Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

The management of diabetic foot: a clinical practice guideline by the Society for Vascular Surgery in collaboration with the American Podiatric Medical Association and the Society for Vascular Medicine.

Bibliographic Source(s)

Hingorani A, LaMuraglia GM, Henke P, Meissner MH, Loretz L, Zinszer KM, Driver VR, Frykberg R, Carman TL, Marston W, Mills JL Sr, Murad MH. The management of diabetic foot: a clinical practice guideline by the Society for Vascular Surgery in collaboration with the American Podiatric Medical Association and the Society for Vascular Medicine. J Vasc Surg. 2016 Feb;63(2 Suppl):3S-21S. [174 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Definitions of the strength of the recommendations (Grade 1 or 2) and quality of the evidence (Level A–C) are provided at the end of the "Major Recommendations" field.

Prevention of Diabetic Foot Ulcers (DFUs)

1. The committee recommends that patients with diabetes undergo annual interval foot inspections by physicians (MD, DO, DPM) or advanced practice providers with training in foot care (Grade 1C).

2. The committee recommends that foot examination include testing for peripheral neuropathy using the Semmes-Weinstein test (Grade 1B).

3. The committee recommends education of the patients and their families about preventive foot care (Grade 1C).

4a. The committee suggests against the routine use of specialized therapeutic footwear in average-risk diabetic patients (Grade 2C).

4b. The committee recommends using custom therapeutic footwear in high-risk diabetic patients, including those with significant neuropathy, foot deformities, or previous amputation (Grade 1B).

5. The committee suggests adequate glycemic control (hemoglobin A_{1c} <7% with strategies to minimize hypoglycemia) to reduce the incidence of DFUs and infections, with subsequent risk of amputation (Grade 2B).

6. The committee recommends against prophylactic arterial revascularization to prevent DFU (Grade 1C).

Off-Loading DFUs

1. In patients with plantar DFU, the committee recommends offloading with a total contact cast (TCC) or irremovable fixed ankle walking boot (Grade 1B).

2. In patients with DFU requiring frequent dressing changes, the committee suggests off-loading using a removable cast walker as an alternative to TCC and irremovable fixed ankle walking boot (Grade 2C). The committee suggests against using postoperative shoes or standard or customary footwear for off-loading plantar DFUs (Grade 2C).

3. In patients with nonplantar wounds, the committee recommends using any modality that relieves pressure at the site of the ulcer, such as a surgical sandal or heel relief shoe (Grade 1C).

4. In high-risk patients with healed DFU (including those with a prior history of DFU, partial foot amputation, or Charcot foot), the committee recommends wearing specific therapeutic footwear with pressure-relieving insoles to aid in prevention of new or recurrent foot ulcers (Grade 1C).

Diagnosis of Diabetic Foot Osteomyelitis (DFO)

1. In patients with a diabetic foot infection (DFI) with an open wound, the committee suggests doing a probe to bone (PTB) test to aid in diagnosis (Grade 2C).

2. In all patients presenting with a new DFI, the committee suggests that serial plain radiographs of the affected foot be obtained to identify bone abnormalities (deformity, destruction) as well as soft tissue gas and radiopaque foreign bodies (Grade 2C).

3. For those patients who require additional (i.e., more sensitive or specific) imaging, particularly when soft tissue abscess is suspected or the diagnosis of osteomyelitis remains uncertain, the committee recommends using magnetic resonance imaging (MRI) as the study of choice. MRI is a valuable tool for diagnosis of osteomyelitis if the PTB test is inconclusive or if the plain film is not useful (Grade 1B).

4. In patients with suspected DFO for whom MRI is contraindicated or unavailable, the committee suggests a leukocyte or antigranulocyte scan, preferably combined with a bone scan as the best alternative (Grade 2B).

5. In patients at high risk for DFO, the committee recommends that the diagnosis is most definitively established by the combined findings on bone culture and histology (Grade 1C). When bone is débrided to treat osteomyelitis, the committee recommends sending a sample for culture and histology (Grade 1C).

6. For patients *not* undergoing bone débridement, the committee suggests that clinicians consider obtaining a diagnostic bone biopsy when faced with diagnostic uncertainty, inadequate culture information, or failure of response to empirical treatment (Grade 2C).

Wound Care for DFUs

1. The committee recommends frequent evaluation at 1- to 4-week intervals with measurements of diabetic foot wounds to monitor reduction of wound size and healing progress (Grade 1C).

1.1. The committee recommends evaluation for infection on initial presentation of all diabetic foot wounds, with initial sharp débridement of all infected diabetic ulcers, and urgent surgical intervention for foot infections involving abscess, gas, or necrotizing fasciitis (Grade 1B).

