Management of diabetic foot ulcers

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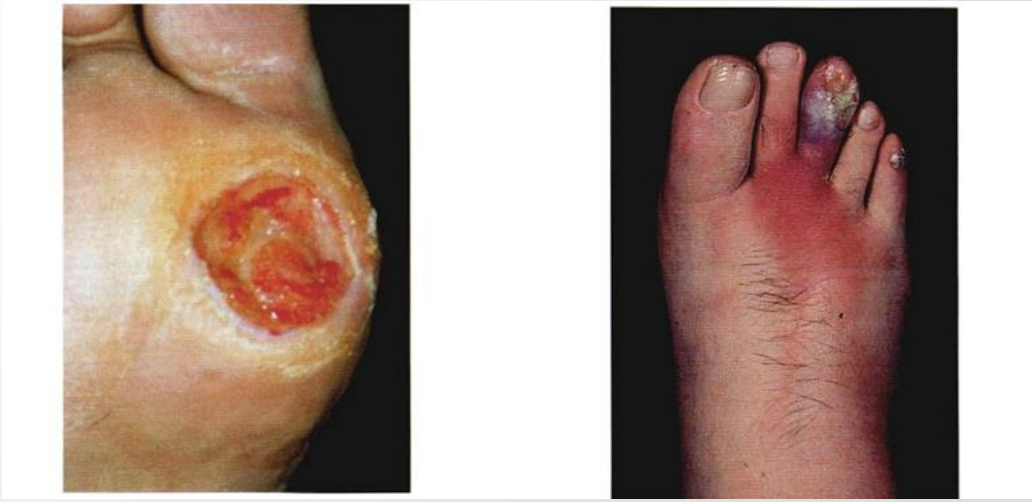
2025



- IWGDF/IDSA Guidelines on the Diagnosis and Treatment of Diabetes-related Foot Infections (IWGDF/IDSA 2023)
- Retinopathy, Neuropathy, and Foot Care: Standards of Care in Diabetes—2025
- Clinical manifestations, diagnosis, and management of diabetic infections of the lower extremities2025 UpToDate
- Approach to imaging modalities in the setting of suspected nonvertebral osteomyelitis, 2025 UpToDate
- Management of diabetic foot ulcers,2025 UpToDate
- Overview of peripheral artery disease in patients with diabetes mellitus, 2025 UpToDate

- Screening
- Severity of wounds
- Indication of hospitalization
- Antibiotic selection
- Surgical consultation
- Vascular surgery consultation
- Off loading
- Debridement
- Dressing
- Adjuvant therapies
- Follow-up

غربالگری

معاینات و فواصل انجام

تشخیص افتراقی علایم نوروپاتی

درمان نوروپاتی دیابتی

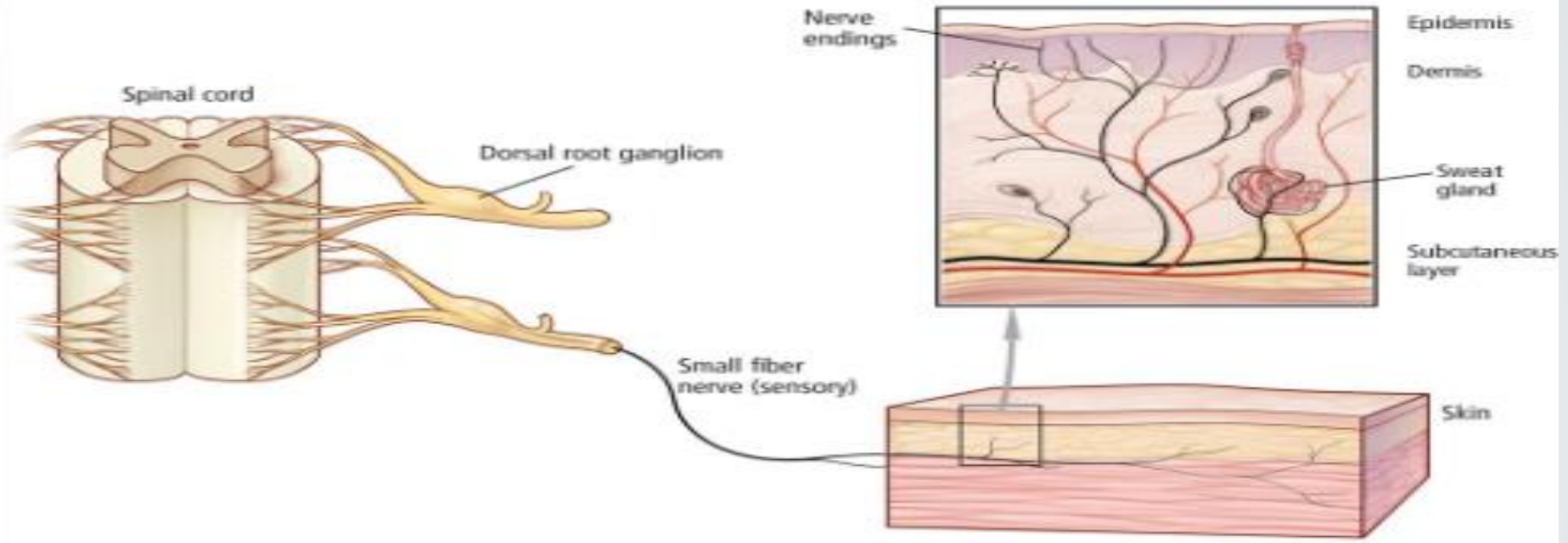
غربالگری PAD

- All people with diabetes should be assessed for diabetic peripheral neuropathy starting at diagnosis of type 2 diabetes and 5 years after the diagnosis of type 1 diabetes and at least annually thereafter.

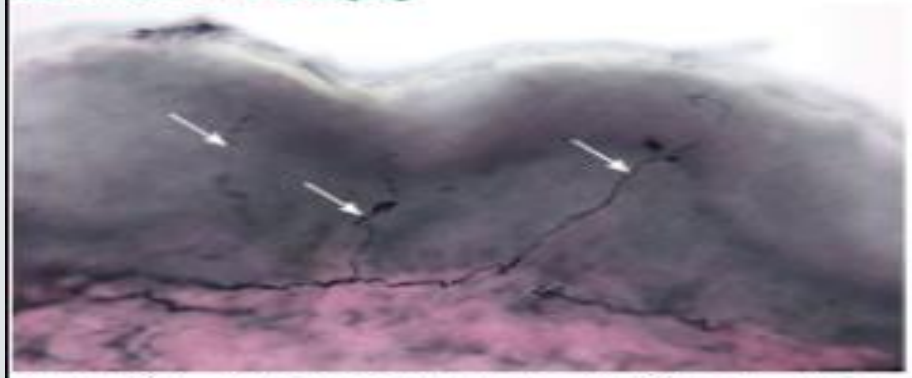
- Assessment for distal symmetric polyneuropathy should include a careful history and assessment of either temperature or pinprick sensation (**small**-fiber function) and vibration sensation using a 128-Hz tuning fork (for **large**-fiber function).
- All people with diabetes should have annual 10-g mono flament testing to identify feet at risk for ulceration and amputation.

Small fiber neuropathy affects sensory nerves

Small fiber neuropathy is a major cause of pain in the hands and feet, especially in the elderly. Diabetes mellitus is the most common identifiable cause, but there are many others. The nerve fibers affected are small-diameter myelinated A-delta fibers and unmyelinated C fibers, which mediate pain, thermal sensation, and autonomic function. Large fibers that innervate muscles are not affected. Skin biopsy may show a paucity of nerve fibers. Quantitative sudomotor axon reflex testing may show a lack of sweating in response to acetylcholine.

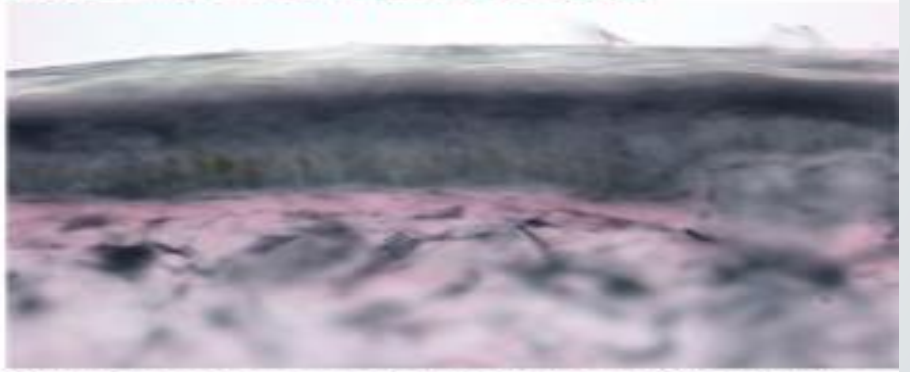


Normal skin biopsy



Normal innervation with small nerve fibers seen in the epidermis (arrows). Skin biopsy specimens with protein gene product 9.5 immunostaining.

Small fiber neuropathy biopsy



A specimen from a patient with small fiber neuropathy shows denervation, with no small nerve fibers seen in the epidermis.

Tavee J, Zhou L. Small fiber neuropathy: a burning problem. Cleve Clin J Med 2009; 76(5):297–305. doi:10.3949/ccjm.76a.08070

- Screening can include asking about orthostatic dizziness, syncope, early sa tiety, erectile dysfunction, changes in sweating patterns, or dry cracked skin in the extremities.
- Signs of autonomic neuropathy include orthostatic hypotension, a resting tachycardia, or evidence of peripheral dryness or cracking of skin

- Cardiovascular Autonomic Neuropathy CAN is associated with mortality independent of other cardiovascular risk factors . In its early stages, CAN may be completely asymptomatic and detected only by decreased heart rate variability with deep breathing. **Advanced disease** may be associated with resting tachycardia (>100 bpm) and orthostatic hypotension.

- hypotension (a fall in systolic or diastolic blood pressure by >20 mmHg or >10 mmHg, respectively, upon standing without an appropriate increase in heart rate). CAN treatment is generally focused on alleviating symptoms.

Categories of risk for foot complications

Risk category	Definition	Treatment recommendations	Suggested follow-up
0	No LOPS, no PAD, no deformity	▪ Patient education including advice on appropriate footwear.	Annually (by generalist and/or specialist)
1	LOPS ± deformity	▪ Consider prescriptive or accommodative footwear. ▪ Consider prophylactic surgery if deformity is not able to be safely accommodated in shoes. Continue patient education.	Every three to six months (by generalist or specialist)
2	PAD ± LOPS	▪ Consider prescriptive or accommodative footwear. ▪ Consider vascular consultation for combined follow-up.	Every two to three months (by specialist)
3	History of ulcer or amputation	▪ Same as category 1. ▪ Consider vascular consultation for combined follow-up if PAD present.	Every one to two months (by specialist)

- Assess and treat pain related to diabetic peripheral neuropathy and symptoms of autonomic neuropathy to improve quality of life.

- In all people with diabetes and DPN,causes of neuropathy other than diabetes should be considered, including toxins (e.g., alcohol), neurotoxic medications (e.g., chemotherapy), vitamin B12 defciency, hypothyroidism, kidney disease, malignancies (e.g., multiple myelomaneuropathy, **inherited** neuropathies, an vasculitis **.**

- Gabapentinoids, serotonin norepinephrine reuptake inhibitors, tricyclic antidepressants, and sodium channel blockers are recommended as initial pharmacologic treatment for neuropathic pain in diabetes.
- Opioids, including tramadol and ta pentadol, should not be used for neuropathic pain treatment in diabe tes given the potential for adverse events.

- Capsaicin has received FDA approval for treatment of pain in DPN using an 8% patch, with one high-quality study reported.
- One medium-quality study of0.075% capsaicin cream has been reported. In individuals with contraindications to oral pharmacotherapy or who prefer topical treatments, the use of topical capsaicin can be considered.

