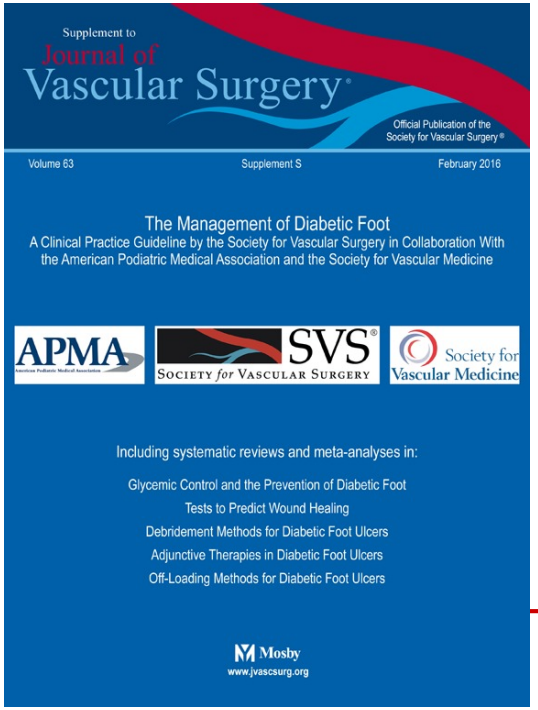
The Management of the Diabetic Foot

A Clinical Practice Guideline by the Society for Vascular Surgery in Collaboration with the American Podiatric Medical Association and the Society for Vascular Medicine



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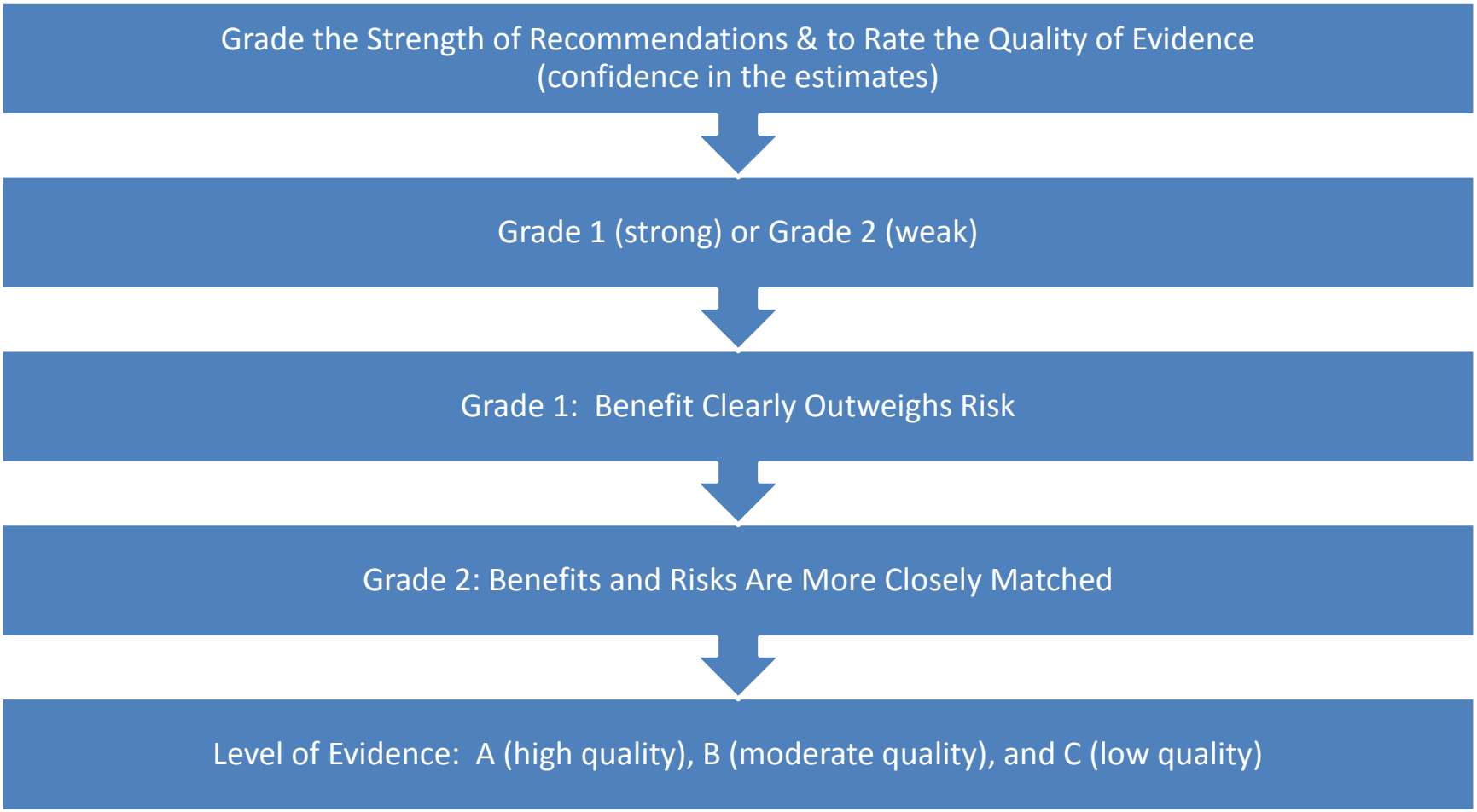
5 Areas of Focus - DFU