1.2. The committee suggests that treatment of DFIs should follow the most current guidelines published by the Infectious Diseases Society of America (IDSA) (Ungraded).

2. The committee recommends use of dressing products that maintain a moist wound bed, control exudate, and avoid maceration of surrounding intact skin for diabetic foot wounds (Grade 1B).

3. The committee recommends sharp débridement of all devitalized tissue and surrounding callus material from DFUs at 1- to 4-week intervals (Grade 1B).

4. Considering lack of evidence for superiority of any given débridement technique, the committee suggests initial sharp débridement with subsequent choice of débridement method based on clinical context, availability of expertise and supplies, patient tolerance and preference, and cost-effectiveness (Grade 2C).

5. For DFUs that fail to demonstrate improvement (>50% wound area reduction) after a minimum of 4 weeks of standard wound therapy, the committee recommends adjunctive wound therapy options. These include negative pressure therapy, biologics (platelet-derived growth factor

[PDGF], living cellular therapy, extracellular matrix products, amnionic membrane products), and hyperbaric oxygen therapy. Choice of adjuvant therapy is based on clinical findings, availability of therapy, and cost-effectiveness; there is no recommendation on ordering of therapy choice. Re-evaluation of vascular status, infection control, and off-loading is recommended to ensure optimization before initiation of adjunctive wound therapy (Grade 1B).

6. The committee suggests the use of negative pressure wound therapy for chronic diabetic foot wounds that do not demonstrate expected healing progression with standard or advanced wound dressings after 4 to 8 weeks of therapy (Grade 2B).

7. The committee suggests consideration of the use of PDGF (becaplermin) for the treatment of DFUs that are recalcitrant to standard therapy (Grade 2B).

8. The committee suggests consideration of living cellular therapy using a bilayered keratinocyte/fibroblast construct or a fibroblast-seeded matrix for treatment of DFUs when recalcitrant to standard therapy (Grade 2B).

9. The committee suggests consideration of the use of extracellular matrix products employing acellular human dermis or porcine small intestinal submucosal tissue as an adjunctive therapy for DFUs when recalcitrant to standard therapy (Grade 2C).

10. In patients with DFU who have adequate perfusion that fails to respond to 4 to 6 weeks of conservative management, the committee suggests hyperbaric oxygen therapy (Grade 2B).

Peripheral Arterial Disease (PAD) and the DFU

1.1. The committee suggests that patients with diabetes have ankle-brachial index (ABI) measurements performed when they reach 50 years of age (Grade 2C).

1.2. The committee suggests that patients with diabetes who have a prior history of DFU, prior abnormal vascular examination, prior intervention for peripheral vascular disease, or known atherosclerotic cardiovascular disease (e.g., coronary, cerebral, or renal) have an annual vascular examination of the lower extremities and feet including ABI and toe pressures (Grade 2C).

2. The committee recommends that patients with DFU have pedal perfusion assessed by ABI, ankle and pedal Doppler arterial waveforms, and either toe systolic pressure or transcutaneous oxygen pressure ($TcPO_2$) annually (Grade 1B).

3. In patients with DFU who have PAD, the committee recommends revascularization by either surgical bypass or endovascular therapy (Grade 1B).

Recommendation 3 Technical and Implementation Remarks

- Prediction of patients most likely to require and to benefit from revascularization can be based on the Society for Vascular Surgery (SVS) Wound, Ischemia, and foot Infection (WIfI) lower extremity threatened limb classification.
- A combination of clinical judgment and careful interpretation of objective assessments of perfusion along with consideration of the wound and infection extent is required to select patients appropriately for revascularization.
- In functional patients with long-segment occlusive disease and a good autologous conduit, bypass is likely to be preferable.
- In the setting of tissue loss and diabetes, prosthetic bypass is inferior to bypass with vein conduit.
- The choice of intervention depends on the degree of ischemia, the extent of arterial disease, the extent of the wound, the presence or absence of infection, and the available expertise.

Definitions

Grading of Recommendations Assessment, Development and Evaluation (GRADE) Recommendations Based on Level of Evidence

Grade	Description of Recommendation	Benefit vs. Risk	Methodologic Quality of Supporting Evidence	Implications
1A	Strong recommendation, high-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Randomized controlled trials (RCTs) without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1B	Strong recommendation, moderate-quality	Benefits clearly outweigh risk and burdens, or vice versa	RCTs with important limitations (inconsistent results, methodologic flaws, indirect, or imprecise) or exceptionally	Strong recommendation, can apply to most patients in most circumstances without

