied to assess the ulcer's site, area, depth, infection, ischaemia, and neuropathy.[7] It

**TABLE 2** SINBAD system for classifying and scoring foot ulcers.

| Category | Definition | SINBAD score |
|---|---|---|
| Site | Forefoot | 0 |
| | Midfoot and hindfoot | 1 |
| Ischaemia | Pedal blood flow intact: At least one pulse palpable | 0 |
| | Clinical evidence of reduced pedal blood flow | 1 |
| Neuropathy | Protective sensation intact | 0 |
| | Protective sensation lost | 1 |
| Bacterial infection | None | 0 |
| | Present | 1 |
| Area | Ulcer <1cm2 | 0 |
| | Ulcer ≥1cm2 | 1 |
| Depth | Ulcer confined to skin and subcutaneous tissue | 0 |
| | Ulcer reaching muscle, tendon or deeper | 1 |

is simple and quick to use, seldom requires specialised equipment beyond clinical examination, and contains the necessary information for triage by a specialist team. If a classification is used for the purpose of interprofessional communication within the health care field, it is crucial to utilise the specific clinical descriptions rather than solely relying on the overall score. This SINBAD classification system has undergone validation for both ulcer healing and amputation prediction,[38] which have demonstrated favourable outcomes and reliable results.

The selection of therapeutic options for diabetic foot ulcer complicated with lower extremity vasculopathy should be based on the severity of toe perfusion loss, the amount of foot tissue loss, infection degree, mechanical pressure on the ulcer, and other factors.[18] Therefore, the WIfI classification[8] (Table 3) proposed in the International Working Group on the Diabetic Foot (IWGDF) classification guidelines[39] can guide clinicians in evaluating the risk of amputation and the possible benefits of vascular reconstruction. This system classifies patients by foot ulcers, ischaemia severity based on noninvasive tests and infection severity based on the IWGDF and Infectious Diseases Society of America (IDSA) classifications. The WIfI classification is applied to a wide range of patients with varying severity and distribution of lower extremity atherosclerotic occlusive disease, including patients with ischaemic rest pain and chronic PAD. Since each of the three categories (wound, ischaemia, and foot infection) has four severity levels, the system generates a clinical combination of 64 theoretical possibilities. These combinations are currently classified and summarised by experts to solve two major clinical problems: the 1-year risk of amputation for each possible combination; and the benefits of each possible combination after revascularisation. The following tables show the clinical grade of 1-year amputation risk and revascularisation benefit (Tables 4 and 5).

***Recommendation 1***. When checking patients with diabetic foot ulcers, it is crucial to inquire about clinical symptoms such as intermittent claudication, resting pain, and sensory retardation of lower extremity vascular lesions, as well as physical examinations such as the skin temperature, colour, pulse palpation and auscultation of the lower extremity arteries (**Recommended Grade: A**). However, the clinical manifestations do not correspond to the presence (or absence) of arterial diseases and their severity. Further examination by instruments and other auxiliary means is still required (**Recommended Grade: B**).

***Recommendation 2***. In addition to symptom consultations and physical examinations, ABI tests and $TcPO_2$ tests are recommended as first-line examinations for patients with diabetic foot ulcers after admission (**Recommended Grade: A**).

***Recommendation 3***. For diabetic foot patients, the above indicators have certain limitations when applied individually, and can be comprehensively determined by combining multiple examination results. The risk of lower extremity vasculopathy is not considered when the ABI >0.9 or the $TcPO_2$ > 60 mmHg. Colour-flow Doppler ultrasound was recommended for a comprehensive evaluation when 40 mmHg ≤ $TcPO_2$ < 60 mmHg or when the ABI indicated mild-to-moderate reduced blood flow. When the $TcPO_2$ < 30 mmHg or the ABI indicates a severe decrease in blood flow, active vascular imaging and revascularisation therapy should be performed. The higher the $TcPO_2$, the more likely the diabetic foot ulcer is to heal (**Recommended Grade: A**).

***Recommendation 4***. Colour-flow Doppler ultrasound is easy to perform and has a high diagnostic accuracy for diabetic foot with lower extremity vasculopathy. It is suitable for large-scale vasculopathy screening and tracking disease progression and can be used as a second-line examination for patients with diabetic foot ulcer after admission (**Recommended Grade: B**). However, a colour-flow Doppler ultrasound operator is required to have sufficient clinical experience, and this examination has low sensitivity for detecting severe vascular calcification and multiple segment PAD. Therefore, it is not recommended as an operation indicator for interventional surgery or amputation of diabetic foot (**Recommended Grade: D**).