- Prevention of Diabetic Foot Ulceration
- Off-loading DFUs
- Wound Care for DFUs
- Diagnosis of Diabetic Foot Osteomyelitis (DFO)
- Peripheral Arterial Disease (PAD) and the DFU

Grades of Recommendation Assessment, Development, and Evaluation (GRADE)



5 Systematic Reviews and Meta-Analysis

5 key questions were deemed 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.

5 systematic reviews addressed the effect of glycemic control on preventing DFU, the evidence supporting different off-loading methods, adjunctive therapies, débridement, and tests to predict wound healing.

Numerous randomized controlled trials were identified in every systematic review; however, most of these trials were small. Therefore, searches were expanded to include nonrandomized trials as well.

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

Objective

The objective of this review was to synthesize the available randomized controlled trials (RCTs) estimating the relative efficacy and safety of intensive vs less intensive glycemic control in preventing diabetic foot syndrome.

Methods

We used the umbrella design (systematic review of systematic reviews) to identify eligible RCTs. Two reviewers determined RCT eligibility and extracted descriptive, methodologic, and diabetic foot outcome data. Random-effects meta-analysis was used to pool outcome data across studies, and the I^2 statistic was used to quantify heterogeneity.

Results

Nine RCTs enrolling 10,897 patients with type 2 diabetes were included and deemed to be at moderate risk of bias. Compared with less intensive glycemic control, intensive control (hemoglobin A_{1c}, 6%-7.5%) was associated with a significant decrease in risk of amputation (relative risk [RR], 0.65; 95% confidence interval [CI], 0.45-0.94; I^2 = 0%). Intensive control was significantly associated with slower decline in sensory vibration threshold (mean difference, −8.27; 95% CI, −9.75 to −6.79). There was no effect on other neuropathic changes (RR, 0.89; 95% CI, 0.75-1.05; I^2 = 32%) or ischemic changes (RR, 0.92; 95% CI, 0.67-1.26; I^2 = 0%). The quality of evidence is likely moderate.

Conclusions

Compared with less intensive glycemic control therapy, intensive control may decrease the risk of amputation in patients with diabetic foot syndrome. The reported risk reduction is likely overestimated because the trials were open and the decision to proceed with amputation could be influenced by glycemic control.

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

Background

This systematic review summarized the evidence on noninvasive screening tests for the prediction of wound healing and the risk of amputation in diabetic foot ulcers.

Methods

We searched 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. We pooled sensitivity, specificity, and diagnostic odds ratio (DOR) and compared test performance.

Results

Thirty-seven studies met the inclusion criteria. Eight tests were used to predict wound healing in this setting, including ankle-brachial index (ABI), ankle peak systolic velocity, transcutaneous oxygen measurement ($TcPo_2$), toe-brachial index, toe systolic blood pressure, microvascular oxygen saturation, skin perfusion pressure, and hyperspectral imaging. For the $TcPo_2$ test, the pooled DOR was 15.81 (95% confidence interval [CI], 3.36-74.45) for wound healing and 4.14 (95% CI, 2.98-5.76) for the risk of amputation. ABI was also predictive but to a lesser degree of the risk of amputations (DOR, 2.89; 95% CI, 1.65-5.05) but not of wound healing (DOR, 1.02; 95% CI, 0.40-2.64). It was not feasible to perform meta-analysis comparing the remaining tests. The overall quality of evidence was limited by the risk of bias and imprecision (wide CIs due to small sample size).

Conclusions

Several tests may predict wound healing in the setting of diabetic foot ulcer; however, most of the available evidence evaluates only $TcPo_2$ and ABI. The overall quality of the evidence is low, and further research is needed to provide higher quality comparative effectiveness evidence.