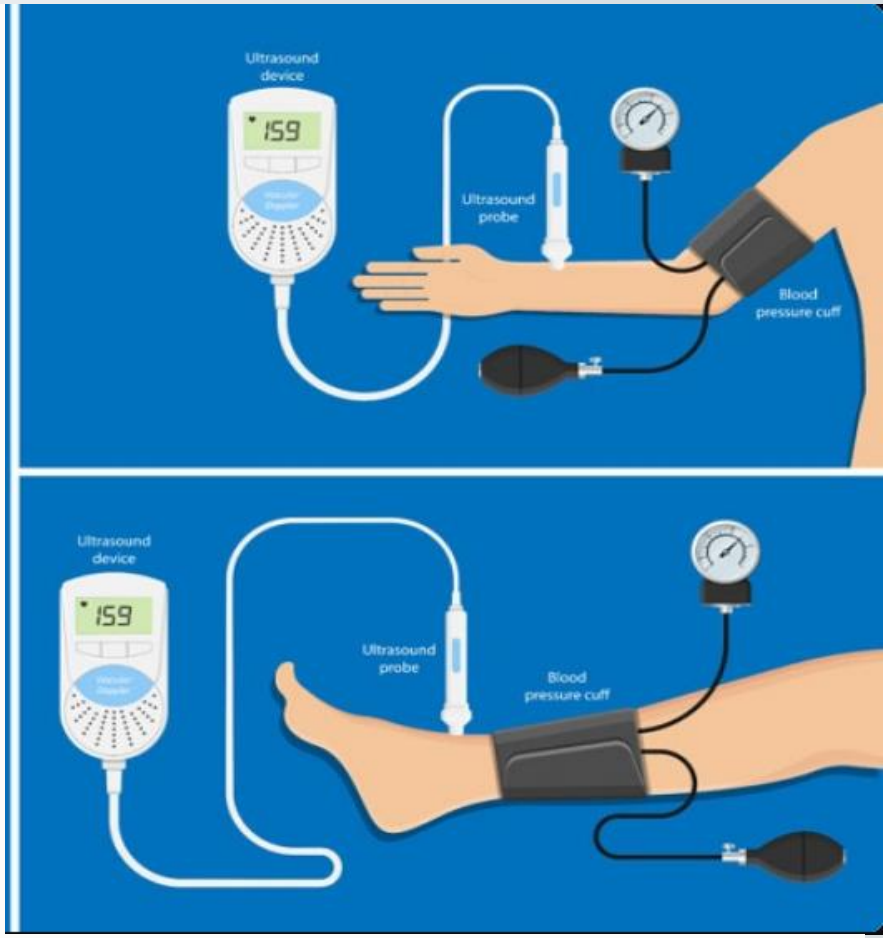
گاباپنتینوئیدها	- گاباپنتین (Neurontin)	مهار کانال‌های کلسیم و کاهش ترشح نوروترنسمیترهای تحریکی	معمولا به عنوان خط اول درمان استفاده می‌شود؛ عوارض جانبی شامل خواب‌آلودگی و سرگیجه است.
	- پرگابالین (Lyrica)		اثربخشی بالا در کاهش درد نوروپاتیک؛ عوارض مشابه گاباپنتین.
مهارکننده‌های بازجذب سروتونین و نوراپی‌نفرین (SNRIs)	- دولوکستین (Cymbalta)	افزایش سطح سروتونین و نوراپی‌نفرین در مغز، تنظیم احساس درد	علاوه بر کاهش درد، به بهبود خلق‌وخو نیز کمک می‌کند؛ عوارض شامل تهوع و خشکی دهان است.
	- ونلافاکسین (Effexor)		ممکن است در دوزهای بالاتر مؤثرتر باشد؛ نیاز به تنظیم دوز تدریجی دارد.
ضدافسردگی‌های سه‌حلقه‌ای (TCAs)	- آمی‌تریپتیلین	مسدود کردن بازجذب سروتونین و نوراپی‌نفرین، افزایش دسترسی آن‌ها در فضای سیناپسی	مؤثر اما با عوارض جانبی بیشتر مانند خواب‌آلودگی، خشکی دهان و افت فشار خون وضعیتی.
	- نورتریپتیلین (Pamelor)		نسبت به آمی‌تریپتیلین عوارض کمتری دارد اما همچنان نیاز به نظارت دقیق دارد.
مسدودکننده‌های کانال سدیم	- کاربامازپین	مهار کانال‌های سدیم، تثبیت غشاهای عصبی و جلوگیری از انتشار	بیشتر برای نورالژی سه‌قلو استفاده می‌شود؛ ممکن است عوارضی مانند

peripheral artery disease

Screening

- The American Diabetes Association has recommended that a screening ABI should be performed in patients >50 years of age with DM and, if normal, should be repeated every five years .
- The guideline further recommends consideration of screening ABI in patients with DM age <50 years with other PAD risk factors, such as **smoking**, **hypertension**, **hyperlipidemia**, **or diabetes duration >10 years**

- Initial screening for peripheral arterial disease (PAD) should include assessment of lower-extremity pulses, capillary refll time, rubor on depen dency, pallor on elevation, and venous flling time.
- Individuals with a history of leg fatigue, claudication, and rest pain relieved with dependency or de creased or absent pedal pulses should be referred for ankle-brachial index with toe pressures and for further vascular assessment as appropriate.



شکل زیر نمایانگر مقادیر مختلف ABI و تفسیر آن‌هاست:

مقدار ABI	وضعیت
1.4 - 1.0	طبیعی
1.0 - 0.9	احتمال PAD خفیف
0.9 - 0.8	PAD خفیف
0.7 - 0.5	PAD متوسط
0.5 >	PAD شدید (احتمال زخم یا گانگرن)

محدودیت‌ها

ABI ممکن است در بیماران مبتلا به کلسیفیکاسیون شریانی (تصلب شرایین) یا در افرادی که دیابت دارند، غیرقابل اعتماد باشد زیرا شریان‌های سفت ممکن است فشار کاذب را افزایش دهند [2] [5] . همچنین، عدم وجود استانداردسازی پروتکل‌ها و نیاز به اپراتورهای ماهر می‌تواند بر دقت نتایج تأثیر بگذارد [2] [3] .

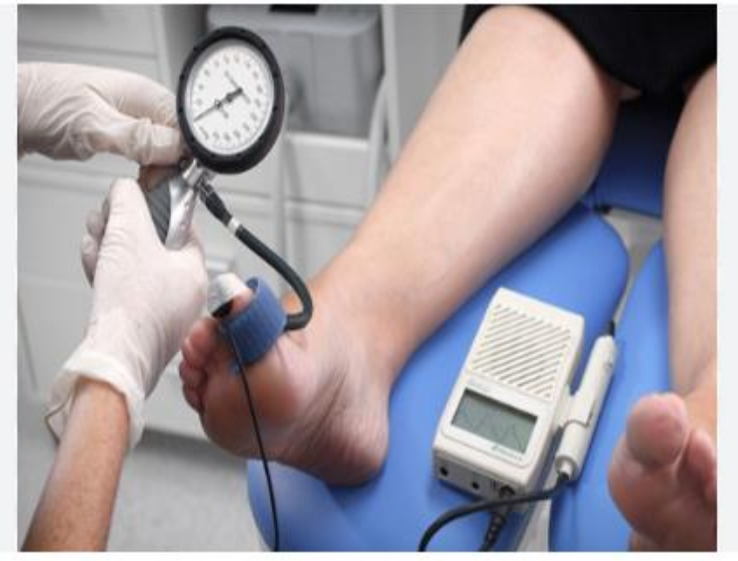
روش انجام تست ABI

1. آماده‌سازی: بیمار باید در حالت خوابیده قرار گیرد و هیچ بخشی از بدن او نباید از لبه تخت آویزان باشد.
2. اندازه‌گیری فشار خون: از یک کاف فشار خون و یک پروب داپلر برای اندازه‌گیری فشار خون سیستولیک در مچ پا و بازو استفاده می‌شود.
3. محاسبه ABI: نسبت فشار خون سیستولیک در مچ پا به فشار خون سیستولیک در بازو محاسبه می‌شود:

$$\frac{{}_{\text{Leg}}P}{{}_{\text{Arm}}P} = \text{ABI}$$

که در آن ${}_{\text{Leg}}P$ فشار خون مچ پا و ${}_{\text{Arm}}P$ فشار خون بازو است.

- While ankle brachial indices will be calculated, they should be interpreted carefully, as they are known to be inaccurate in people with diabetes due to noncompressible vessels.
- Toe systolic blood pressure tends to be more accurate. Toe systolic blood pressure <30 mmHg is suggestive of PAD and an inability to heal foot ulcerations. Individuals with abnormal pulse volume recording tracings and toe pressures <30 mmHg with foot ulcers should be referred for immediate vascular evaluation. Due to the high prevalence of PAD in people with diabetes.

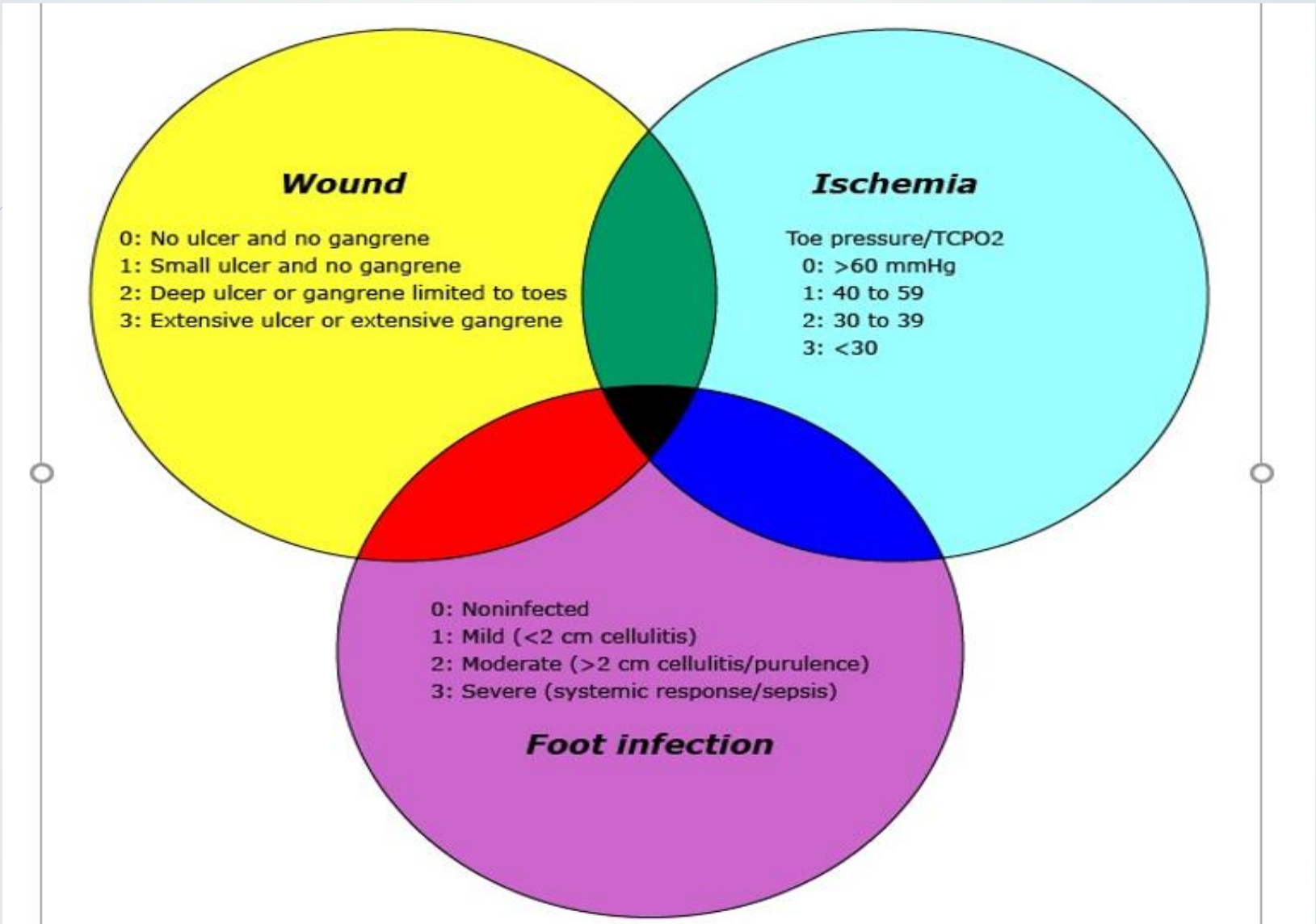


MANAGEMENT

- **Smoking cessation**
- **Lipid-lowering therapy**
- Thus, we suggest that all patients with PAD and DM should be treated with the maximum tolerated dose of a high-intensity statin (eg, rosuvastatin 20 to 40 mg, atorvastatin 40 to 80 mg daily)
- **Antithrombotic therapy:**Long term antithrombotic therapy using aspirin (75 to 100 mg/day) or clopidogrel (75 mg daily) is **recommended** for all patients with PAD, including those with DM, to reduce the risk of overall cardiovascular events and death unless contraindications exist.
- We do not routinely recommended dual antiplatelet therapy (DAPT) for patients with DM and PAD, unless there is a clear indication such as coronary or peripheral arterial intervention.

- Glycemic control
- Antihypertensive therapy
- Diet and exercise

شدت زخم



The conceptual diagram illustrates the interaction between the main factors that contribute to tissue loss. This scheme is appropriate for any patient with a chronic wound/tissue loss. The clinician should ask, "Which factor or combination of factors contributes the most to the pathophysiology of the wound? Ischemia? Infection? Wound extent?" Early assessment helps determine initial wound management priorities, but frequent reassessment is important since the wound environment is dynamic, and the balance toward one or another factor can change.