***Recommendation 5***. Currently, CTA/MRA examination should be selected for patients who can tolerate noninvasive screening for vasculopathy of the lower extremities and patients suspected of having a diabetic foot combined with vasculopathy of the lower extremities. DSA examination should be the first choice and the most important therapeutic choice for patients who are considered to need vascular reconstruction. (**Recommended Grade: B**). If the diabetic foot ulcer persists for more than 1 month with no signs of wound healing, a DSA examination should be performed for the patients, regardless of whether the early vascular examination results indicate the presence of lesions, and interventional vascular therapy should be considered according to the results (**Recommended Grade: A**).

***Recommendation 6***. The SINBAD and WIfI grading systems have practical clinical guiding significance in the assessment of diabetic foot ulcers complicated with lower extremity vasculopathy. The SINBAD system is recommended to facilitate communication about the characteristics of diabetic foot ulcers among health professionals (**Recommended Grade: A**). The WIfI classification is recommended for evaluating the risk of amputation and the benefit of revascularisation and making treatment recommendations (**Recommended Grade: A**).

## 3.3 | Surgical treatment of diabetic foot ulcer complicated with vasculopathy

### 3.3.1 | Therapeutic principle

In treating diabetic foot ulcer complicated with vasculopathy, the principle of internal-surgical coordination and individual treatment

**TABLE 3** WIfI classification of diabetic foot.

| **Wound** | | |
|---|---|---|
| **Grade** | **DFU** | **Gangrene** |
| 0 | No ulcer | No gangrene |
| Clinical description: Ischaemic resting pain (requires classic symptoms + grade 3 ischaemia), without wound | | |
| 1 | Small, shallow ulcer(s) on distal leg or foot; no exposed bone, unless limited to distal phalanx | No gangrene |
| Clinical description: Minor tissue loss. Salvageable with simple digital amputation (1 or 2 digits) or skin coverage. | | |
| 2 | Deeper ulcer with exposed bone, joint or tendon; generally not involving the heel; shallow heel ulcer, without calcaneal involvement | Gangrenous changes limited to digits |
| Clinical description: Major tissue loss salvageable with multiple (≥3) digital amputations or standard transmetatarsal amputation (TMA) ± skin coverage. | | |
| 3 | Extensive, deep ulcer involving forefoot and/or midfoot; deep, full thickness heel ulcer ± calcaneal involvement | Extensive gangrene involving forefoot and/or midfoot; full thickness heel necrosis six calcaneal involvement |
| Clinical description: Extensive tissue loss salvageable only with a complex foot reconstruction or non-traditional TMA (Chopart or Lisfranc); flap coverage or complex wound management needed for large soft tissue defect | | |

| **Ischaemia** | | | |
|---|---|---|---|
| **Grade** | **ABI** | **Ankle systolic pressure (mmHg)** | **$TcPO_2$ (mmHg)** |
| 0 | ≥0.80 | >100 | ≥60 |
| 1 | 0.6–0.79 | 70–100 | 40–59 |
| 2 | 0.4–0.59 | 50–70 | 30–39 |
| 3 | ≤0.39 | <50 | <30 |

| **Foot infection** | |
|---|---|
| **Grade** | **Clinical manifestations** |
| 0 | ① No symptoms or signs of infection<br>② Infection present, as defined by the presence of at least two of the following items:<br>• Local swelling or induration<br>• Erythema >0.5 to ≤2 cm around the ulcer<br>• Local tenderness or pain<br>• Local warmth<br>• Purulent discharge (thick, opaque to white, or sanguineous secretion) |
| 1 | ① Local infection involving only the skin and the subcutaneous tissue (without involvement of deeper tissues and without systemic signs as described below).<br>② Exclude other causes of an inflammatory response of the skin (e.g., trauma, gout, acute Charcot neuro-osteoarthropathy, fracture, thrombosis, and venous stasis) |
| 2 | ① Local infection (as described above) with erythema >2 cm or involving structures deeper than the skin and subcutaneous tissues (eg, abscess, osteomyelitis, septic arthritis, and fasciitis)<br>② No systemic inflammatory response signs (as described below) |
| 3 | Local infection (as described above) with the signs of SIRS, as manifested by two or more of the following:<br>• Temperature >38°C or <36°C<br>• Heart rate >90 beats/min<br>• Respiratory rate >20 breaths/min or PaCO2 <32 mmHg<br>• White blood cell count >12,000 or <4000 cu/mm or 10% immature (band) forms |

*Note*: The WIfI classification includes three assessments for wound (W) ischaemia (I) and foot infection (fI), which is the guidance for clinicians in assessing the risk of amputation and the possible benefits of revascularisation.