Grade	Description of Recommendation	Benefit vs. Risk	Methodologic Quality of Supporting Evidence	Implications
1C	Strong recommendation, low-quality or very-low-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Observational studies or case series	Strong recommendation but may change when higher quality evidence becomes available
2A	Weak recommendation, high-quality evidence	Benefits closely balanced with risks and burdens	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2B	Weak recommendation, moderate-quality evidence	Benefits closely balanced with risks and burdens	RCTs with important limitations (inconsistent results, methodologic flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2C	Weak recommendation, low-quality or very-low-quality evidence	Uncertainty in the estimates of benefits and risk, and burdens; Risk, benefit, and burdens may be closely balanced	Observational studies or case series	Very weak recommendations; Other alternatives may be reasonable

Note: Modified from Guyatt G, Gutterman D, Baumann MH, Addrizzo-Harris D, Hylek EM, Phillips B, et al. Grading strength of recommendations and quality of evidence in clinical guidelines: Report from an American College of Chest Physicians task force. Chest 2006;129:174-81.

Clinical Algorithm(s)

An algorithm titled "Algorithm for care and prevention of diabetic foot" is provided in the original guideline document.

Scope

Disease/Condition(s)

Diabetic foot

Guideline Category

Diagnosis

Management

Prevention

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Podiatry

Surgery

Intended Users

Advanced Practice Nurses

Physician Assistants

Physicians

Podiatrists

Guideline Objective(s)

To improve the care of patients with diabetic foot and to provide an evidence-based multidisciplinary management approach to improving the care of patients with diabetic foot

Target Population

All diabetics regardless of etiology

Interventions and Practices Considered

1. Prevention of diabetic foot ulcer (DFU)
    - Annual interval foot inspections
    - Testing for peripheral neuropathy using Semmes-Weinstein test
    - Education for patients and their families
    - Custom therapeutic footwear
    - Adequate glycemic control
2. Off-loading DFUs
    - Total contact cast (TCC) or irremovable fixed ankle walking boot
    - Removable cast walker
    - Surgical sandal or heel relief shoe
    - Pressure relieving insoles
3. Diagnostic tests
    - Probe to bone (PTB)
    - Serial plain radiograph
    - Magnetic resonance imaging (MRI)
    - Leukocyte or antigranulocyte scan with a bone scan
    - Bone culture and histology
    - Diagnostic bone biopsy
4. Wound care
    - 1- to 4-week intervals
    - Sharp débridement
    - Evaluation for infection
    - Dressing products with moist wound bed
5. Adjunctive wound therapy
    - Negative pressure therapy
    - Biologics (e.g., platelet-derived growth factor, living cellular therapy, extracellular matrix products, amnionic membrane products)
    - Hyperbaric oxygen therapy
6. Peripheral arterial disease (PAD) and the DFU
    - Measurement of ankle-brachial index (ABI)
    - Annual vascular examination
    - Pedal perfusion
    - Revascularization
    - Bypass

Note: The following practices were considered but not recommended: routine use of specialized therapeutic footwear in average-risk diabetic patients, prophylactic arterial revascularization, postoperative shoes or standard or customary footwear for off-loading plantar DFUs.

Major Outcomes Considered

- Percentage reduction in wound size
- Wound healing
- Amputation

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): Five systematic reviews were prepared to support the development of this guideline (see the "Availability of Companion Documents" field). Detailed search strategies and additional information on eligibility criteria, study identification, data collection, and study selection is available in the systematic reviews.

A Systematic Review and Meta-Analysis of Glycemic Control for the Prevention of Diabetic Foot Syndrome

Because glycemic control can be achieved by multiple interventions and in multiple settings and because its effect has been evaluated previously in multiple systematic reviews, the reviewers used an umbrella systematic review approach. Additional information on this approach is available in the systematic review.

Information Sources and Search Methods

A comprehensive literature search was conducted by an expert reference librarian with input from study investigators with experience in systematic reviews. The reviewers searched the electronic databases (MEDLINE, EMBASE, Web of Science, and the Cochrane Central Register of Controlled Trials [CENTRAL]) for systematic reviews using various combinations of controlled vocabulary supplemented by keywords for the concepts of prevention and diabetic foot. Results were limited to systematic reviews.

Two reviewers working independently identified systematic reviews eligible for further review by performing a screen of abstracts and titles. If a systematic review was deemed relevant, the manuscript was obtained and reviewed in full-text versions. The included randomized controlled trials (RCTs) from the reviewed systematic reviews were retrieved in full-text versions (all available versions of each study) for further assessment.

Eligibility Criteria

The reviewers included RCTs that enrolled patients with diabetes (of any type) without DFUs, comparing intensive glycemic control against less intensive glycemic control and evaluating the incidence of diabetic foot syndrome.