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

Background

Several methods of débridement of diabetic foot ulcers are currently used. The relative efficacy of these methods is not well established.

Methods

This systematic review and meta-analysis was conducted to find the best available evidence for the effect of débridement on diabetic foot wound outcomes. We searched MEDLINE, Embase, Cochrane Central Register of Controlled Trials, Web of Science, and Scopus through October 2011 for randomized controlled studies (RCTs) and observational comparative studies.

Results

We identified 11 RCTs and three nonrandomized studies reporting on 800 patients. The risk of bias was moderate overall. Meta-analysis of three RCTs showed that autolytic débridement significantly increased the healing rate (relative risk [RR], 1.89; 95% confidence interval [CI] 1.35-2.64). Meta-analysis of four studies (one RCT) showed that larval débridement reduced amputation (RR, 0.43; 95% CI, 0.21-0.88) but did not increase complete healing (RR, 1.27; 95% CI, 0.84-1.91). Surgical débridement was associated with shorter healing time compared with conventional wound care (one RCT). Insufficient evidence was found for comparisons between autolytic and larval débridement (one RCT), between ultrasound-guided and surgical débridement, and between hydrosurgical and surgical débridement.

Conclusions

The available literature supports the efficacy of several débridement methods, including surgical, autolytic, and larval débridement. Comparative effectiveness evidence between these methods and supportive evidence for other methods is of low quality due to methodologic limitations and imprecision. Hence, the choice of débridement method at the present time should be based on the available expertise, patient preferences, the clinical context and cost.

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

Background

Multiple adjunctive therapies have been proposed to accelerate wound healing in patients with diabetes and foot ulcers. The aim of this systematic review is to summarize the best available evidence supporting the use of hyperbaric oxygen therapy (HBOT), arterial pump devices, and pharmacologic agents (pentoxifylline, cilostazol, and iloprost) in this setting.

Methods

We searched MEDLINE, Embase, Cochrane Central Register of Controlled Trials, Web of Science, and Scopus through October 2011. Pairs of independent reviewers selected studies and extracted data. Predefined outcomes of interest were complete wound healing and amputation.

Results

We identified 18 interventional studies; of which 9 were randomized, enrolling 1526 patients. The risk of bias in the included studies was moderate. In multiple randomized trials, the addition of HBOT to conventional therapy (wound care and offloading) was associated with increased healing rate (Peto odds ratio, 14.25; 95% confidence interval, 7.08-28.68) and reduced major amputation rate (odds ratio, 0.30; 95% confidence interval, 0.10-0.89), compared with conventional therapy alone. In one small trial, arterial pump devices had a favorable effect on complete healing compared with HBOT and in another small trial compared with placebo devices. Neither iloprost nor pentoxifylline had a significant effect on amputation rate compared with conventional therapy. No comparative studies were identified for cilostazol in diabetic foot ulcers.

Conclusions

There is low- to moderate-quality evidence supporting the use of HBOT as an adjunctive therapy to enhance diabetic foot ulcer healing and potentially prevent amputation. However, there are only sparse data regarding the efficacy of arterial pump devices and pharmacologic interventions.

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

Background

Increased plantar foot pressure is one of several key factors that lead to diabetic foot ulcers. Multiple methods have been proposed to relieve this pressure and thus enhance wound healing and potentially prevent relapse. We aimed in this systematic review to find the best available evidence for off-loading methods.

Methods

We searched MEDLINE, Embase, Cochrane CENTRAL, Web of Science, and Scopus through October 2011. Pairs of independent reviewers selected studies and extracted data. Predefined outcomes of interest included complete wound healing, time to complete wound healing, amputation, infection, and relapse rates.

Results

We identified 19 interventional studies, of which 13 were randomized controlled trials, including data from 1605 patients with diabetic foot ulcers using an off-loading method. The risk of bias in the included studies was moderate. This analysis demonstrated improved wound healing with total contact casting over removable cast walker, therapeutic shoes, and conventional therapy. There was no advantage of irremovable cast walkers over total contact casting. There was improved healing with half-shoe compared with conventional wound care. Therapeutic shoes and insoles reduced relapse rate in comparison with regular footwear. Data were sparse regarding other off-loading methods.

Conclusions

Although based on low-quality evidence (ie, evidence warranting lower certainty), benefits are demonstrated for use of total contact casting and irremovable cast walkers in the treatment of diabetic foot ulcers. Reduced relapse rate is demonstrated with various therapeutic shoes and insoles in comparison with regular footwear.