Abbreviations: ABI, ankle brachial index; DFU, diabetic foot ulcer; $TcPO_2$, transcutaneous oxygen pressure; TMA, transmetatarsal amputation.

**TABLE 4** Estimated risk of amputation at 1 year for each combination.

| | I-0 | | | | I-1 | | | | I-2 | | | | I-3 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| W-0 | VL | VL | L | M | VL | L | M | H | L | L | M | H | L | M | M | H |
| W-1 | VL | VL | L | M | VL | L | M | H | L | M | H | H | M | M | H | H |
| W-2 | L | L | M | M | M | M | H | H | M | H | H | H | H | H | H | H |
| W-3 | M | M | H | H | H | H | H | H | H | H | H | H | H | H | H | H |
| | fI-0 | fI-1 | fI-2 | fI-3 | fI-0 | fI-1 | fI-2 | fI-3 | fI-0 | fI-1 | fI-2 | fI-3 | fI-0 | fI-1 | fI-2 | fI-3 |

*Note*: VL, Very Low (clinical stage 1); L, Low (clinical stage 2); M, Middle (clinical stage 3); H, High (clinical stage 4).

Abbreviations: fI, foot infection; I, ischaemia; W, wound.

**TABLE 5** Estimate likelihood of benefit of/requirement for revascularisation.

| | I-0 | | | | I-1 | | | | I-2 | | | | I-3 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| W-0 | VL | VL | VL | VL | VL | L | L | M | L | L | M | M | M | H | H | H |
| W-1 | VL | VL | VL | VL | L | M | M | H | M | H | H | H | H | H | H | H |
| W-2 | VL | VL | VL | VL | M | M | H | H | H | H | H | H | H | H | H | H |
| W-3 | VL | VL | VL | VL | M | M | M | H | H | H | H | H | H | H | H | H |
| | fI-0 | fI-1 | fI-2 | fI-3 | fI-0 | fI-1 | fI-2 | fI-3 | fI-0 | fI-1 | fI-2 | fI-3 | fI-0 | fI-1 | fI-2 | fI-3 |

*Note*: VL, Very Low (clinical stage 1); L, Low (clinical stage 2); M, Middle (clinical stage 3); H, High (clinical stage 4).

Abbreviations: fI, foot infection; I, ischaemia; W, wound.

should be adopted. For such patients, blood glucose, blood pressure, blood lipids and other indicators should be actively controlled.[40] If the vascular lesions are in the mild-to-moderate stage and have not yet progressed to meet the criteria for surgical treatment, the principle of "early, individual, reasonable combination" can be followed for the treatment of vascular lesions, and the wound dressings on the diabetic foot should be changed. The medication for vasculopathy should be as accessible as possible. If combination drug treatment is needed, the medications should be complementary, the interaction between drugs should be monitored, and the liver, kidneys, heart, lungs and other organ functions of patients should be monitored. Vasodilator drugs such as beraprost sodium, carvedilol and nebivolol are currently considered.[41,42] Antiplatelet drugs such as aspirin and clopidogrel[43] and anticoagulant drugs such as low molecular weight heparin and rivaroxaban[44] can be selected according to the specific situation. For patients who need surgical treatment, revascularisation treatment should be selected based solely on the patient's situation.

***Recommendation 7***. For patients with diabetic foot ulcers complicated with lower extremity vasculopathy, blood glucose, blood pressure and blood lipids should be individually controlled. Aspirin alone (75–325 mg per day) or clopidogrel alone (75 mg per day) can reduce the incidence of serious vascular events among patients with PAD. The addition of low-dose rivaroxaban (2.5 mg twice daily) to aspirin in patients with symptomatic PAD reduced the incidence of MALEs (major adverse limb events) (**Recommended Grade: A**).

### 3.3.2 | Treatment plan for vascular reconstruction

Vascular surgeons have extensive experience in vascular reconstruction or recanalisation treatment for lower extremity vasculopathy. However, compared with simple vascular lesions of the lower extremities, diabetic foot ulcers with lower extremity vasculopathy have their own characteristics. For example, the lesions may be multihorizontal, long vascular segments, or show complete occlusion, or even serious calcification, poor collateral circulation, and more involvement of small vessels under the knee, as well as other related characteristics.[45] These characteristics increase the difficulty of surgical intervention for lower extremity vasculopathy and significantly reduce the long-term patency rate. Even so, most studies have reported that the healing rate of diabetic ulcers at 12 months after revascularisation therapy is over 60%, and the extremity retention rate is in the range of 80%–85%.[46] Therefore, surgical intervention for diabetic foot ulcers with low extremity vasculopathy is crucial (Figure 2).