Clinical classification of infection, definitions	IWGDF/IDSA classification
No systemic or local symptoms or signs of infection	1/Uninfected
Infected: At least two of these items are present: • Local swelling or induration • Erythema >0.5 but <2 cm[b] around the wound • Local tenderness or pain • Local increased warmth • Purulent discharge	2/Mild
And, no other cause of an inflammatory response of the skin (e.g., trauma, gout, acute charcot neuro-arthropathy, fracture, thrombosis, or venous stasis)	3/Moderate
Infection with no systemic manifestations and involving: • Erythema extending ≥2 cm[b] from the wound margin, *and/or* • Tissue deeper than skin and subcutaneous tissues (e.g., tendon, muscle, joint, and bone)[c]	

Infection involving bone (osteomyelitis)	Add "(O)"
Any foot infection with associated systemic manifestations (of the systemic inflammatory response syndrome [SIRS]), as manifested by ≥2 of the following: • Temperature, > 38°C or <36°C • Heart rate, > 90 beats/min • Respiratory rate, > 20 breaths/min, *or* PaCO2 < 4.3 kPa (32 mmHg) • White blood cell count >12,000/mm^3, *or* < 4G/L, *or* >10% immature (band) forms	4/Severe
- Infection involving bone (osteomyelitis)	Add "(O)"

The presence of clinically significant foot ischaemia makes both diagnosis and treatment of infection considerably more difficult. [a]infection refers to any part of the foot. [b]in any direction, from the rim of the wound.

[c]if osteomyelitis is demonstrated in the absence of ≥2 signs/symptoms of local or systemic inflammation, classify the foot as either grade 3(O) (if <2 SIRS criteria) or grade 4(O) if ≥2 SIRS criteria) (see text).

A. Findings suggesting a more serious diabetes-related foot infection

Wound specific	
Wound	Penetrates to subcutaneous tissues (e.g., fascia, tendon, muscle, joint, or bone)
Cellulitis	Extensive (>2 cm), distant from ulceration, or rapidly progressive (including lymphangitis)
Local signs/symptoms	Severe inflammation or induration, crepitus, bullae, discolouration, necrosis or gangrene, ecchymoses or petechiae, and new anaesthesia or localised pain
General	
Presentation	Acute onset/worsening or rapidly progressive
Systemic	Fever, chills, hypotension, confusion, and volume depletion
Laboratory tests	Leucocytosis highly elevated C-reactive protein, or erythrocyte sedimentation rate, severe or worsening hyperglycemia, acidosis, new/worsening azotaemia and electrolyte abnormalities tests
Complicating features	Presence of a foreign body (accidently or surgically implanted), puncture wound, deep abscess, arterial or venous insufficiency, lymphoedema, immunosuppressive illness or treatment, acute kidney injury
Failing treatment	Progression while on apparently appropriate antibiotic and supportive therapy

Osteomyelitis

- In a person with diabetes, consider using a combination of probe-to-bone test, plain X-rays, and ESR, or CRP, or PCT as the initial studies to diagnose osteomyelitis of the foot. (Conditional; Low).
- Perform magnetic resonance imaging (MRI) when the diagnosis of diabetes-related osteomyelitis of the foot remains in doubt despite clinical, plain X-rays and laboratory findings. (Strong; Moderate).
- Consider using positron emission tomography (PET), leucocyte scintigraphy, or single photon emission computed tomography (SPECT) as an **alternative to MRI** for the diagnosis of diabetes-related osteomyelitis of the foot. (Conditional; Low).

likelihood of osteomyelitis

- following factors increase the likelihood of osteomyelitis:

- Grossly visible bone or ability to probe to bone
- Ulcer size larger than 2 cm^2
- Ulcer duration longer than one to two weeks
- Erythrocyte sedimentation rate (ESR) >70 mm/hour

تشخیص افتراقی

DIFFERENTIAL DIAGNOSIS

- Charcot arthropathy – Onset of Charcot arthropathy may be acute or subacute.
- Patients characteristically present with sudden onset of unilateral warmth, **redness**, and **edema** over the **foot or ankle**, often **with history of minor trauma .**
- The a infected foot may be discernably warmer than the contralateral foot.
- Alternatively, in some cases, patients present with a slowly progressing arthropathy with insidious onset of swelling over months or years.
- Occasionally, recurrent acute attacks may occur. The most frequently involved joints are the tarsus and tarsometatarsal joints, followed by the metatarsophalangeal joints and the ankle

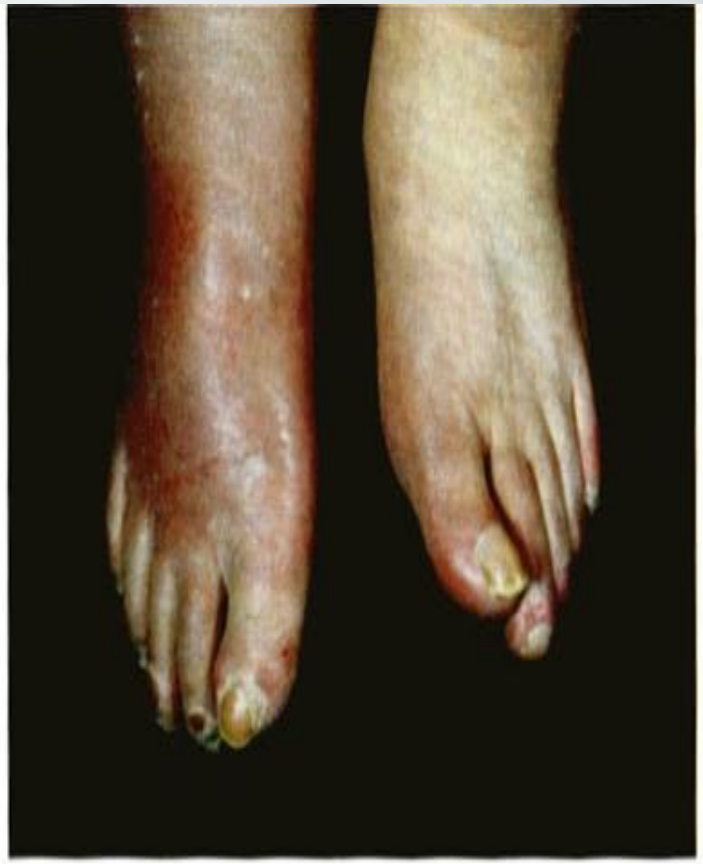


Fig. 3.15 Unilateral oedema and erythema in acute onset Charcot's osteoarthropathy.

DIFFERENTIAL DIAGNOSIS

- **Venous stasis**.
- **Deep vein thrombosis**.
- **Crystal-associated arthritis**.
- **Fracture and other trauma-associated injuries**.
- Usually, these can be distinguished from infection based on clinical history, physical exam, and imaging finndings.
- However, infection may coexist with other processes, and empiric antimicrobial therapy may be warranted in some cases when the diagnosis is uncertain.

اندیکاسیون بستری

- Consider hospitalising all persons with diabetes and a foot infection who have either a severe foot infection as classified by the IWGDF/IDSA classification or a moderate infection which is associated with key relevant morbidities. (Conditional; Low).
- Assess inflammatory serum biomarkers such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), or procalcitonin (PCT) in a person with diabetes and a possible infected foot ulcer for whom the clinical examination is diagnostically equivocal or uninterpretable. (Best Practice Statement).

B. Factors that should lead to considering hospitalisation
Severe infection (see findings suggesting a more serious diabetes-related foot infection above)
Metabolic or haemodynamic instability
Intravenous therapy needed (and not available/appropriate as an outpatient)
Diagnostic tests needed that are not available as an outpatient
Severe foot ischaemia is present
Surgical procedures (more than minor) required
Failure of outpatient management
Need for more complex dressing changes than patient/caregivers can provide
Need for careful, continuous observation

کشت از زخم

Obtaining samples for culture

- Wound culture is often helpful in cases of moderate or severe infection and when the concern for multidrug-resistant organisms is high.
- Ideally, samples for culture should be obtained prior to the initiation of empiric antibiotics. However, in cases of systemic toxicity or limb-threatening infections, antibiotic therapy should not be withheld before surgical cultures are obtained.
- The preferred clinical specimens for reliable culture include aspirate from an abscess or curettage from the ulcer base following supercial debridement of necrotic tissue.
- Organisms cultured from superficial swabs are not reliable for predicting the pathogens responsible for deeper infection .

Obtaining samples for culture

- In the setting of osteomyelitis, bone biopsy is the preferred method of sample collection for culture.
- If performed percutaneously, sampling through uninvolved tissue under radiographic guidance is preferred.
- Although sinus tract cultures may be of some use for prediction of osteomyelitis if *S. aureus* or *Salmonella* species are identified, in general, such cultures are not worthwhile .
- Samples should be sent for Gram stain and both aerobic and anaerobic bacterial cultures.

- If infection in a clinically stable patient fails to respond to more than one antibiotic course, some favor discontinuing antimicrobial therapy for a few days (eg, 48 to 72 hours) in order to obtain a biopsy for culture of antibiotics and optimize the fyield .
- In general, this is a safe and reasonable approach, although deep cultures are often positive even if therapy is continued up to the time of debridement.

تصویر برداری

Table 3. Features characteristic of diabetes-related osteomyelitis of the foot on plain X-rays.

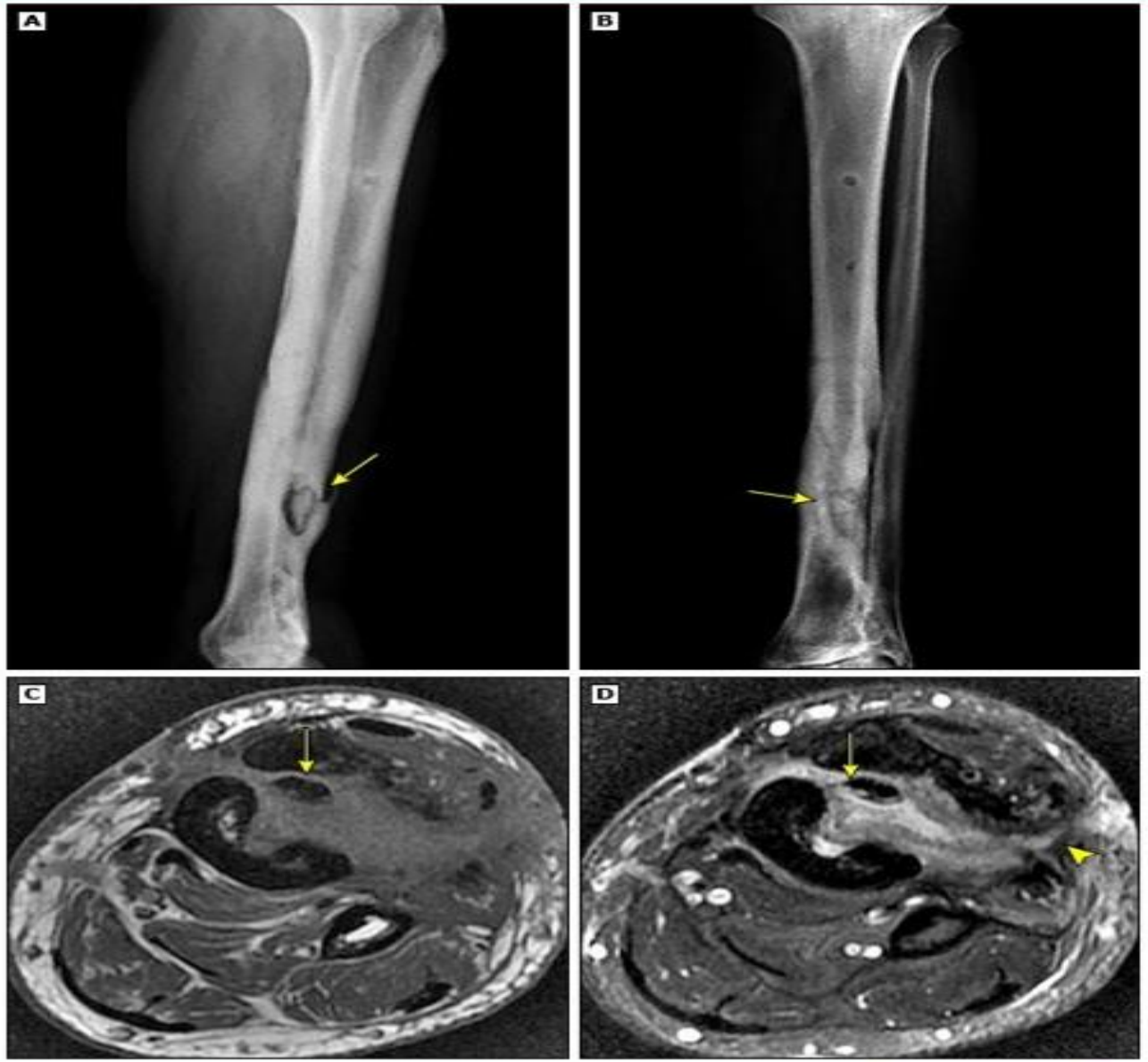
- New or evollistaving radiographic features[a] on serial radiographs,[b] including:
  - Loss of bone cortex, with bony erosion or demineralisation
  - Focal loss of trlistaabecular pattern or marrow radiolucency (demineralisation)
  - Periosteal reaction or elevation
- Bone sclerosis, with or without erosion
- Abnormal soft tissue density in the subcutaneous fat, or gas density, extending from skin towards underlying bone, suggesting a deep ulcer or sinus tract
- Presence of sequestruma: devitalised bone with radiodense appearance separated from normal bone
- Presence of involucrum[a]: layer of new bone growth outside previously existing bone resulting, and originating, from stripping off the periosteum
- Presence of cloacae[a]: opening in the involucrum or cortex through which sequestrum or granulation tissue may discharge

اصطلاح	تعریف و توضیحات
سکستروم (Sequestrum)	به استخوان مرده‌ای اطلاق می‌شود که به دلیل عفونت (استئومیلیت) دچار نکروز شده و دیگر خون‌رسانی ندارد. این استخوان به عنوان محلی برای پناه گرفتن میکروب‌ها عمل می‌کند و می‌تواند باعث مزمن شدن عفونت شود 2 1 .
اینولکروم (Involucrum)	استخوان جدیدی است که در اثر جدا شدن پریوست (پرده بافتی دور استخوان) از استخوان اصلی ایجاد می‌شود. این استخوان جدید به عنوان یک پاسخ التهابی به عفونت شکل می‌گیرد 2 1 .
کلواک (Cloaca)	به مجرایی اشاره دارد که از طریق آن چرک و بافت‌های عفونی از ناحیه عفونی خارج می‌شوند. این مجرا معمولاً به سطح پوست باز می‌شود و نشان‌دهنده وجود عفونت مزمن است 4 3 .