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Prevention of Diabetic Foot Ulceration

Recommendation 1: We recommend 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)

Suggested Frequency for Follow-up Evaluation

Category	Risk Profile	Evaluation Frequency
0	Normal	Annual
1	Peripheral Neuropathy	Semiannual
2	Neuropathy with Deformity and/or PAD	Quarterly
3	Previous Ulcer or Amputation	Monthly or Quarterly

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Prevention of Diabetic Foot Ulceration

Recommendation 2: We recommend that foot examination include testing for peripheral neuropathy using the Semmes-Weinstein test (Grade 1B)

Prevention of Diabetic Foot Ulceration

Recommendation 3: We recommend education of the patients and their families about preventive foot care (Grade 1C)

Prevention of Diabetic Foot Ulceration

Recommendation 4:

a. We suggest against the routine use of specialized therapeutic footwear in average-risk diabetic patients (Grade 2C)

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

Prevention of Diabetic Foot Ulceration

Recommendation 5: We suggest adequate glycemic control (hemoglobin A1c < 7% with strategies to minimize hypoglycemia) to reduce the incidence of diabetic foot ulcers (DFUs) and infections, with subsequent risk of amputation (Grade 2B)

Prevention of Diabetic Foot Ulceration

Recommendation 6: We recommend against prophylactic arterial revascularization to prevent DFU (Grade 1C)

Off-loading DFUs

Recommendation 1: In patients with plantar DFU, we recommend offloading with a total contact cast (TCC) or irremovable fixed ankle walking boot (Grade 1B)

Off-loading DFUs

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

Off-loading DFUs

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

Off-loading DFUs

Recommendation 4: In high-risk patients with healed DFU (including those with a prior history of DFU, partial foot amputation, or Charcot foot), we recommend 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)

Recommendation 1: In patients with a diabetic foot infection (DFI) with an open wound, we suggest doing a probe to bone (PTB) test to aid in diagnosis (Grade 2C)

Diagnosis of DFO

Recommendation 2: In all patients presenting with a new DFI, we suggest 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)

Diagnosis of DFO

Recommendation 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, we recommend 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 of if the plain film is not useful (Grade 1B)

Diagnosis of DFO

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

Diagnosis of DFO

Recommendation 5: In patients at high risk for DFO, we recommend 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, we recommend sending a sample for culture and histology (Grade 1C)

Diagnosis of DFO

Recommendation 6: For patients not undergoing bone débridement, we suggest 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

Recommendation 1: We recommend 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)

Recommendation 1.1: We recommend 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)

Recommendation 1.2: We suggest that treatment of DFIs should follow the most current guidelines published by the Infectious Diseases Society of America (IDSA) (Ungraded)

Wound Care for DFUs

Recommendation 2: We recommend 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)

Wound Care for DFUs

Recommendation 3: We recommend sharp débridement of all devitalized tissue and surrounding callus material from diabetic foot ulcerations at 1- to 4-week intervals (Grade 1B)

Wound Care for DFUs

Recommendation 4: Considering lack of evidence for superiority of any given débridement technique, we suggest 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)

Wound Care for DFUs

Recommendation 5: For DFUs that fail to demonstrate improvement (>50% wound area reduction) after a minimum of 4 weeks of standard wound therapy, we recommend 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)

Wound Care for DFUs

Recommendation 6: We suggest 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)

Wound Care for DFUs

Recommendation 7: We suggest consideration of the use of PDGF (becaplermin) for the treatment of DFUs that are recalcitrant to standard therapy (Grade 2B)

Wound Care for DFUs

Recommendation 8: We suggest 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)

Wound Care for DFUs

Recommendation 9: We suggest 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)

Wound Care for DFUs

Recommendation 10: In patients with DFU who have adequate perfusion that fails to respond two 4 to 6 weeks of conservative management, we suggest hyperbaric oxygen therapy (Grade 2B)

Peripheral Arterial Disease (PAD) and the DFU

Recommendation 1.1: We suggest that patients with diabetes have ankle-brachial index (ABI) measurements performed when they reach 50 years of age (Grade 2C).

Peripheral Arterial Disease (PAD) and the DFU

Recommendation 1.2: We suggest 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 (eg, coronary, cerebral, or renal) have an annular vascular examination of the lower extremities and feet including ABI and toe pressures (Grade 2C)

PAD and the DFU

Recommendation 2: We recommend 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 (TcPO2) annually (Grade 1B)

PAD and the DFU

Recommendation 3: In patients with DFU with PAD, we recommend revascularization by either surgical bypass or endovascular therapy (Grade 1B)

PAD and the DFU

Recommendation 3 *(continued)*: 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.