For patients with no-option critical limb ischaemia disease, there are few treatment options. Some studies have reported that effective treatment can be achieved through methods such as venous-arterialisation,[47] autologous stem cell transplantation,[48] omentum majus transplantation[49] and bioengineering materials.[50] Although most of these techniques are generally applicable for chronic lower limb ischaemia, they may not always be suitable for diabetic foot ulcers complicated with lower extremity vasculopathy because of the limited time for treatment.

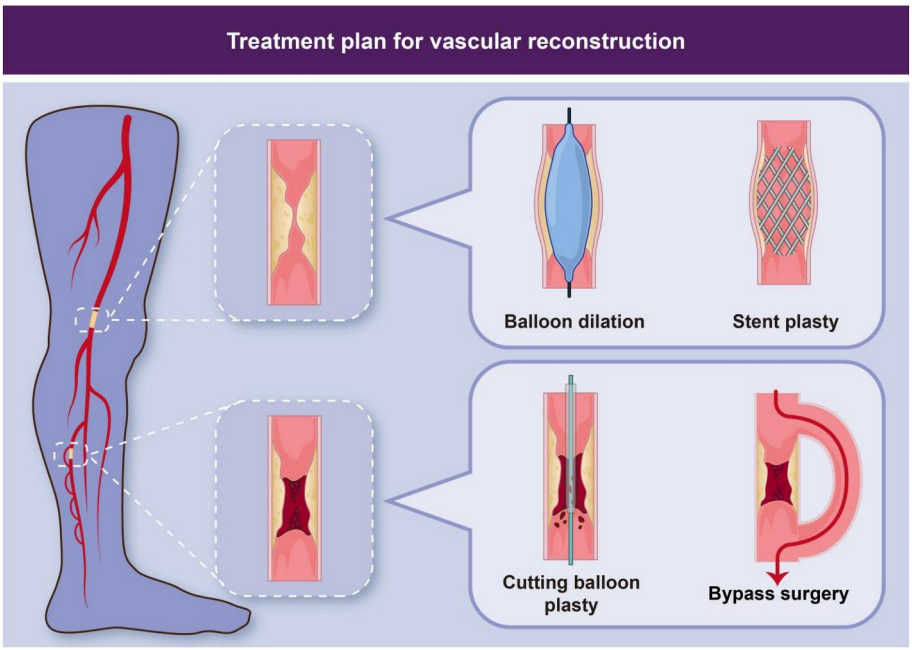


**FIGURE 2** Representative treatment plan for revascularisation of diabetic foot ulcer complicated with lower extremity vasculopathy (incomplete obstruction: balloon dilatation, stent plasty; complete obstruction: cutting balloon plasty, bypass surgery).

(1) **Endovascular therapy** Endovascular therapy primarily comprises balloon dilatation, stent plasty, atherectomy, ultrasound ablation, cutting balloon plasty and laser-assisted angioplasty. Balloon dilation and stent plasty are currently primarily applied in clinical practice. The main advantages of endovascular therapy include safety, minimal invasiveness, repeatability and effectiveness. It can be solved by conventional bypass surgery, even if endovascular surgery fails.[51] Endovascular surgery can rapidly improve the blood supply of the ischaemic extremity, so it can improve the healing of diabetic foot ulcer and the rate of extremity rescue. Moreover, restenosis occurs even after vasodilatation, and restenosis often has to go through a lengthy process during which the collateral circulation of the ischaemic extremity is established; therefore, this type of surgery is widely applied in clinical practice.

(2) **Traditional bypass surgical treatment** Traditional bypass surgical treatment generally comprises autologous great saphenous vein bypass, artificial vascular bypass and profunda arterioplasty. Only patients with Trans-Atlantic Inter-Society Consensus (TASC) grade D or grade C lesions and no high-risk factors for surgery need to be treated with conventional bypass surgery, and the bypass surgery method should be considered carefully.[52] A combination of multiple methods can be applied for complex and extensive extremity artery lesions. When autogenous greater saphenous veins or artificial vessels were used as bypass grafts for above-knee femoral artery bypass, the difference in the 5-year postoperative patency rate was not statistically significant between the two. However, when the distal anastomosis was below the knee, the 5-year postoperative patency rate of the former was significantly higher than that of the latter.[53]