A Systematic Review and Meta-Analysis of Tests to Predict Wound Healing in Diabetic Foot

Study Selection

To be eligible for this review, studies had to be clinical trials or observational studies that used one of these eight noninvasive tests: ankle brachial index (ABI), ankle peak systolic velocity (APSV), transcutaneous oxygen measurement ($TcPO_2$), toe-brachial index (TBI), toe systolic blood pressure (TBP), microvascular oxygen saturation (SaO_2), skin perfusion pressure (SPP), and hyperspectral imaging. Studies had to report the incidence of subsequent healing of diabetic foot ulcers (DFUs) or the need for subsequent amputation. DFU patients, regardless of age, gender, ethnicity, and underlying symptoms, were included in analysis.

Literature Search

The reviewers conducted a broad search of six electronic databases, including Ovid MEDLINE In-Process & Other Non-Indexed Citations, MEDLINE, EMBASE, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, and Scopus, from database inception to October 2011. The appropriate database search terms were developed for the concept of DFUs and for the concept of each noninvasive test. The search terms were broad without language or country restrictions.

Data Abstraction

Two independent reviewers screened the study titles and abstracts using a predefined protocol. Full texts of the relevant studies were further assessed for inclusion by the same pair of reviewers. All discrepancies between the reviewers were resolved through consensus.

A Systematic Review and Meta-Analysis of Débridement Methods for Chronic Diabetic Foot Ulcers

Eligibility Criteria

Eligible studies were RCTs and controlled observational studies that enrolled patients with DFUs treated by any method of débridement and compared with any different method and reported the outcomes of interest.

Study Identification

An expert reference librarian designed and conducted the electronic search strategy with input from a study investigator with expertise in conducting systematic reviews. The reviewers searched MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Web of Science, and Scopus through October 2011. The reviewers identified additional candidate studies by review of the bibliographies of included articles and contact with experts. Controlled vocabulary supplemented with keywords was used to search for the topic of diabetic foot débridement, limited to randomized and nonrandomized studies.

Data Collection

All relevant abstracts were downloaded into an Endnote library and uploaded into an online reference management system (DistillerSR; Evidence Partners, Ottawa, ON, Canada). Reviewers working independently and in duplicate screened the abstracts for eligibility. Disagreements were automatically upgraded to the next level of screening. Full text of eligible abstracts were retrieved and screened in duplicate. Disagreements at this level were resolved by discussion and consensus.

A Systematic Review and Meta-Analysis of Adjunctive Therapies in Diabetic Foot Ulcers

Eligibility Criteria

Eligible studies were randomized trials and controlled observational studies in patients with DFUs in which a discrete list of adjunctive therapies was compared with other adjunctive therapies or with a control group and reported the outcomes of interest. The control group is a group of patients in the same study that received comprehensive wound care (dressing changes, offloading, and débridement) but did not receive the intervention being tested.

Study Identification

The search strategy was designed and conducted by an experienced reference librarian with input from the study's principal investigator. The reviewers used controlled vocabulary (e.g., Medical Subject Headings terms) with keywords to define the concepts of adjunctive therapy and diabetic foot. The reviewers conducted a comprehensive search of several databases from each database's earliest inclusive dates to October 2011. Databases included were Ovid Medline In-Process & Other Non-Indexed Citations, Ovid MEDLINE, Ovid EMBASE, Ovid Cochrane Database of Systematic Reviews, Ovid Cochrane Central Register of Controlled Trials, and Scopus. The committee identified additional candidate studies by review of the bibliographies of included articles and contact with experts.

Study Selection and Data Collection

All relevant abstracts were downloaded into an Endnote library and uploaded into an online reference management system (DistillerSR; Evidence Partners, Ottawa, ON, Canada). Reviewers working independently and in duplicate screened the abstracts for eligibility. Included abstracts were screened in full text. When reviewers disagreed on including an abstract, the full-text article was automatically reviewed. Full-text screening was also done in duplicate (see Figure 1 in the systematic review). Disagreements at this level were resolved by discussion and consensus.

A Systematic Review and Meta-Analysis of Off-Loading Methods for Diabetic Foot Ulcers

Eligibility Criteria

Eligible studies were randomized trials and controlled observational studies that enrolled patients with DFUs treated by any off-loading method compared with a different one and reported the outcomes of interest.

Study Identification

The search strategy was designed and conducted by an experienced reference librarian with input from the study's principal investigator. A comprehensive search of several databases from each database's earliest inclusive dates to October 2011 was conducted. The databases included Ovid MEDLINE In-Process & Other Non-Indexed Citations, Ovid MEDLINE, Ovid EMBASE, Ovid Cochrane Database of Systematic Reviews, Ovid Cochrane Central Register of Controlled Trials, and Scopus. The reviewers identified additional candidate studies by review of bibliography of included articles and contact with experts. Controlled vocabulary supplemented with keywords was used to search for the topic: diabetic foot off-loading, limited to randomized and nonrandomized studies.