PAD and the DFU

Recommendation 3 *(continued)*: 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.

PAD and the DFU

Recommendation 3 *(continued)*: In functional patients with long-segment occlusive disease and a good autologous conduit, bypass is likely to be preferable.

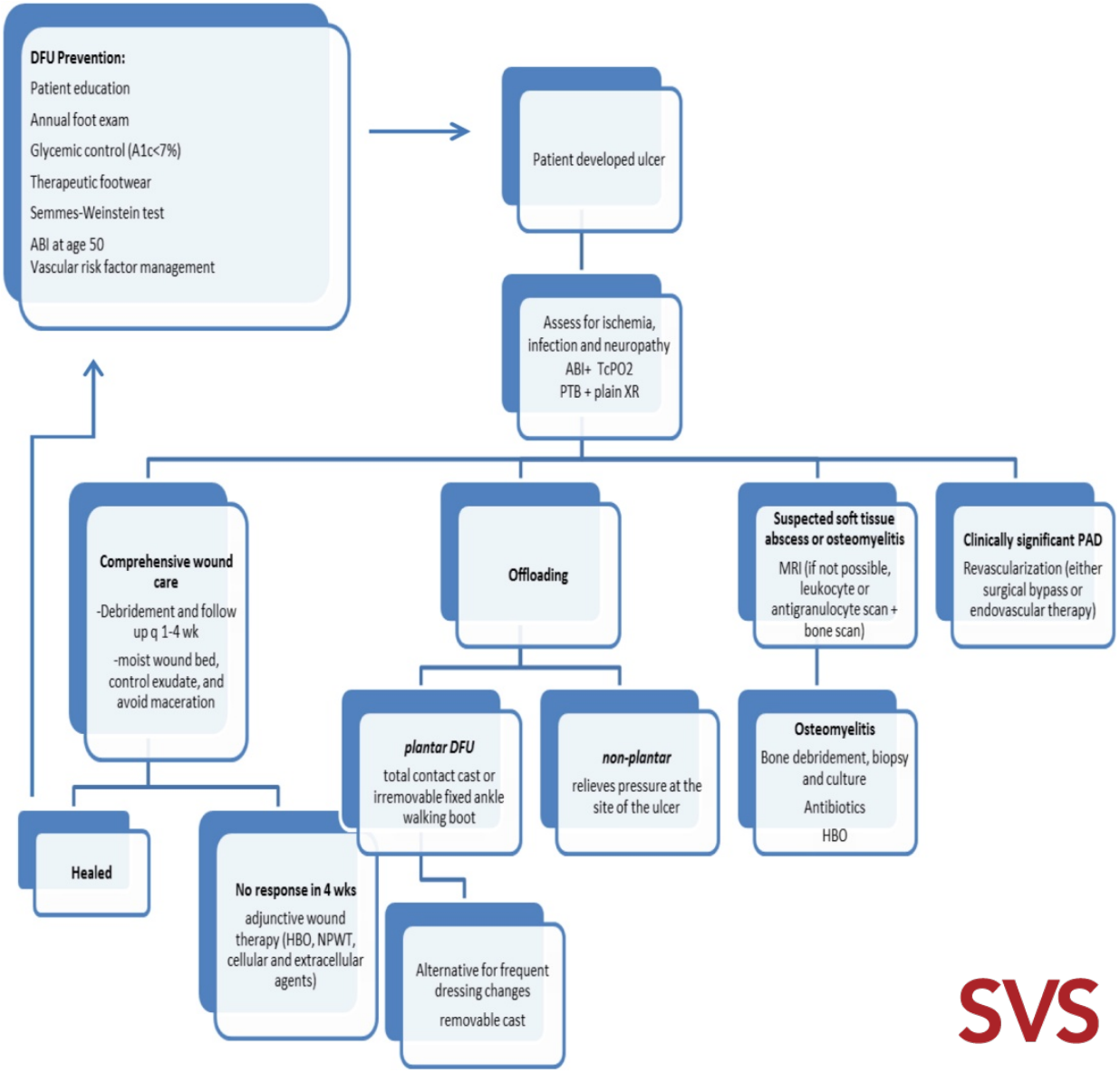
PAD and the DFU

Recommendation 3 *(continued)*: In the setting of tissue loss and diabetes, prosthetic bypass is inferior to bypass with vein conduit.

PAD and the DFU

Recommendation 3 *(continued)*: 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.

Overview of Assessment and Treatment of Diabetic Foot Ulcers



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