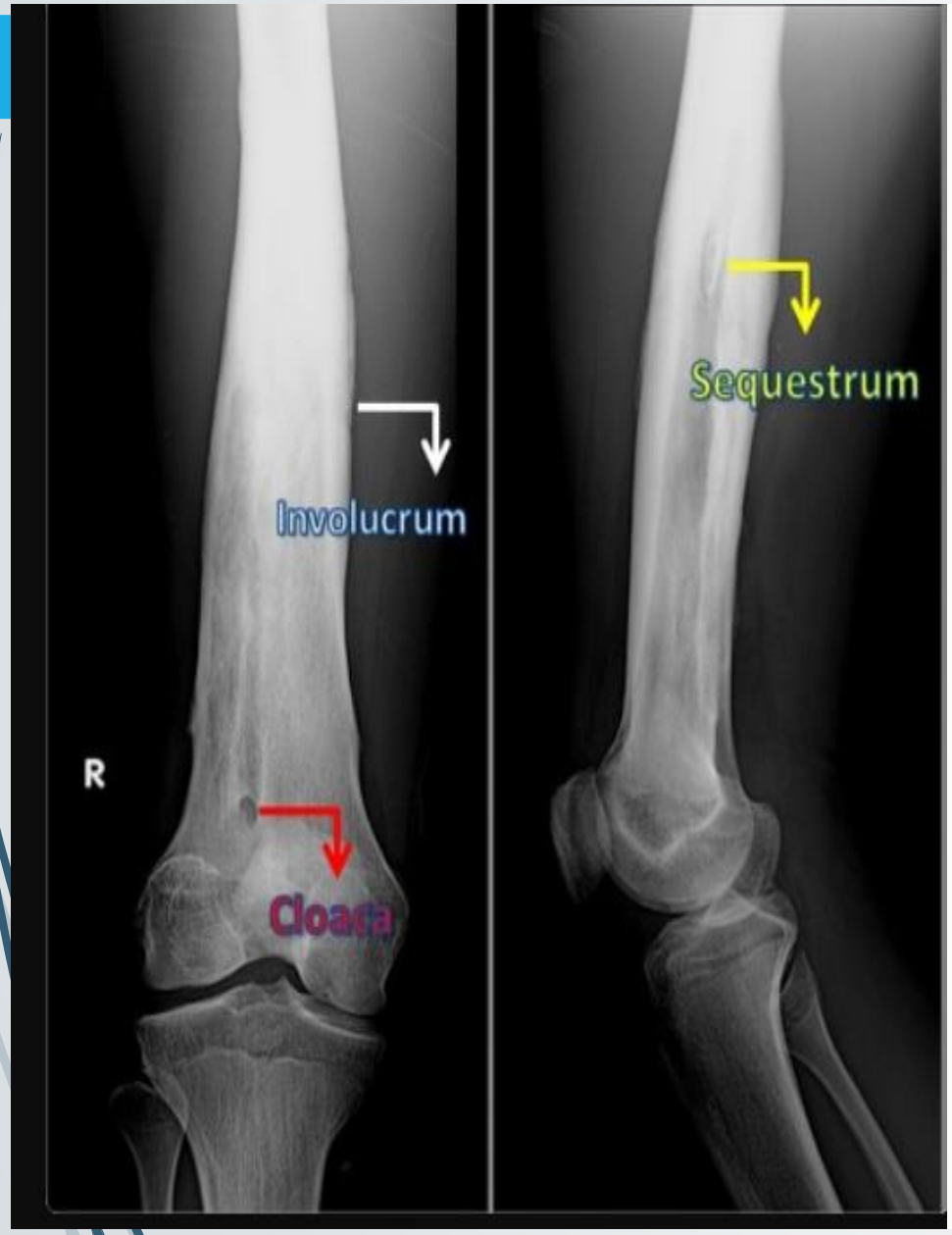
تغییرات رادیولوژیکی در بیماران مبتلا به زخم دیابتی و استئومیلیت معمولاً نشانه‌های خاصی را نشان می‌دهند. در زیر جدولی از این تغییرات بر اساس منابع معتبر علمی ارائه شده است:

نوع تغییر	توضیحات	منبع
کاهش تراکم استخوان	کاهش تراکم استخوان معمولاً به عنوان اولین نشانه استئومیلیت در رادیوگرافی مشاهده می‌شود. این تغییرات ممکن است چند هفته پس از شروع عفونت ظاهر شوند.	2 5
نواحی تیره (لکول‌ها)	وجود نواحی تیره در تصاویر رادیوگرافی ممکن است نشان‌دهنده تخریب بافت استخوانی باشد که به دلیل عفونت ایجاد شده است.	1 4
وجود گاز در بافت عمقی	وجود گاز در بافت‌های نرم اطراف استخوان می‌تواند نشانه‌ای از عفونت‌های خاص مانند کلستریدیوم باشد.	1 2
تخریب استخوان	تخریب استخوان به صورت چرخه‌های لیتیک و حلقه‌های اسکلروزیس قابل مشاهده است که نشان‌دهنده فعالیت عفونی است.	5 6
آبسه‌ها	آبسه‌های استخوانی و تجمع مایعات در تصاویر رادیوگرافی قابل مشاهده هستند، که نشان‌دهنده عفونت شدید است.	1 3
تغییرات در بافت نرم	تغییرات در بافت نرم اطراف استخوان، مانند ادم و التهاب، که می‌تواند به وضوح در MRI یا سونوگرافی دیده شود.	1 4

Adult with chronic osteomyelitis

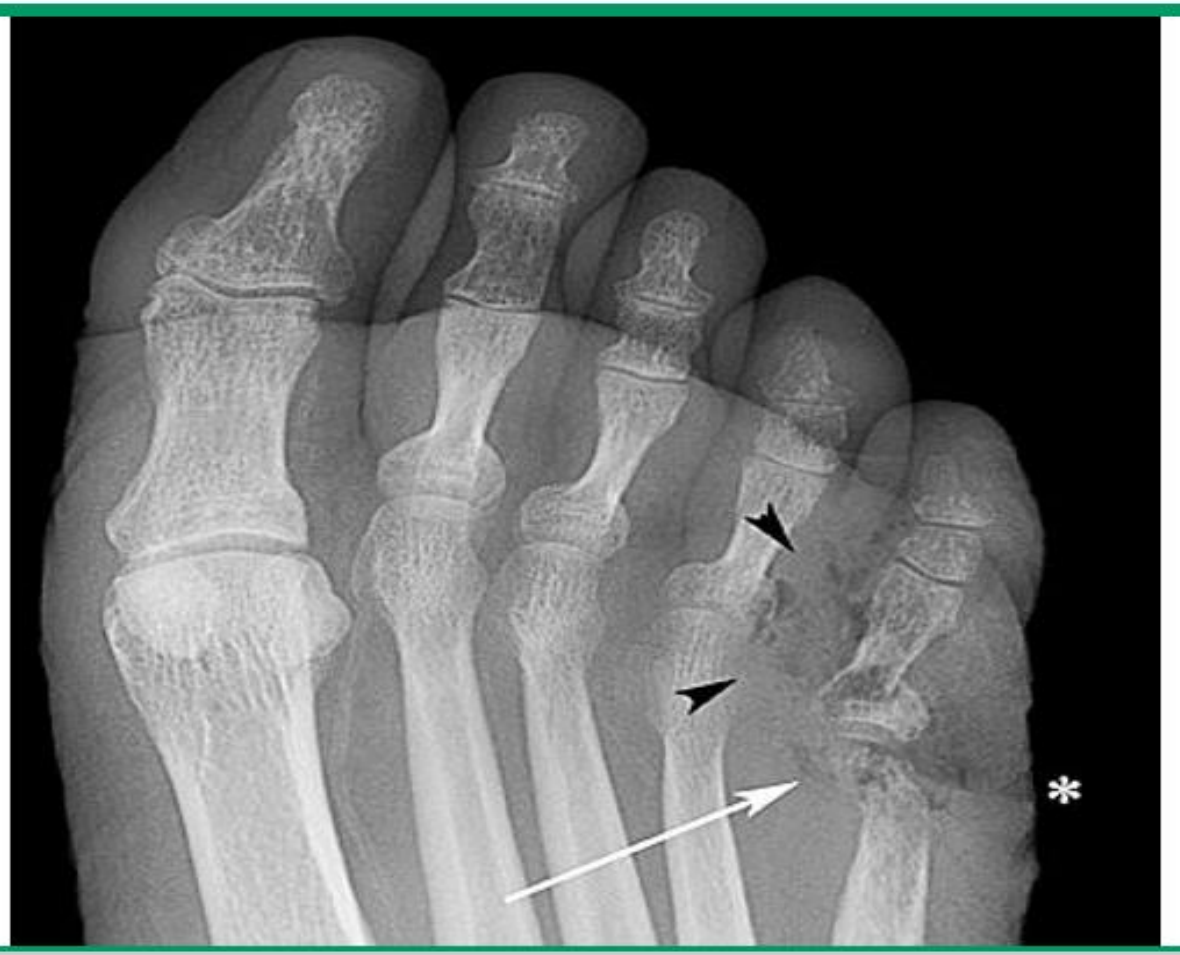


39-year-old man with chronic osteomyelitis of the tibia and a draining wound. Plain rays (A and B) demonstrate a sclerotic sequestrum in the defect of the tibia (arrow). Magnetic resonance imaging axial T1 & T2 images (C and D) show the sequestrum (arrow) in the intraosseous abscess. The abscess/sinus tract can be seen extending to the skin on the T2 image (arrowhead).



ویژگی	سکسترووم (Sequestrum)	اینولکروم (Involucrum)
تعریف	استخوان مرده جدا شده از استخوان سالم	استخوان جدیدی که بین پریوست و استخوان تشکیل می‌شود
منشأ	ناشی از نکروز و مرگ سلول‌های استخوانی به دلیل عفونت یا کاهش خون‌رسانی	ناشی از تلاش بدن برای جداسازی ناحیه عفونی و نکروزه
وضعیت خون‌رسانی	فاقد عروق خونی (آواسکولار)	دارای عروق خونی (واسکولار)
نقش در عفونت	محل تجمع عفونت مزمن	جداسازی ناحیه عفونی و کمک به ترمیم
درمان	معمولاً نیاز به جراحی برای برداشتن دارد	ممکن است نیازی به مداخله نداشته باشد، مگر در صورت عفونت

Osteomyelitis of the toe



Radiograph of the foot demonstrates air in the soft tissues about the 5th toe (black arrowheads). Cortical destruction of the 5th metatarsal head is also seen (white arrow). Irregular contour of the overlying skin represents associated soft tissue ulceration (asterisk).

Courtesy of Perry Horwich, MD.