Data Collection

All relevant abstracts were downloaded into an Endnote library and uploaded into an online reference management system (DistillerSR). Reviewers working independently and in duplicate screened the abstracts for eligibility. Disagreements were automatically upgraded to the next level of screening. Full texts of eligible abstracts were retrieved and screened in duplicate. Disagreements at this level were resolved by discussion and consensus.

Number of Source Documents

See the "Availability of Companion Documents" field for the systematic reviews.

A Systematic Review and Meta-Analysis of Glycemic Control for the Prevention of Diabetic Foot Syndrome

Of 555 full-text articles assessed for eligibility, 9 randomized controlled trials (RCTs) were published in 26 articles. See Figure 1 and the "Results" section in the systematic review for additional information.

A Systematic Review and Meta-Analysis of Tests to Predict Wound Healing in Diabetic Foot

Of 95 full-text articles assessed for eligibility, 37 met inclusion criteria and were included in the analysis. See Figure 1 and the "Results" section in the systematic review for additional information.

A Systematic Review and Meta-Analysis of Débridement Methods for Chronic Diabetic Foot Ulcers

Of 57 articles selected for full-text retrieval, 14 studies were included in analysis. See Figure 1 and the "Results" section in the systematic review for additional information.

A Systematic Review and Meta-Analysis of Adjunctive Therapies in Diabetic Foot Ulcers

Of 86 articles selected for full-text retrieval, 19 studies fulfilled inclusion criteria and were included in the analysis. See Figure 1 and the "Results" section in the systematic review for additional information.

A Systematic Review and Meta-Analysis of Off-Loading Methods for Diabetic Foot Ulcers

Of 56 articles selected for full-text retrieval, 19 studies were included in the analysis. See Figure 1 and the "Results" section in the systematic review for additional information.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

See the "Rating Scheme for the Strength of the Recommendations" field.

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): Five systematic reviews were prepared to support the development of this guideline (see the "Availability of Companion Documents" field). Additional information about all topics in the field is available in the systematic reviews.

A Systematic Review and Meta-Analysis of Glycemic Control for the Prevention of Diabetic Foot Syndrome

Data Collection and Extraction

The data from randomized controlled trials (RCTs) were extracted using a standardized, piloted, and Web-based data extraction form and working in duplicates. The reviewers abstracted data on patient demographics, baseline characteristics, study design, sample size, intervention type, fasting blood glucose and hemoglobin A_{1c} levels, and diabetic foot outcome measures. The number of events in each trial was extracted, when available, and attributed to the arm to which patients were randomized (i.e., the basis of the intention-to-treat approach).

Statistical Analysis and Data Synthesis

The reviewers estimated the relative risk (RR) and the mean difference with the associated 95% confidence interval (CI) and pooled across studies using a random-effects model, as described by DerSimonian and Kacker. The committee chose the random-effects method as primary analysis because of its conservative summary estimate and incorporation of between- and within-study variance. The analysis was repeated using the fixed-effect method, and discrepancies, if present, were outlined. To assess heterogeneity of treatment effect among trials, the reviewers used the I^2 statistic; the I^2 statistic represents the proportion of heterogeneity of treatment effect across trials that is not attributable to chance or random error. Analyses were conducted using features on RevMan version 5.1 (The Nordic Cochrane Center, Copenhagen, Denmark). The study was reported in accordance with the recommendations set forth by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) work groups.

Refer to the systematic review for information on risk of bias assessment.

A Systematic Review and Meta-Analysis of Tests to Predict Wound Healing in Diabetic Foot

Data Abstraction

Two reviewers extracted study details independently, in duplicate, using a standardized pilot-tested form.

Risk of Bias and Methodologic Quality Assessment

Considering that the included studies were either nonrandomized or randomized for purposes other than the goal of this systematic review, the committee applied the Newcastle and Ottawa quality assessment tool and evaluated representativeness of study samples, exposure ascertainment, blinding of outcome assessors, and loss to follow-up. The quality of evidence was evaluated using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methods.

Data Synthesis

To evaluate the effectiveness of each test in predicting outcomes of interest, the reviewers calculated sensitivity and specificity for each test using bivariate binominal mixed models. Developed by Reitsma et al. and later refined by Chu and Cole, the bivariate binominal mixed model assumes independent exact binomial distributions of number of true positives and number of true negatives conditional on sensitivity and specificity for each study and constructs a bivariate normal model on the logit transforms of sensitivity and specificity between studies.

The reviewers also pooled difference of test score across the included studies and constructed random-effects models using the DerSimonian and Laird method.