(3) **Venous-arterialisation**: Venous-arterialisation is a technique of use as a revascularisation strategy for patients with chronic limb-threatening ischaemia and no options for distal revascularisation. Deep venous arterialisation (DVA) is performed on patients with resting pain or nonhealing wounds who lack distal arterial targets for conventional open or endovascular arterial revascularisation due to advanced small-artery disease.[47] Therefore, it is considered a last resort to try limb salvage in situations where amputation is an unavoidable option. In the literature, the rates of limb salvage range from 25% to 100% for open DVA, 60%–71% for percutaneous DVA, and 46%–69% for hybrid DVA approaches. Percutaneous DVA provides a minimally invasive choice for patients with sufficient endoluminal access.[54]

***Recommendation 8***. Patients with diabetic foot ulcers complicated with lower extremity vasculopathy should be evaluated using the WIfI classification to evaluate the benefit of revascularisation. When the benefit of revascularisation is "very low" or "low" or the benefit of revascularisation is "medium" and the risk of amputation within 1 year is "low" or "medium", vascular surgical treatment can be temporarily delayed, and only dressing changes or surgical treatment of the wound can be performed. When the benefit of revascularisation is "medium" and the risk of amputation within 1 year is "high" revascularisation is recommended, and microsurgery is considered to repair the wound. When the revascularisation benefit is "high", vascular surgical treatment is strongly recommended, followed by surgical management of the wound (Recommended Grade: A). The timing of vascular reconstruction for patients with diabetic foot ulcers complicated with lower extremity vasculopathy is crucial. When

a patient is identified as requiring vascular reconstruction treatment, surgery should be performed to restore distal blood flow to the lower limbs as soon as possible.

***Recommendation 9***. Balloon dilation is recommended as the first choice of treatment for patients with diabetes with below-knee artery diseases. Because of the elastic retraction of the blood vessels after traditional balloon dilatation, the treatment effect is not ideal. A drug-coated balloon can improve the patency rate of target lesions in the short and long term and avoid the potential need for stent implantation. It is the most commonly used treatment method for below-knee artery stenosis and occlusion, and is recommended as the first-line treatment (**Recommended Grade: A**).

***Recommendation 10***. For endovascular stent implantation, salvage stent implantation is recommended for peripheral blood vessels, especially for lower extremity blood vessels. That is, stent implantation is recommended only when residual stenosis >30% or when flow-limiting dissection occurs after balloon dilatation. Stent implantation across joints, important branch blood vessels and long segment stents should be avoided as much as possible. The use of covered stents is recommended after reopening the original stent occlusion or stenosis or when stent implantation is required for thrombosis (**Recommended Grade: B**). Endovascular volume reduction technology can remove hardened and calcified plaques from the lumen during the treatment of lesions. It has unique advantages that balloon dilation and stent implantation do not have, and can be used as a second-line option (**Recommended Grade: C**).

***Recommendation 11***. Bypass grafting is a better choice for young patients with long occlusive lesions, good distal outflow tract conditions, and good surgical tolerance. The long-term patency rate after autologous vascular bypass grafting is generally good (**Recommended Grade: B**).

***Recommendation 12***. In situations where amputation is deemed the only viable solution, percutaneous DVA is viewed as a last resort for limb preservation. This technique is a minimally invasive alternative for patients with adequate endoluminal access (**Recommended Grade: B**).

***Recommendation 13***. The goal of revascularisation should be to optimise perfusion to the foot, which will differ depending on the individual patient's circumstances. The efficacy of a revascularisation operation should be assessed utilising objective measures of perfusion. Because of insufficient evidence, we have refrained from providing specific targets for perfusion pressures in this recommendation. Our suggestion is that revascularisation should produce a minimum toe pressure of >30 mmHg or $TcPO_2$ of >25 mmHg to be deemed effective[55] (**Recommended Grade: D**). In addition, the skin oxygen levels rise gradually in the weeks following successful percutaneous transluminal angioplasty. For this reason, $TcPO_2$ measurements are ideally taken 1 week after surgery[56] (**Recommended Grade: D**).

### 3.3.3 | Wound treatment of diabetic foot ulcer complicated with lower extremity vasculopathy

Diabetic foot ulcer patients with vasculopathy need further wound treatment to improve the blood supply. Diabetic foot ulcers have varying treatment methods according to the WIfI classification (Figure 3). Generally, patients with diabetic foot ulcers and no foot infection should refrain from bearing weight on the foot and their wound dressings should be changed. Vascular reconstruction therapy can be considered when the WIfI classification for ischaemia is grade 2–3. For patients with diabetic foot and infection, lower extremity vascular function should be evaluated on the basis of anti-infection therapy. Vascular reconstruction therapy should be actively performed for ischaemia with WIfI classification grades 2–3, but patients should be informed that the risk of amputation within 1 year is very high. Most diabetic foot wounds can be treated with surgical debridement to achieve the purpose of removing necrotic tissues, reducing infection and preserving healthy tissues, thus creating opportunities for wound repair. However, when the wound or foot infection score is 3 in diabetic foot patients, the risk of toe or lower extremity amputation is very high.[57]