Conventional radiography

- Conventional radiography (eg, plain x-ray) is a reasonable initial imaging modality for evaluation of suspected osteomyelitis in patients with at least two weeks of clinical symptoms; it is not adequate for detection of early osteomyelitis .
- Bony destructive changes on radiography lag at least two weeks behind clinical infection; approximately 50 to 75 percent of the bone matrix must be destroyed before plain radiographs demonstrate lytic changes

MRI

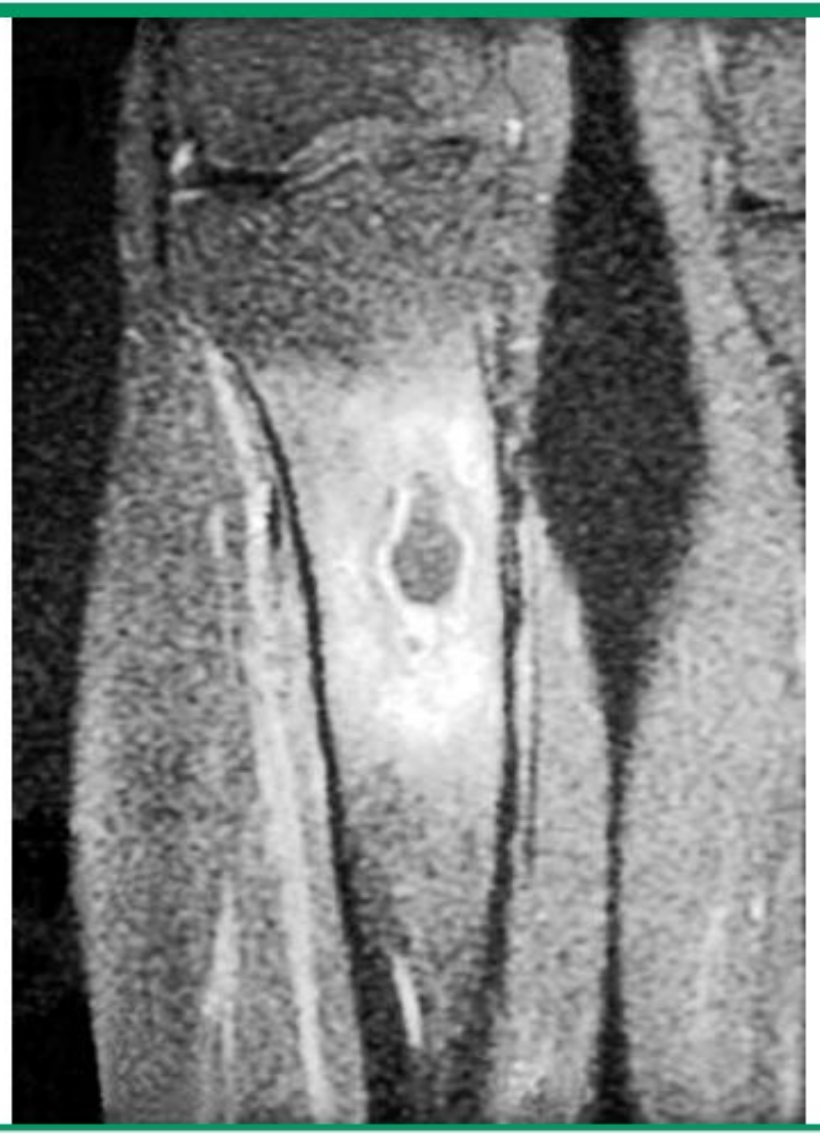
- Bone marrow signal abnormality on MRI is a nonspecifc finding that can be seen with a variety of other pathologies including contusion, **fracture**, **postsurgical change, arthritis**, **neoplasm**, and **Charcot** arthropathy .
- Establishing the correct diagnosis depends on the clinical setting and on additional imaging findings. Moreover, if infection coexists with additional pathology that can cause bone marrow edema, MRI cannot reliably distinguish between marrow changes attributable to infection and those attributable to other pathology.
- Lastly, bone marrow changes may persist for weeks to months after osteomyelitis begins to respond to therapy.

MRI

- Intravenous contrast does not improve the detection of osteomyelitis on MRI but does improve the distinction between phlegmon, necrotic tissue, and abscess.
- Preliminary data suggest that techniques such as difusion-weighted MRI and dynamic contrast-enhanced MRI (DCE-MRI) may help in the diferentiation of Charcot arthropathy from osteomyelitis

اصطلاح	تعریف و توضیحات
Penumbra Sign	"Penumbra sign" یک نشانه رادیولوژیک در تصویربرداری با MRI است که به طور خاص در تشخیص عفونت استخوان (استئومیلیت) و به ویژه آبسه برودی (Brodie's abscess) مشاهده می‌شود. این نشانه به ناحیه‌ای اطلاق می‌شود که حاوی سیگنال‌های ضعیف هایپراینستنس است و توسط بافت گرانولاسیون احاطه شده است. این ویژگی به عنوان یک علامت اولیه عفونت استخوان شناخته می‌شود و می‌تواند در تشخیص افتراقی با تومورهای استخوانی مفید باشد 1 .
اهمیت بالینی	شناسایی "penumbra sign" می‌تواند به تشخیص سریع‌تر استئومیلیت کمک کند و از عوارض جدی مانند آرتریت سپتیک جلوگیری نماید. این نشانه به ویژه در بیمارانی که سابقه جراحی دارند یا علائم غیرقابل توجیه درد استخوان را تجربه می‌کنند، اهمیت دارد 2 1 .
تشخیص افتراقی	این نشانه ممکن است در سایر شرایط مانند استئوید اوستئوم، کوندروسارکوم، و گرانولوم ائوزینوفیلیک نیز دیده شود، بنابراین باید در تشخیص افتراقی در نظر گرفته شود 1 .

Penumbra sign in osteomyelitis

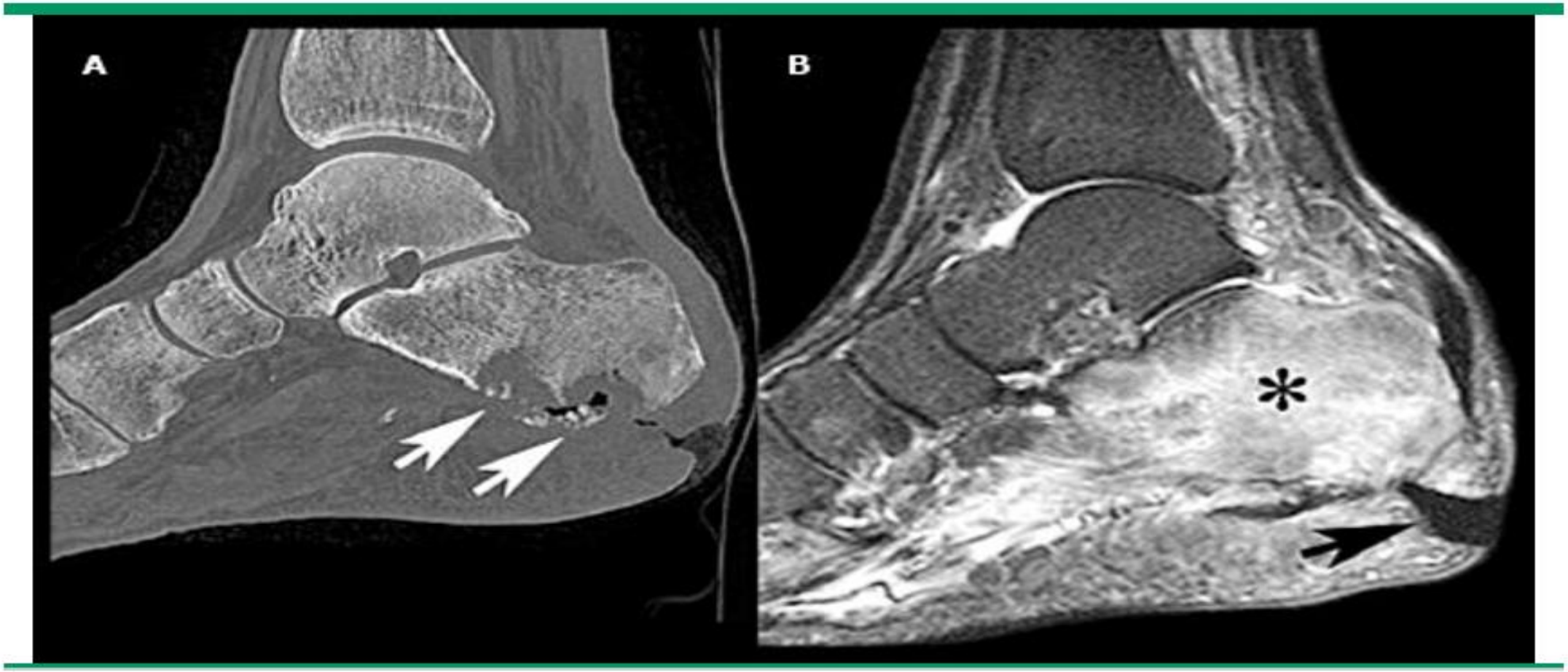


Magnetic resonance imaging (MRI) scan shows the penumbra sign (a transitional zone with relative signal intensity between abscess and sclerotic bone marrow on T1-weighted MRI).

CT

- CT is more sensitive than conventional radiography for assessing cortical and trabecular integrity, periosteal reaction, intraosseous gas, soft tissue gas, and the extent of sinus tracts It is useful in **chronic osteomyelitis** and may be the most useful modality to evaluate for the presence of osseous sequestra and involucrum .
- Intravenous contrast is required for detection of soft tissue abnormalities such as sinus tracts.
- Noncontrast CT allows assessment of gas but does not evaluate soft tissue pathology as well as a contrasted CT.
- Metallic hardware can give rise to artifact that may degrade CT image quality and limit diagnostic capability .

Osteomyelitis in the heel



(A) Sagittal computed tomography image demonstrates cortical fragmentation of the plantar aspect of thecalcaneus (arrows) and adjacent air and soft tissue ulceration.

(B) Corresponding fluid-sensitive short inversion time inversion recovery (STIR) image demonstrates extensive high-signal edema in the calcaneus (asterisk) and again demonstrates posterior plantar ulcer overlying the calcaneus (arrow).

Ultrasound

- Ultrasound may be a useful diagnostic tool for circumstances in which other modalities are not readily available.

Typically, bone is not well depicted by ultrasound, because the cortical surface of the bone

refelects the acoustic energy that is used to generate ultrasound images.

However, changes superfcial to cortical bone can be visualized by ultrasound.

- In osteomyelitis, ultrasound can demonstrate elevation and/or thickening of the periosteum due to pus emanating from the bone
- Ultrasound may be more useful for detection of these findings in pediatric patients, since the periosteum in the pediatric skeleton is more loosely adherent to the cortex than in the adult skeleton .
- Ultrasonography is considered excellent for aspirating suspected infected fluid collections or abscesses

درمان آنتی بیوتیک

- Do not treat clinically uninfected foot ulcers with systemic or local antibiotic therapy when the goal is to reduce the risk of new infection or to promote ulcer healing.(Best Practice Statement.)

Oral agents for empiric treatment of mild to moderate diabetic foot infections

Regimens with activity against streptococci and staphylococci (MSSA)
Cephalexin **or**
Dicloxacillin **or**
Amoxicillin-clavulanate **or**
Clindamycin
Regimens with activity against streptococci and MRSA
Clindamycin* **or**
Linezolid **or**
Cephalexin **or** dicloxacillin **PLUS** Trimethoprim-sulfamethoxazole **or** doxycycline
Regimens with activity against streptococci, MRSA, aerobic gram-negative bacilli ¶ and anaerobes
Trimethoprim-sulfamethoxazole **PLUS** Amoxicillin-clavulanate **or** Moxifloxacin **-OR-**
Clindamycin* **PLUS** Ciprofloxacin ¶ **or** Levofloxacin ¶

Antibiotic dosing for adults with normal renal function Δ	
Cephalexin	500 mg every 6 hours
Dicloxacillin	500 mg every 6 hours
Clindamycin	300 to 450 mg every 6 to 8 hours
Linezolid	600 mg every 12 hours
Trimethoprim-sulfamethoxazole (co-trimoxazole)	2 double-strength tablets (trimethoprim 160 mg and sulfamethoxazole 800 mg per tablet) every 12 hours
Doxycycline	100 mg orally every 12 hours
Amoxicillin-clavulanate	875/125 mg every 12 hours
Ciprofloxacin	500 mg every 12 hours (or, if there is concern for *Pseudomonas aeruginosa*, 750 mg every 12 hours)
Levofloxacin	500 mg every 24 hours (or, if there is concern for *P. aeruginosa*, 750 mg every 24 hours)
Moxifloxacin ◊	400 mg every 24 hours

MSSA: methicillin-susceptible *Staphylococcus aureus*; MRSA: methicillin-resistant *S. aureus*. * Check susceptibility testing.

¶ Only the regimens containing ciprofloxacin or levofloxacin have expected activity against *Pseudomonas aeruginosa*. Empiric coverage for *P. aeruginosa* may not be necessary unless the patient has a particular risk for involvement with this organism, such as a macerated wound or one with significant water exposure. When there is concern for *P. aeruginosa*, higher dosing of ciprofloxacin or levofloxacin is appropriate, as described in the dosing section above. Δ Many of these agents require adjustment of the dose in the setting of renal dysfunction. ◊ Moxifloxacin is not recommended for the treatment of *P. aeruginosa*.