The reviewers assessed heterogeneity across individual studies using the I^2 statistic and Cochran Q test. Publication bias was assessed by the Begg

adjusted rank correlation test. All statistical analyses were conducted using Stata version 12 (StataCorp, College Station, Tex).

Sensitivity Analysis

The reviewers constructed multivariate nested random-effects meta-regression models across all included studies to further compare prognostic accuracy of clinical tests. The sensitivity analysis provided an alternative method to evaluate the findings.

A Systematic Review and Meta-Analysis of Débridement Methods for Chronic Diabetic Foot Ulcers

Data Collection

Data were extracted in duplicate using a standardized, piloted, Web-based form. For each study the reviewers abstracted a detailed description of baseline characteristics (main demographic characteristics, type and duration of diabetes, size, and duration of the ulcer, etc.) and interventions received (active or control) for all participants enrolled. They also collected the quality assessment and outcome data. A third reviewer compared the reviewers' data and resolved inconsistencies by referring to the full-text article.

Methodologic Quality Assessment

Two reviewers independently assessed the quality of studies included. Nonrandomized studies were evaluated using the Newcastle-Ottawa scale. The reviewers assessed outcome ascertainment, adjustment for confounders, proportion of patients lost to follow-up, and sample selection in each study. RCTs were evaluated using the Cochrane risk of bias assessment tool. The quality of evidence was evaluated using the GRADE methods.

Statistical Analysis

The committee pooled the RR and 95% CI across included studies using random-effect meta-analysis described by Der-Simonian and Laird. Between-studies heterogeneity was calculated by the I^2 statistic, which estimates the proportion of variation in results across studies that is not due to chance. Meta-analysis was completed using Comprehensive Meta-analysis (CMA) 2.2 software (Biostat Inc, Englewood, NJ).

Subgroup Analysis and Publication Bias

The reviewers did not perform subgroup analyses because of the limited number of studies that compared each intervention. Evaluation of publication bias was not feasible due to the small number of included studies.

A Systematic Review and Meta-Analysis of Adjunctive Therapies in Diabetic Foot Ulcers

Study Selection and Data Collection

For each study, at least one reviewer abstracted the following descriptive data: detailed description of baseline characteristics (main demographic characteristics, type and duration of diabetes, size and duration of the ulcer, etc.) and interventions received (active or control) for all participants enrolled. The reviewers also collected quality assessment and outcome data. Another reviewer checked the entered data for accuracy and resolved inconsistencies by referring to the full-text article.

Risk of Bias Assessment

Two reviewers independently assessed the quality of studies included. Nonrandomized studies were evaluated using the Newcastle-Ottawa scale, and the committee assessed outcome ascertainment, adjustment for confounders, proportion of patients lost to follow-up, and sample selection in each study. Randomized trials were evaluated using the Cochrane risk of bias assessment tool. Domains assessed included randomization, blinding, allocation concealment, baseline imbalances, loss to followup, and bias due to funding. The quality of evidence was evaluated using the GRADE methods.

Statistical Analysis

The committee estimated from each study Peto odds ratios (ORs) with the 95% CI due to the small number of events. Between-studies heterogeneity was calculated by the I^2 statistic, which estimates the proportion of variation in results across studies that is not due to chance. Meta-analysis was completed using Comprehensive Meta-Analysis 2.2 software (Biostat Inc, Englewood, NJ).

Data were insufficient to perform subgroup analysis. Evaluation of publication bias was not feasible due to the small number of included studies per comparison.

A Systematic Review and Meta-Analysis of Off-Loading Methods for Diabetic Foot Ulcers

Data Collection

For each study, the reviewers abstracted the following descriptive data: detailed description of baseline characteristics (e.g., main demographic characteristics, type and duration of diabetes, size and duration of the ulcer) and interventions received (active or control) for all participants enrolled. The reviewers also extracted data for outcomes and assessment of methodologic quality. Extracted data were collated by a third independent reviewer, and inconsistencies were resolved by referring to the full-text article.

Methodologic Quality and Risk of Bias Assessment

Two reviewers independently assessed the quality of studies included. Nonrandomized studies were evaluated using the Newcastle-Ottawa scale; the reviewers assessed outcome ascertainment, adjustment for confounders, proportion of patients lost to follow-up, and sample selection in each study. Randomized trials were evaluated using the Cochrane risk of bias assessment tool; domains assessed included randomization, blinding, allocation concealment, baseline imbalances, loss to follow-up data, and bias due to funding. The quality of evidence was evaluated using the GRADE methods.

Statistical Analysis

The reviewers pooled RR and 95% CI across included studies using random-effects meta-analysis described by DerSimonian and Laird. For continuous outcomes, they pooled the weighted mean difference across studies. Between-studies heterogeneity was calculated by I^2 statistic, which estimates the proportion of variation in results across studies that is not due to chance. Meta-analysis was completed using CMA version 2.2 (Biostat Inc, Englewood, NJ).