(1) **Wound debridement**: Timely and effective wound debridement is crucial to promote wound healing. The identification and removal of necrotic tissue and the preservation and protection of healthy tissue during surgical debridement are key factors in determining the effect of debridement. Debridement can remove necrotic tissue, reduce the number of bacteria on the wound surface, reduce local pressure and promote wound drainage. Debridement can be divided into surgical debridement, enzymatic debridement, biological debridement, and ultrasonic debridement, among others.[58] Surgical debridement is the most effective treatment for these methods.
(2) **NPWT**: Negative pressure wound therapy (NPWT) is a noninvasive wound drainage method and closure treatment technology that applies controllable local negative pressure to assist in the treatment of chronic and acute wounds.[59] Several clinical studies have confirmed that, compared with traditional debridement and dressing changes, NPWT can reduce the degree of interstitial oedema, the capillary afterload of local tissues, and the number of bacteria on the wound by draining excess fluid.[60] The shear force formed by negative pressure on the wound can cause cell deformation and form a hypoxic gradient in the tissues surrounding it, promote cell recruitment, proliferation and differentiation, accelerate blood vessel formation, granulate tissue proliferation and epithelial cell growth and facilitate wound healing.[61,62] In addition, NPWT can effectively reduce the frequency of dressing changes and shorten the preparation time

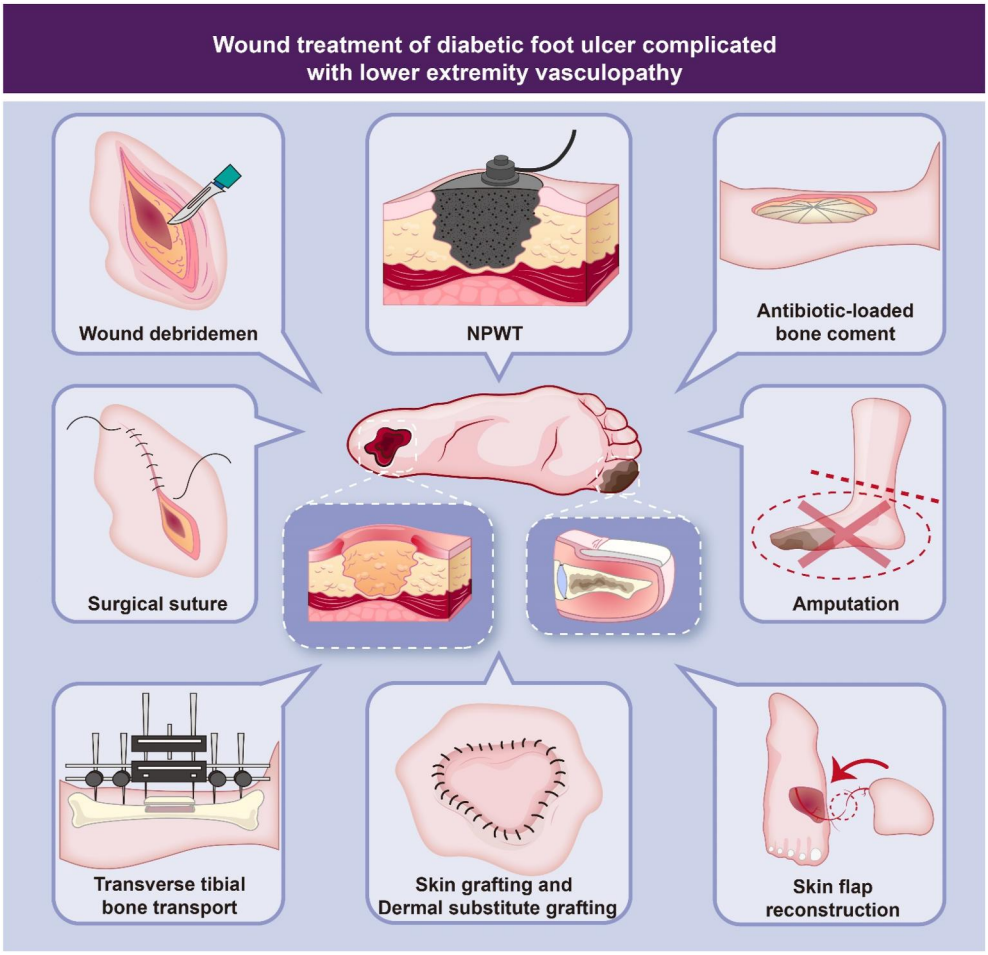


**FIGURE 3** Different surgical treatment methods for diabetic foot ulcer complicated with lower extremity vasculopathy.

of the wound bed while immobilising grafts during surgery, controlling wound exudation and blocking the surgical area to reduce postoperative wound contamination.[63] Its combined application with a variety of materials and drugs in the treatment of diabetic foot ulcers has also been reported to have remarkable effects.[26,64]