Parenteral agents for empiric treatment of moderate to severe diabetic foot infections*

	Dosing (for adults with normal renal function) ¶	Activity against *Pseudomonas* Δ
Beta-lactam/beta-lactamase inhibitors		
Ampicillin-sulbactam	3 g every 6 hours	No
Piperacillin-tazobactam ◊	3.375 g every 6 hours or 4.5 g every 6 to 8 hours	Yes, when dosed 4.5 g every 6 hours
Carbapenems		
Imipenem-cilastatin ◊	500 mg every 6 hours	Yes
Meropenem ◊	1 g every 8 hours	Yes
Ertapenem	1 g every 24 hours	No
Combination regimens		
Metronidazole PLUS one of the following:	500 mg every 8 hours	No
Ceftriaxone	1 to 2 g every 24 hours	No
Ceftazidime ◊	1 to 2 g every 8 hours §	Yes, when 2 g dose is used
Cefepime ◊	2 g every 8 to 12 hours ¥	Yes
Ciprofloxacin ‡	400 mg IV every 8 to 12 hours	Yes †
Levofloxacin	750 mg IV every 24 hours	Yes †
Moxifloxacin	400 mg every 24 hours	No
Aztreonam ‡	2 g every 8 hours	Yes †

PLUS one of the following if MRSA coverage is warranted		
Vancomycin**	15 to 20 mg/kg every 8 to 12 hours	
Linezolid ¶¶	600 mg every 12 hours	
Daptomycin ΔΔ	4 to 6 mg/kg every 24 hours	

AUC: area under the 24-hour time-concentration curve.

* These regimens do not have activity against carbapenem-resistant Enterobacteriaceae. Patients who have suspected or documented infection with a carbapenem-resistant organism should be managed in consultation with an expert in infectious diseases.

¶ Many of these agents require adjustment of the dose in the setting of renal dysfunction.

Δ Empiric coverage for *Pseudomonas aeruginosa* may not be necessary except in severe cases or when the patient has particular risk for involvement with this organism, such as a macerated wound or one with significant water exposure.

◊ These antibiotics can be given as a prolonged infusion over 3 to 4 hours. Patients who have a high risk of infection with drug-resistant pathogens or who are critically ill in the setting of a severe infection are most likely to bene t from prolonged infusion dosing. For additional information, refer to other UpToDate content on prolonged infusions of beta-lactams.

§ We aim to use the higher cefepime dose, particularly for severe infections or neutropenic patients, but dosing should take into account the condition treated, the minimum inhibitory concentration of the isolate, the potential for toxicity, and other patient-speci c factors.

¥ In certain circumstances, such as prolonged outpatient antibiotic therapy, a dosing interval of every 12 hours may be considered; however, this dosing regimen has not been well-studied.

‡ These agents should be used in combination with an agent that has good gram-positive coverage, such as vancomycin, linezolid, or daptomycin.

† Variable activity against *Pseudomonas*. Consult local susceptibility data before use.

** For severely ill patients, a vancomycin loading dose (20 to 35 mg/kg) is appropriate; within this range, we use a higher dose for critically ill patients. The loading dose is based on actual body weight, rounded to the nearest 250 mg increment and not exceeding 3000 mg. The initial maintenance dose and interval are determined by nomogram (typically 15 to 20 mg/kg every 8 to 12 hours for most patients with normal renal function). Subsequent dose and interval adjustments are based on AUC-guided or trough-guided serum concentration monitoring. Refer to the UpToDate topic on vancomycin dosing for sample nomogram and discussion of vancomycin monitoring

¶¶ Because of the toxicity associated with long-term linezolid use, we do not recommend this agent for treatment of osteomyelitis. ΔΔ Higher doses may be needed if there is concomitant osteomyelitis.

Table 5. Duration of antibiotic therapy according to the clinical situation.

	Route	Duration
Infection severity (skin and soft tissues)		
Class 2: Mild	Oral	1–2 weeks[a]
Class 3/4: Moderate/severe	Oral/initially iv	2–4 weeks
Bone/joint		
Resected	Oral/initially iv	2–5 days
Debrided (soft tissue infection)	Oral/initially iv	1–2 weeks
Positive culture or histology of bone margins after bone resection	Oral/initially iv	3 weeks
No surgery or dead bone	Oral/initially iv	6 weeks

Abbreviation: iv, intravenous. [a] 10 days following surgical debridement.

(a) Administer antibiotic therapy to a patient with a skin or soft tissue diabetic foot infection for a duration of 1–2 weeks. (Strong; High).

(b) Consider continuing treatment, perhaps for up to 3–4 weeks, if the infection is improving but is extensive and is resolving slower than expected or if the patient has severe peripheral artery disease (PAD). (Conditional, Low).

(c) If evidence of infection has not resolved after 4 weeks of apparently appropriate therapy, re-evaluate the patient, and reconsider the need for further diagnostic studies or alternative treatments. (Strong; Low).

Targeted therapy

- — If appropriate wound cultures were submitted, antimicrobial therapy should be tailored to culture and susceptibility results when available.
- However, it is not always necessary to cover all microorganisms isolated from cultures .Virulent species such as *S. aureus* and streptococci (group A or B) should always be covered, but in polymicrobial infections, less virulent organisms (such as coagulase negative staphylococci and enterococci) may be less important.

- Furthermore, if isolates are resistant to an empiric regimen to which the patient is clearly responding well, broadening the spectrum to include those isolates may not be necessary.
- On the other hand, if the patient is not responding, expanding therapy to target all isolated organisms may be warranted.
- For those patients who were initiated on parenteral therapy, a switch to an oral regimen is reasonable following clinical improvement.

- Do not empirically target antibiotic therapy **against *Pseudomonas aeruginosa*** in cases of DFI in temperate climates, but use empirical treatment of *P. aeruginosa* if it has been isolated from cultures of the affected site within the previous few weeks, in a person with **moderate or severe infection** who resides in Asia or North Africa. (Best Practice Statement.

- Consider a duration of up to 3 weeks of antibiotic therapy after minor amputation for diabetes-related osteomyelitis of the foot and positive bone margin culture and 6 weeks for diabetes-related foot osteomyelitis without bone resection or amputation. (Conditional; Low).
- Use the outcome at a minimum follow-up duration of 6 months after the end of the antibiotic therapy to diagnose remission of diabetes-related osteomyelitis of the foot.
- Best Practice Statement.

در زیر جدولی از باکتری‌های گرم مثبت و گرم منفی که می‌توانند در انسان عفونت ایجاد کنند، ارائه شده است:

باکتری‌های گرم مثبت	باکتری‌های گرم منفی
استافیلوکوکوس اورئوس	اشرشیا کلی (Escherichia coli)
استرپتوکوکوس پیوژنز	سودوموناس آئروژینوزا (Pseudomonas aeruginosa)
استرپتوکوکوس پنومونیه	کلامیدیا تراکوماتیس (Chlamydia trachomatis)
انتروکوکوس فکالیس	کامپیلوباکتر (Campylobacter)
لیستریا مونوسیتوژنز	هلیکوباکتر پیلوری (Helicobacter pylori)
باسیلوس آنتراسیس	ویبریو کلرا (Vibrio cholerae)
کورینه باکتریوم دیفتریا	لپتوسپیرا (Leptospira)

در زیر جدولی از تفاوت‌های باکتری‌های گرم مثبت و گرم منفی که می‌توانند در بدن عفونت ایجاد کنند، ارائه شده است:

ویژگی	باکتری‌های گرم مثبت	باکتری‌های گرم منفی
ساختار دیواره سلولی	لایه ضخیم پپتیدوگلایکان	لایه نازک پپتیدوگلایکان و وجود غشای خارجی
رنگ‌آمیزی گرم	بنفش (به دلیل جذب کریستال ویوله)	قرمز یا صورتی (به دلیل جذب سافرانین)
حساسیت به آنتی‌بیوتیک‌ها	معمولاً حساس‌تر به آنتی‌بیوتیک‌ها مانند پنی‌سیلین	معمولاً مقاوم‌تر به آنتی‌بیوتیک‌ها
وجود آنتی‌ژن O	فاقد آنتی‌ژن O اختصاصی	دارای آنتی‌ژن O اختصاصی
عفونت‌های شایع	استافیلوکوکوس اورئوس، استرپتوکوکوس پیوژنز	اشرشیا کلی، سودوموناس آئروژینوزا
سموم تولیدی	ممکن است سموم خارج سلولی تولید کنند	معمولاً تولید اندوتوکسین (LPS)
شرایط رشد	نیاز غذایی ساده‌تر	نیاز غذایی پیچیده‌تر

در زیر جدولی از باکتری‌های گرم مثبت هوازی و غیرهوازی که می‌توانند در بدن عفونت ایجاد کنند، ارائه شده است:

نوع باکتری	نام باکتری	ویژگی‌ها
گرم مثبت هوازی	استافیلوکوکوس اورئوس	عامل عفونت‌های پوستی، عفونت‌های تنفسی و مسمومیت غذایی.
	استرپتوکوکوس پنومونیه	عامل پنومونی اکتسابی و منتژیت.
	انتروکوکوس فکالیس	عامل عفونت‌های ادراری و عفونت‌های قلبی-عروقی.
	باسیلوس سرئوس	عامل مسمومیت غذایی و عفونت‌های پوستی.
گرم مثبت غیرهوازی	کلستریدیوم پرفرنجنز	عامل گانگرن گازی و مسمومیت غذایی.
	کلستریدیوم دیفیسیل	عامل عفونت‌های روده‌ای و اسهال ناشی از آنتی‌بیوتیک.
	اکتینومایسس	می‌تواند باعث عفونت‌های مزمن و عفونت‌های بافت نرم شود.

باکتری‌های گرم مثبت هوازی و غیرهوازی تفاوت‌های مهمی دارند که به ویژگی‌های ساختاری، متابولیسم و نیازهای اکسیژنی آن‌ها مربوط می‌شود. در زیر به این تفاوت‌ها اشاره می‌شود:

ویژگی	باکتری‌های گرم مثبت هوازی	باکتری‌های گرم مثبت غیرهوازی
نیاز به اکسیژن	نیاز به اکسیژن برای رشد و تولید انرژی دارند.	قادر به رشد در شرایط بدون اکسیژن هستند.
متابولیسم	متابولیسم تنفسی (تنفس هوازی) دارند.	متابولیسم تخمیری یا تنفس بی‌هوازی دارند.
مثال‌ها	استافیلوکوکوس اورئوس، استرپتوکوکوس پنومونیه	کلستریدیوم پرفرنجنز، باکتروئیدها
حساسیت به آنتی‌بیوتیک‌ها	معمولاً نسبت به آنتی‌بیوتیک‌ها حساس‌تر هستند.	ممکن است نسبت به برخی آنتی‌بیوتیک‌ها مقاوم‌تر باشند.
محیط رشد	در محیط‌های غنی از اکسیژن بهتر رشد می‌کنند.	در محیط‌های بی‌هوازی یا کم‌اکسیژن بهتر رشد می‌کنند.
ساختار دیواره سلولی	دارای لایه ضخیم پپتیدوگلیکان و فاقد غشای خارجی هستند.	مشابه باکتری‌های هوازی، اما ممکن است دارای ویژگی‌های خاصی باشند که آن‌ها را در شرایط بی‌هوازی سازگار کند.

عوامل مختلفی باعث افزایش مقاومت به آنتی‌بیوتیک در باکتری‌های *Pseudomonas aeruginosa* می‌شوند. این عوامل شامل ویژگی‌های ژنتیکی، محیطی و رفتاری هستند که به شرح زیر است:

عامل	توضیحات
کاهش نفوذپذیری غشای خارجی	*Pseudomonas aeruginosa* قادر است به طور انتخابی مانع از نفوذ آنتی‌بیوتیک‌ها به داخل سلول خود شود. این ویژگی به دلیل ساختار خاص غشای خارجی و وجود پروتئین‌های خاص مانند oprI و oprL است که بر روی سیستم انتشار دارو تأثیر می‌گذارند [1] [3] .
تولید آنزیم‌های تخریب‌کننده	این باکتری می‌تواند آنزیم‌هایی مانند بتالاکتاماز ها تولید کند که قادر به تخریب آنتی‌بیوتیک‌ها، به ویژه بتالاکتام‌ها هستند [2] [4] .
وجود پلاسمیدهای مقاوم	پلاسمیدها می‌توانند ژن‌های مقاومت را از یک باکتری به باکتری دیگر منتقل کنند، که این امر باعث گسترش سریع مقاومت در میان جمعیت‌های باکتریایی می‌شود [5] [6] .
جهش‌های ژنتیکی	تغییرات ژنتیکی در *Pseudomonas aeruginosa* می‌تواند باعث ظهور مقاومت به آنتی‌بیوتیک‌ها شود. این جهش‌ها ممکن است به طور طبیعی یا تحت فشار های انتخابی ایجاد شوند [5] [6] .
فشار انتخابی ناشی از استفاده نادرست از آنتی‌بیوتیک‌ها	استفاده نادرست و غیرضروری از آنتی‌بیوتیک‌ها، مانند تجویز نامناسب یا طولانی‌مدت، فشار انتخابی را بر روی باکتری‌ها افزایش می‌دهد و منجر به بقای سویه‌های مقاوم می‌شود [4] [6] .
محیط‌های بیمارستانی و عفونت‌های مزمن	*Pseudomonas aeruginosa* معمولاً در محیط‌های بیمارستانی و در عفونت‌های مزمن مانند عفونت‌های ریه در بیماران مبتلا به فیبروز کیستیک یافت می‌شود، که این شرایط موجب افزایش احتمال

Table 4. Proposals for the empirical antibiotic therapy according to clinical presentation and microbiological data (from Lipsky et al.[11]).[a]