Subgroup Analysis and Publication Bias

The reviewers did not perform any subgroup analyses because of the limited amount of studies that compared each intervention. Evaluation of publication bias was not feasible because of the small number of included studies per comparison.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The Society for Vascular Surgery (SVS), American Podiatric Medical Association, and Society for Vascular Medicine selected a multidisciplinary committee consisting of vascular surgeons, podiatrists, and physicians with expertise in vascular and internal medicine. A guideline methodologist, a librarian, and a team of investigators with expertise in conducting systematic reviews and meta-analysis assisted the committee in the process. The committee communicated in person and remotely repeatedly during a period of 3 years.

Specific questions were grouped into five areas of focus (prevention, diagnosis of osteomyelitis, wound care, offloading, and peripheral arterial disease [PAD]). Each group of the committee was assigned a focus area. The committee deemed five key questions to be in need of a full systematic review and meta-analysis; the evidence in several other areas was summarized by consensus of committee members. The five systematic reviews addressed the effect of glycemic control on preventing diabetic foot ulcer (DFU), the evidence supporting different off-loading methods, adjunctive therapies, débridement, and tests to predict wound healing.

The committee used the Grading of Recommendation Assessment, Development and Evaluation (GRADE) system to rate the quality of evidence (confidence in the estimates) and to grade the strength of recommendations. This system, adopted by >70 other organizations, categorizes recommendations as *strong* Grade 1 or *weak* Grade 2 on the basis of the quality of evidence, the balance between desirable effects and undesirable ones, the values and preferences, and the resources and costs.

Grade 1 recommendations are meant to identify practices for which benefit clearly outweighs risk. These recommendations can be made by clinicians and accepted by patients with a high degree of confidence. Grade 2 recommendations are made when the benefits and risks are more closely matched and are more dependent on specific clinical scenarios. In general, physician and patient preferences play a more important role in the decision-making process in these circumstances.

In GRADE, the level of evidence to support the recommendation is divided into three categories: A (high quality), B (moderate quality), and C (low quality). Conclusions based on high-quality evidence are unlikely to change with further investigation, whereas those based on moderate-quality evidence are more likely to be affected by further scrutiny. Those based on low-quality evidence are the least supported by current data and the most likely to be subject to change in the future.

It is important to recognize that a Grade 1 recommendation can be based on low-quality (C) evidence by the effect on patient outcome. A full explanation of the GRADE system has been presented to the vascular surgery community. A consensus of the recommendations and level of evidence to support it was attained, and every recommendation in this guideline represents the unanimous opinion of the task force. Although some recommendations are Grade 2 with Level 3 data, the task force deemed it appropriate to present these as the unanimous opinion of its members regarding optimal current management. This was done with the understanding that these recommendations could change in the future but that it was unlikely that new data would emerge soon.

Rating Scheme for the Strength of the Recommendations

Grading of Recommendations Assessment, Development and Evaluation (GRADE) Recommendations Based on Level of Evidence

Grade	Description of Recommendation	Benefit vs. Risk	Methodologic Quality of Supporting Evidence	Implications
1A	Strong recommendation, high-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Randomized controlled trials (RCTs) without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1B	Strong recommendation, moderate-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	RCTs with important limitations (inconsistent results, methodologic flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1C	Strong recommendation, low-quality or very-low-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Observational studies or case series	Strong recommendation but may change when higher quality evidence becomes available
2A	Weak recommendation, high-quality evidence	Benefits closely balanced with risks and burdens	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2B	Weak recommendation, moderate-quality evidence	Benefits closely balanced with risks and burdens	RCTs with important limitations (inconsistent results, methodologic flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2C	Weak recommendation, low-quality or very-low-quality evidence	Uncertainty in the estimates of benefits and risk, and burdens; Risk, benefit, and burdens may be closely balanced	Observational studies or case series	Very weak recommendations; Other alternatives may be reasonable

Note: Modified from Guyatt G, Gutterman D, Baumann MH, Addrizzo-Harris D, Hylek EM, Phillips B, et al. Grading strength of recommendations and quality of evidence in clinical guidelines: Report from an American College of Chest Physicians task force. Chest 2006;129:174-81.