(3) **Antibiotic-loaded bone cement**: It has the advantages of anti-infection, high mechanical strength and strong shaping ability. It can be employed to fill the wound cavity of the diabetic foot, release a high concentration of antibiotics locally, inhibit the formation of bacterial biofilms, and limit the effect of ischaemia.[65] Antibiotic-loaded bone cement can also be used in combination with NPWT to improve the treatment efficiency, shorten the treatment time, and accelerate the process of wound repair.[66,67]

(4) **Transverse tibial bone transport**: In 1976, Professor Ilizarov of the Soviet Union invented the lateral remodelling technique of the lower extremity bone and proposed the "tension-stress rule" in 1989. This means that the living tissue can be stimulated to grow and regenerate continuously by promoting stable, slow and continuous tensile stress.[68] After technical improvements and the evolution of surgical instruments in China, this surgical method has also evolved into the "tibial transverse bone transport" technique. Numerous local studies have revealed that this treatment can improve the ABI of the affected extremity, restore the normal skin temperature and sensation, stimulate microcirculation regeneration of the lower extremity, improves peripheral nerve function, control local infection, promote ulcer healing and reduce the risk of recurrence.[69,70]

(5) **Surgical suture**: Diabetic foot ulcers can be directly closed by a surgical suture if there is granulation tissue, fresh bleeding, no obvious tension and no dead space after debridement or other treatments. If the tension of the wound is large, a skin stretching device can be used for wound closure. The wound can be closed gradually by adjusting the tension and changing the wound dressing intermittently.[71,72]

(6) **Dermal substitute grafting**: The current approach to treat diabetic foot ulcers involves thorough cleansing of the wound bed and removal of infected tissue through surgical debridement. Dressings are then applied to protect and cover the wound, while also maintaining a clean and moist environment and effectively absorbing exudate. Various materials have been developed so far. For instance, acellular dermal matrix, an extracellular matrix-based material, enables cellular infiltration and proliferation,

thereby promoting vascularisation, matrix deposition, and re-epithelialisation.[73] The Integra Dermal Regeneration Template is FDA-approved and was developed by Integra Life Sciences, USA. Other biological products, such as Dermagraft, Becaplermin, and Apligraf are widely used for this purpose. In recent years, with the development of functional hydrogel materials[74] and 3D printing technology,[75] an increasing number of wound dressings and dermal substitutes have entered clinical application.

(7) **Skin grafting**: After debridement treatment, the wound base should be surgically sealed as soon as possible. Skin grafting is one of the simplest ways to do this. Skin grafts have high requirements on the wound base and are not wear-resistant. Free skin grafts should be used for diabetic foot wounds with good granulation tissue growth and no tendon or bone exposure, and for wounds at nonweight-bearing sites.[76]

(8) **Skin flap transplantation**: Since diabetic foot ulcers complicated with PAD typically have varying degrees of vascular sclerosis and occlusion, conventional concepts show that skin grafting is the optimal choice for repairing such wounds, and is preferred over flap repair. Recent studies have confirmed that free flaps can improve the local blood supply, reduce the rate of lower extremity amputation and improve the five-year survival rate and can be used in patients with mild vasculopathy or those who have undergone vascular reconstruction surgery.[77,78] In addition, local flaps are often applied and advantageous in the surgical repair of small-scale diabetic foot ulcers because they cause minor damage, can be placed in close proximity to tissues and accelerate the return of normal sensation to cutaneous nerves.[79,80]

(9) **Toe/lower extremity amputation**: Toe/lower extremity amputation can be performed when refractory wounds seriously affect the patient's quality of life or when the toe/extremity has lost its functionality and has no preservation value or is life-threatening.[81] The level of diabetic foot amputation is closely related to the patient's nutritional status, the state of the skin of the affected extremity, the presence or absence of arterial occlusion or neuropathy and infection severity. Following a detailed preoperative evaluation and careful intraoperative exploration, we strive to promote primary healing of the stump and preserve the functionality of the affected extremity as much as possible.[82]

***Recommendation 14***. Surgical debridement should be the initial choice for those with wound or foot infection above grade 1 in the WIfI classification. Surgical debridement should be performed no less than once a week. Foot infections with abscess, gangrene, or necrotising fasciitis should be thoroughly debrided. Multiple debridement procedures are often beneficial for wound healing (**Recommended Grade: A**).