Infection severity	Additional factors	Usual pathogen(s)[b]	Potential empirical regimens[c]
Mild	No complicating features	GPC	Semisynthetic penicillinase-resistant penicillin (cloxacillin) 1st generation cephalosporin (cephalexin)
	ß-lactam allergy or intolerance	GPC	Clindamycin; fluoroquinolone (levo/moxi-floxacin); trimethoprim-sulfamethoxazole; doxycycline
	Recent antibiotic exposure	GPC + GNR	ß-lactam- ß lactamase inhibitor1 (amoxicillin/clavulanate, ampicillin/sulbactam) Fluoroquinolone (levo/moxi-floxacin); trimethoprim-sulfamethoxazole
	High risk for MRSA	MRSA	Linezolid; trimethoprim-sulfamethoxazole; clindamycin; doxycycline, fluoroquinolone (levofloxacin, moxifloxacin)

Moderate or severe[d]	No complicating features	GPC ± GNR	ß-lactam- ß lactamase inhibitor1 (amoxicillin/clavulanate, ampicillin/sulbactam) 2nd, 3rd generation cephalosporine (cefuroxime, cefotaxime, ceftriaxone)
	Recent antibiotics	GPC ± GNR	ß-lactam- ß lactamase inhibitor2 (ticarcillin/clavulanate, piperacillin/tazobactam) 2nd, 3rd generation cephalosporine (cefuroxime, cefotaxime, ceftriaxone) group 1 carbapenem (ertapenem); (depends on prior therapy; seek advice)
	Macerated ulcer or warm climate	GNR, including *Pseudomonas* sp.	ß-lactam- ß lactamase inhibitor2 (ticarcillin/clavulanate, piperacillin/tazobactam) semisynthetic penicillinase-resistant penicillin (cloxacillin) + ceftazidime or ciprofloxacin group 2 carbapenem (mero/imi-penem)
	Ischaemic limb/necrosis/ gas forming	GPC ± GNR ± strict anaerobes	ß-lactam- ß lactamase inhibitor1 (amoxicillin/clavulanate, ampicillin/sulbactam) or ß-lactam- ß lactamase inhibitor2 (ticarcillin/clavulanate, piperacillin/tazobactam) Group 1 (ertapenem) or 2 (mero/imi-penem) carbapenem 2nd (cefuroxime)/3rd (cefotaxime, ceftriaxone) generation cephalosporin + clindamycin or metronidazole
	MRSA risk factors	MRSA	Consider adding, or substituting with, glycopeptides (vancomycin, teicoplanin); llLinezolid; daptomycin; fusidic acid, trimethoprim-sulfamethoxazole; doxycycline
	Risk factors for resistant GNR	ESBL	Carbapenem (erta/mero/imi-penem); fluoroquinolone (ciprofloxacin); Aminoglycoside (amikacin); colistin

Antibiotics enclosed in brackets are cited as examples. High risk for MRSA: previous MRSA infection or colonisation. MRSA risk factors: prolonged hospitalisation, intensive care admission, recent hospitalisation, recent antibiotic use, invasive procedures, HIV infection, admission to nursing homes, open wounds, haemodialysis, discharge with long-term central venous access.

Abbreviations: ESBL, extended-spectrum ß-lactamase; GNR, gram-negative rod; GPC, gram-positive cocci (staphylococci and streptococci); HIV, human immunodeficiency virus; MRSA, methicillin-resistant *Staphylococcus aureus*. [a] Recommendations are based upon theoretical considerations and results of available clinical trials. [b] Refers to isolates from an infected foot ulcer, not just colonisation at another site. [c] Given at the usual recommended doses for serious infections. Where more than one agent is listed, only one of them should be prescribed unless otherwise indicated. Consider modifying doses or agents selected for patients with comorbidities such as azotaemia, liver dysfunction, and obesity. [d] Oral antibiotic agents should generally not be used for severe infections, except as a follow-on (switch) after initial parenteral therapy.

Duration of therapy

- The duration of antibiotic therapy should be tailored to individual clinical circumstances. Patients with mild infection should receive oral antibiotic therapy in conjunction with attentive wound care until there is evidence that the infection has resolved (usually about one to two weeks).
- Antibiotics need not be administered for the entire duration that the wound remains open.

مشاوره جراحی

- The urgent surgical consultation should be obtained in cases of severe infection or moderate DFI complicated by extensive gangrene, necrotising infection, signs suggesting deep (below the fascia) abscess, compartment syndrome, or severe lower limb ischaemia. (Best Practice Recommendation.)
- Consider performing early (within 24–48 h) surgery combined with antibiotics for moderate and severe DFIs to remove the infected and necrotic tissue. (Conditional; Low).

Consultation with a surgeon

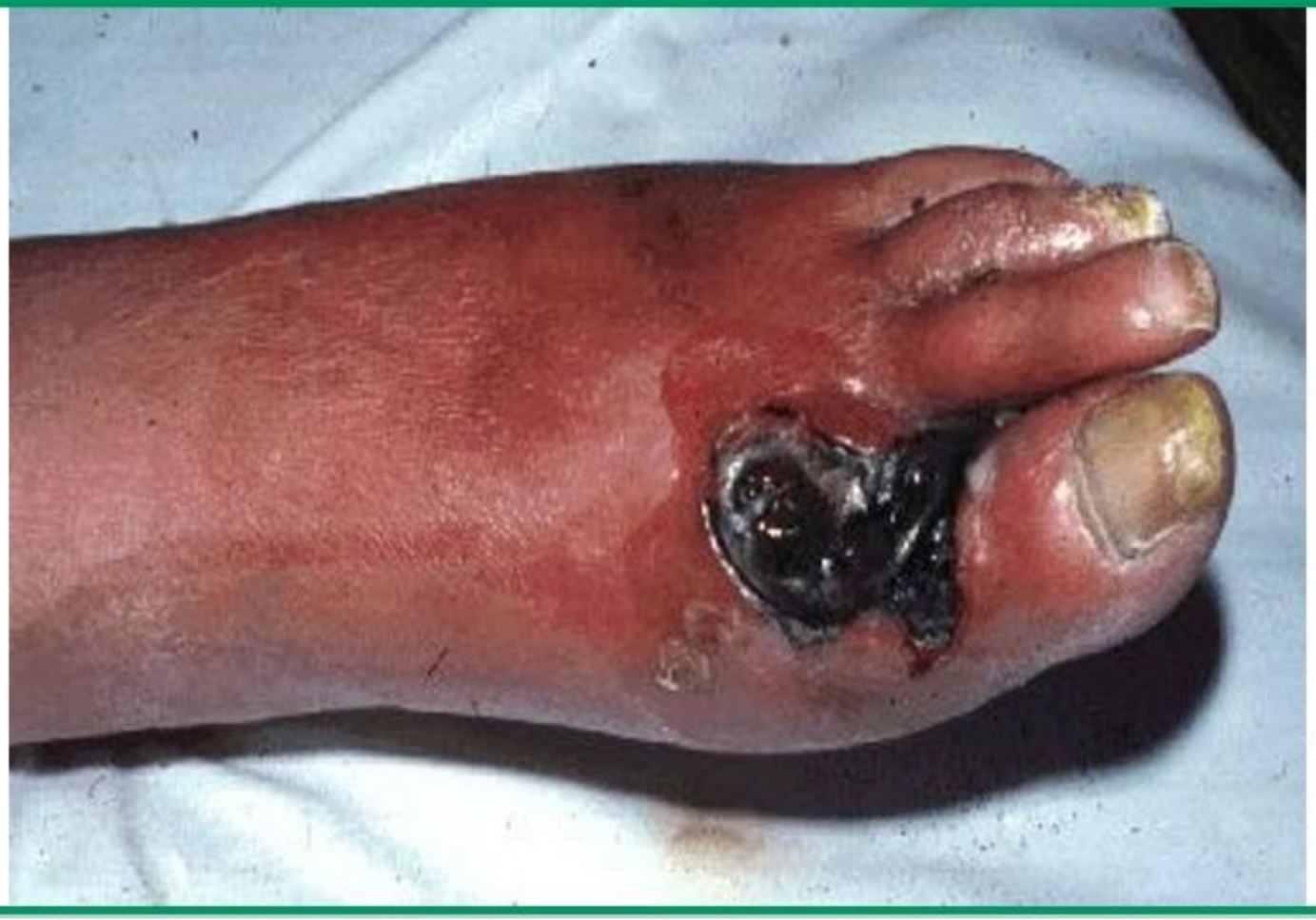
- The utility of early surgical debridement was illustrated in a retrospective review of 112 diabetic patients with severe foot infections .
- Those patients who underwent surgical intervention at the time of presentation had a significantly lower rate of above-ankle amputation than those who received three days of **intravenous antimicrobial** therapy **prior** to surgery.

- In people with diabetes, PAD and a foot ulcer or gangrene with infection involving any portion of the foot obtain an urgent consultation by a surgical specialist as well as a vascular specialist in order to determine the indications and timings of a drainage and/or revascularisation procedure.

(Best Practice Statement.)

- Consider performing surgical resection of infected bone combined with systemic antibiotics in a person with diabetes-related osteomyelitis of the foot. (Conditional; Low).
- Consider antibiotic treatment without surgery in case of (i) **forefoot osteomyelitis without** an immediate need for incision and drainage to control infection, (ii) without PAD, and (iii) without exposed bone. (Conditional; Low).

Infected and ischemic diabetic foot ulcer



Foot from a diabetic patient with an ulcer that extends to the deep layers with signs of local infection, cellulitis, and necrosis. This lesion healed completely after a hospital stay involving excision of necrotic tissue but no amputation.

- Partial amputations of the foot (eg, ray or trans metatarsal amputations) may adversely alter the biomechanics of the foot, increasing the risk of future ulceration.

- Thus, in certain cases, limited surgical debridement combined with prolonged antibiotic therapy may be appropriate .

- However, extensive surgical debridement or resection is preferable in the following clinical circumstances :
- Persistent sepsis without an alternate source
  - Inability to receive or tolerate appropriate antibiotic therapy
  - Progressive bone deterioration despite appropriate antibiotic therapy
  - Mechanics of the foot are compromised by extensive bony destruction requiring correction
  - Surgery is needed to achieve soft tissue wound or primary closure

مراحل درمان زخم

- Of loading of plantar ulcerations
- Debridement of necrotic, nonviable tissue
- Revascularization of ischemic wounds when necessary
- Management of infection: soft tissueor bone
- Use of physiologic, topical dressings

Off Loading

Total contact cast

- Disadvantages of total contact casting include expertise needed in applying the cast, inability to inspect the foot frequently, inconvenience in activities of daily living (eg, bathing), and the risk of developing a secondary ulcer in an ill- fitting cast (particularly in patients with neuropathy) ..

Total contact cast

- Frequent cast changes may be needed to avoid complications. Total contact casts should **not** be used in patients with infected ulcers or wounds, osteomyelitis, peripheral ischemia (ankle-brachial index <0.6), bilateral ulceration, lower extremity amputation, or heel ulceration

Cast walkers

- An alternative to total contact casting is a prefabricated brace called a cast walker that is designed to maintain a total contact .
- Several cast walkers (**nonremovable, removable**) are commercially available and provide the capability to olfoad the foot similar to contact casts.
- A signifcant disadvantage of the cast walker is poor patient compliance if the cast walker is removed.
- Prefabricated products are at least as good as total contact casting for offloading the foot and equalizing foot pressures when the foot anatomy is normal, as illustrated in the studies below, but data are not available demonstrating these effects for patients with diabetic foot deformities.