Cost Analysis

Published cost analyses were reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Independent peer review and oversight have been provided by members of the Society for Vascular Surgery (SVS) Document Oversight Committee.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Several large trials have suggested survival benefit and lower overall morbidity with tight glycemic control.
- Patients treated with negative pressure wound therapy (NPWT) healed to closure faster, experienced significantly fewer secondary amputations, and required significantly fewer home care therapy days than patients treated with advanced moist wound therapy (AMWT). Randomized controlled trials (RCTs) and studies demonstrated reduced time to complete healing of diabetic foot ulcers (DFUs), reduced duration and frequency of hospital admission, and decreased rate of amputation compared with AMWT/debridement; decreased healing time and improved quality of life; increased rate of appearance of granulation tissue; reduced length of hospitalization and reduced amputation rates with functional residual extremity; reduced time to granulation, clearing of bacterial infection, and successful granulation; and significant reduction in wound size compared with conventional therapy.

Potential Harms

- Adverse effects such as maceration, infection, or further loss of tissue should prompt a change in wound dressing modality.
- Adverse events of platelet-derived growth factor (PDGF) use were rare, and the only medication related event was local tissue sensitivity in 2%.
- Ankle-brachial index (ABI) measurements may be falsely elevated in a significant number of patients with diabetes because of medial calcinosis.
- Both open surgical bypass and endovascular revascularization can have significant short-term and long-term complications.

Qualifying Statements

Qualifying Statements

These guidelines are likely to be a "living document" that will be modified as techniques are further refined, technology develops, medical therapy improves, and new data emerge. The committee monitored the literature for new evidence emerging after the search of the five commissioned systematic reviews, and the group periodically updated guidelines as new data became available.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Clinical Algorithm

Mobile Device Resources

Patient Resources

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Hingorani A, LaMuraglia GM, Henke P, Meissner MH, Loretz L, Zinszer KM, Driver VR, Frykberg R, Carman TL, Marston W, Mills JL Sr, Murad MH. The management of diabetic foot: a clinical practice guideline by the Society for Vascular Surgery in collaboration with the American Podiatric Medical Association and the Society for Vascular Medicine. J Vasc Surg. 2016 Feb;63(2 Suppl):3S-21S. [174 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 Feb

Guideline Developer(s)

American Podiatric Medical Association - Medical Specialty Society

Society for Vascular Medicine - Medical Specialty Society

Society for Vascular Surgery - Medical Specialty Society

Source(s) of Funding

Society for Vascular Surgery (SVS)

Guideline Committee

Diabetic Foot Practice Guidelines Committee

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Financial Disclosures/Conflicts of Interest

Author conflict of interest: none

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the Journal of Vascular Surgery Web site .

Availability of Companion Documents

The following are available:

- Hasan R, Firwana B, Elraiyah T, Domecq JP, Prutsky G, Nabhan M, Prokop LJ, Henke P, Tsapas A, Montori VM. A systematic review and meta-analysis of glycemic control for the prevention of diabetic foot syndrome. J Vasc Surg. 2016 Feb;63(2 Suppl):22S-28S. Available from the Journal of Vascular Surgery Web site .
- Wang Z, Hasan R, Firwana B, Elraiyah T, Tapas A, Prokop L, Mills JL, Murad MH. A systematic review and meta-analysis of tests to predict wound healing in diabetic foot. J Vasc Surg. J Vasc Surg. 2016 Feb;63(2 Suppl):29S-36S. Available from the Journal of Vascular Surgery Web site .
- Elraiyah T, Domecq JP, Prutsky G, Tsapas A, Nabhan M, Frykberg RG, Hasan R, Firwana B, Prokop LJ, Murad MH. A systematic review and meta-analysis of débridement methods for chronic diabetic foot ulcers. J Vasc Surg. 2016 Feb;63(2 Suppl):37S-45S. Available from the Journal of Vascular Surgery Web site .
- Elraiyah T, Tapas A, Prutsky G, Domecq JP, Hasan R, Firwana B, Nabhan M, Prokop L, Hingorani A, Claus PL, Steinkraus LW, Murad MH. A systematic review and meta-analysis of adjunctive therapies in diabetic foot ulcers. J Vasc Surg. 2016 Feb;63(2 Suppl):46S-58S.

Available from the Journal of Vascular Surgery Web site .
- Elraiyah T, Prutsky G, Domecq JP, Tsapas A, Nabhan M, Frykberg RG, Firwana B, Hasan R, Prokop LJ, Murad MH. A systematic review and meta-analysis of off-loading methods for diabetic foot ulcers. J Vasc Surg. 2016 Feb;63(2 Suppl):59S-68S. Available from the Journal of Vascular Surgery Web site .

A continuing medical education (CME) activity is available from the Journal of Vascular Surgery Web site . Additionally, a clinical practice guidelines app is available from the Society for Vascular Surgery (SVS) Web site .

Patient Resources

The following is available:

- Patient resources. Vascular treatments: diabetic foot care. Available from the Society for Vascular Surgery (SVS) Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on June 8, 2016. The information was verified by the guideline developer on July 7, 2016.

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