***Recommendation 15***. NPWT can be employed for diabetic foot ulcers with or without infection, especially for wound WIfI classification grades 2–3. Although the negative pressure and drainage effects of NPWT are beneficial for removing wound exudate and bacteria, it must be combined with surgical debridement rather than used individually (**Recommended Grade: A**). NPWT combined with vascular intervention in the treatment of diabetic foot ulcers has good efficacy (**Recommended Grade: B**).

***Recommendation 16***. Although patients with diabetic foot ulcers complicated with vasculopathy have been treated for vascular lesions in the early stages, simple surgeries that cause less secondary damage are preferred for wound repair to solve complex problems with simple methods, and skin grafting remains the first choice. For special parts, such as joints and weight-bearing areas, it is recommended that medium-thickness skin grafts be drilled and transplanted. After skin grafting, NPWT can improve the survival rate of skin grafts (**Recommended Grade: A**).

***Recommendation 17***. For wounds with exposed tendons and bones, in the case of multiple atherosclerosis and occlusion of blood vessels, pretreatment such as antibiotic-loaded bone cement, transverse tibial bone transport and NPWT can be used to improve the blood supply to the wound. Appropriate dermal substitutes could also be used for temporary wound coverage to achieve anti-infection effects, reduce bleeding or promote tissue regeneration. Then, skin grafting or skin flap transplantation can be performed subsequently (**Recommended Grade: B**).

***Recommendation 18***. In cases where the vascular occlusion score is mild to moderate, the above wounds can be covered with local skin flaps or free skin flaps to increase the healing rate and reduce the recurrence rate of ulcers. Retrograde skin flaps should be used to reduce the incidence of flap necrosis (**Recommended Grade: B**). When the wound is complicated and requires surgical repair with a skin flap, DSA examination is recommended to clarify the vascular conditions prior to operation (**Recommended Grade: B**).

***Recommendation 19***. Worse cases of diabetic foot ulcers with vasculopathy will be associated with a high amputation rate. Currently, the amputation risk of patients can be assessed according to the WIfI classification. If amputation is inevitable, the length of the affected extremity should be preserved on the basis of ensuring wound healing to reduce psychological and life inconveniences (**Recommended Grade: B**).

## 4 | CONCLUSIONS

Patients suffering from diabetic foot ulcers complicated with lower extremity vasculopathy have rapid progression and poor clinical outcomes, and amputation is often required if they cannot receive standardized treatment. Early diagnosis could enable targeted treatment to prevent the progression of disease and other adverse outcomes, but diabetic foot ulcers complicated with lower extremity vasculopathy in individuals are frequently underdiagnosed. Among

patients with diabetes, it is recommended that ABI and $TcPO_2$ be measured at least a yearly basis to identify the possible presence of vasculopathy and to predict the risk of progression to the symptomatic stages of the disease. In addition, the decision to manage diabetic foot ulcers with lower extremity vasculopathy should be individualised and may require further diagnostic studies, medical treatment to reduce the risk of vascular occlusion, effective surgical therapies for the wound and vascular lesions, and the involvement of vascular surgeons. This consensus offers a theoretical basis and reasonable operation suggestions for the diagnosis and treatment of individuals with diabetic foot ulcers complicated with vascular lesions, with the goal of ensuring access to optimal, evidence-based management for all. With the introduction of new theoretical knowledge and the progression of treatment concepts and methods, it could be predicted that there will be more breakthrough progress in treating diabetic foot ulcer complicated with lower extremity vasculopathy in the near future.

The recommendations in this consensus were subjected to the evidence grading and recommendation strength standards developed by the OCEBM but not GRADE or PRISMA. This may lead to some differences in the strength of recommendation compared with other consensus or guidelines. We hope to cooperate with IWGDF, EVSVS and SVS to develop more comprehensive clinical guidelines in the near future.

## AUTHOR CONTRIBUTIONS

All authors were responsible for drafting the article and critically revising it for important intellectual content. All authors approved the version to be published.

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## CONFLICT OF INTEREST STATEMENT

No potential conflicts of interest relevant to this article were reported.

## DATA AVAILABILITY STATEMENT

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

## ETHICS STATEMENT

No ethics statement.

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## PEER REVIEW

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