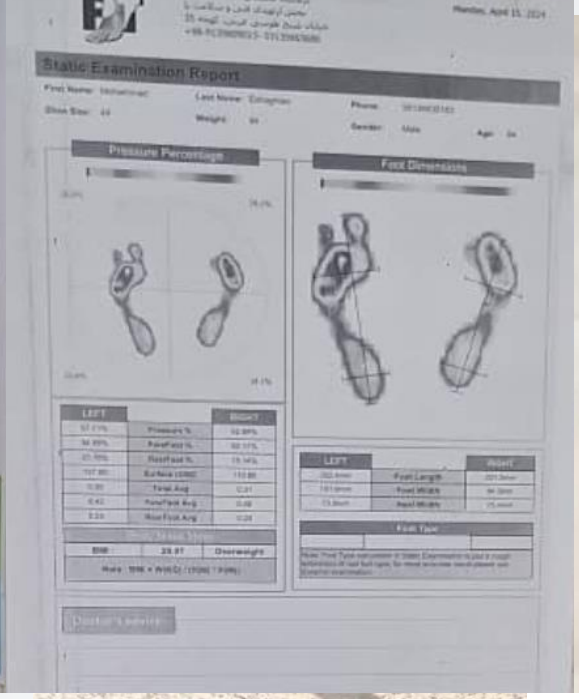
Knee walker

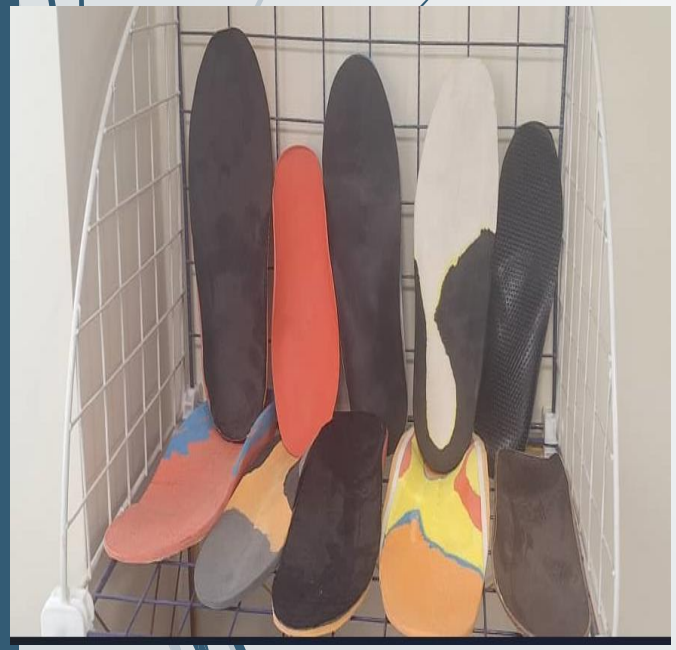
Graphic 73730 Version 2.0

Wedge shoes

Graphic 53678 Version 2.0


غربالگری سلامت پا
آموزش مراقبت از پای دیابتی
طراحی و ساخت کفش و کفی طبی با استفاده از اسکنر 3D و Pressure
انجام گچ گیری TCC برای درمان زخم پای دیابتی با متودهای جدید
طراحی و ساخت انواع کفش ها، صندل ها و کفی های طبی مخصوص:
افراد دارای دیابت، صافی کف پا، خار پاشنه
کوتاهی پا، مشکلات زانو و کمر
سالمندان، کودکان، ورزشکاران و ...


Static Examination Report
Pressure Percentage
Foot Dimensions




PT-3DPLANTAR

WOUND DEBRIDEMENT

Surgical

- Sharp excisional debridement of chronic wounds decreases bacterial load and stimulates contraction and wound epithelialization .
- Surgical debridement is the most appropriate choice for removing large areas of necrotic tissue and is indicated whenever there is any evidence of infection (cellulitis, sepsis).
- Surgical debridement is also indicated in the management of chronic nonhealing wounds to remove infected tissue, handle undermined wound edges, or obtain deep tissue for culture and pathology .

Enzymatic

- Enzymatic debridement involves applying exogenous enzymatic agents to the wound. Many products are commercially available ,but results of clinical studies are mixed and their specific effect remains unclear .
- Ulcer healing rates are not improved with the use of most topical agents, including debriding enzymes .
- However, collagenase may promote **endothelial cell and keratinocyte migration**, thereby stimulating angiogenesis and epithelialization as its mechanism of action, rather than functioning as a strict debridement agent .
- It also remains a good option in patients who require debridement but are not surgical candidates.

Biologic

- Maggot therapy has been used in the treatment of pressure ulcers ,chronic venous ulceration, diabetic ulcers .and other acute and chronic wounds .
- The larvae secrete proteolytic enzymes that liquefy necrotic tissue, which is subsequently ingested while leaving healthy tissue intact.
- Basic and clinical research suggests that maggot therapy has additional benefits, including antimicrobial action and stimulation of wound healing .

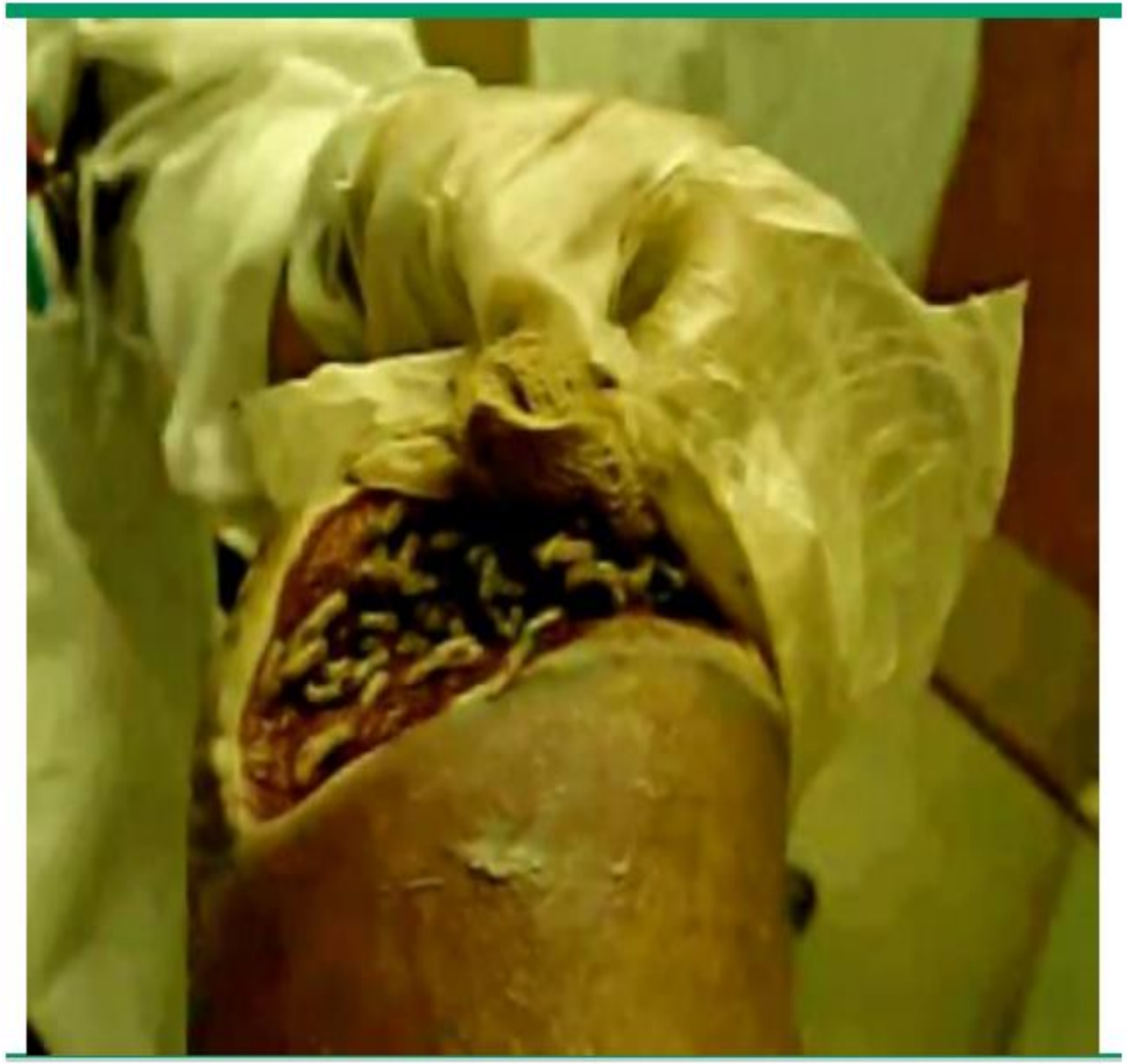
Biologic

- Maggot therapy can be used as a bridge between debridement procedures, or for debridement of chronic wounds when surgical debridement is not available or cannot be performed .Maggot therapy may also reduce the duration of antibiotic therapy in some patients
- Larvae are generally changed every 48 to 72 hours.

Treatment of necrotic tissue with maggots

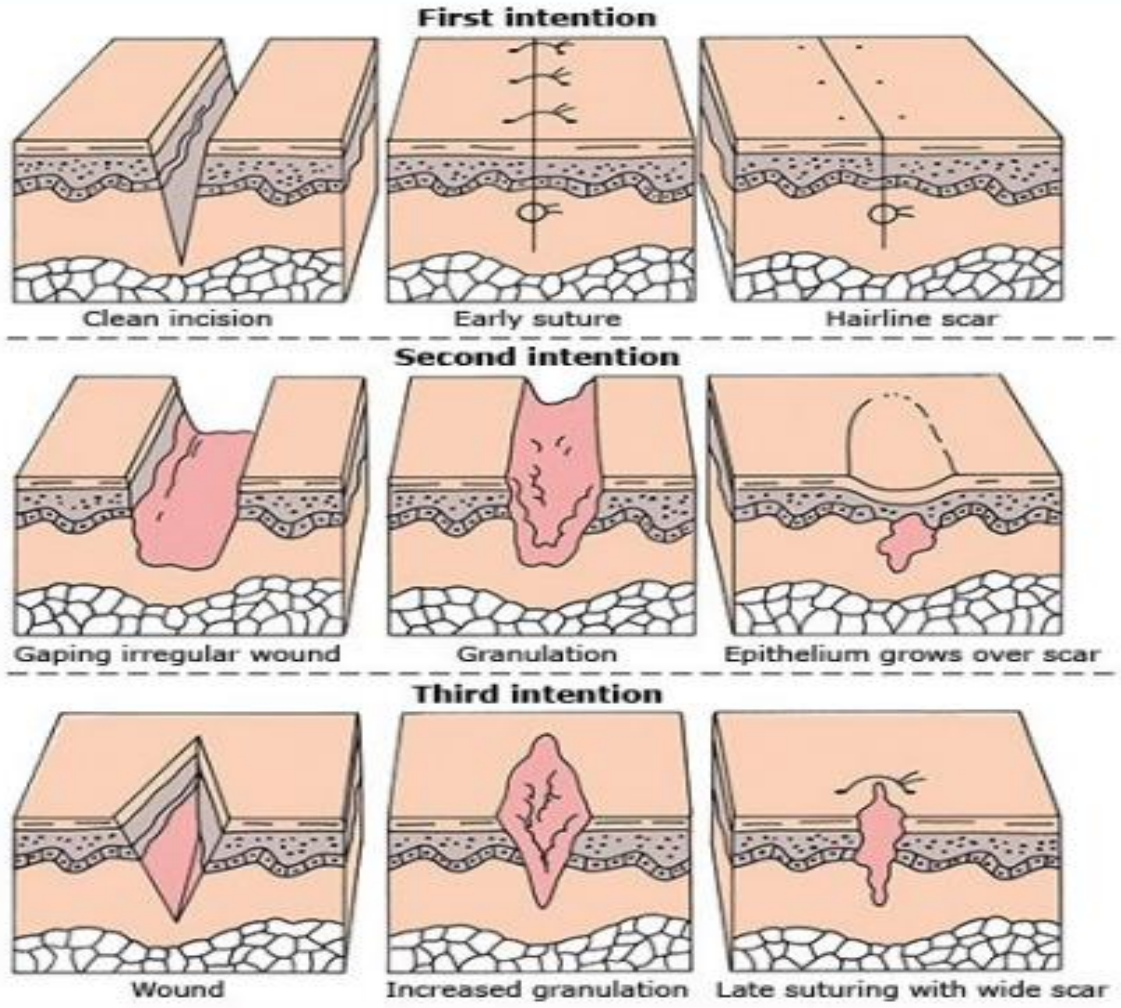
(A) Infection of necrotic skin associated with ulcerated cancer.
(B) After treatment with maggots.
(C) Maggots in a tea bag.

Biologic debridement with larvae



Courtesy of Dr. David G Armstrong/SALSA. For more information, visit www.toeandflow.com.

Types of wound healing



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WOUND DRESSINGS

Irrigation

- There is no high-level evidence to support the use of any particular additive to the irrigant, nor any particular additive over another.
- The act of irrigation and the volume of irrigant probably provides the primary positive benefits.

Warm, isotonic (normal) saline is typically used; however, systematic reviews have found no significant diferences in rates of infection for tap water compared with saline for wound cleansing .

The addition of dilute iodine or other antiseptic solutions (eg, chlorhexidine, hydrogen peroxide, sodium hypochlorite) is generally unnecessary. Such additives have minimal action against bacteria, and some, but not all, may impede wound healing.

WOUND PACKING

- A traditional gauze dressing is often used to pack wounds to aid in continuing debridement of devitalized tissue from the wound bed.
- The gauze is moistened with normal saline or tap water and placed into the wound and covered with dry layers of gauze.
- As the moistened gauze dries, it adheres to surface tissues, which are then removed when the dressing is changed. Dressing changes should be frequent enough that the gauze does not dry out completely, which can be two to three times daily.

WOUND PACKING

- A disadvantage of gauze dressings is that they can also remove developing granulation tissue, resulting in reinjury.
- Thus, these dressings are discontinued when all the necrotic tissue has been removed and granulation is occurring.
- An alternative to gauze dressing for managing wounds with significant dead space is negative pressure wound therapy.

WOUND PACKING

- Many of the materials that are used as topical dressings for wounds (foams, alginates, hydrogels) can be molded into the shape of the wound and are useful for wound packing.
- As with their use in dressing wounds, there is little consensus over what constitutes the best material for wound packing.
- Wound dressing changes associated with large defects can be managed without repeated applications of tape to the skin by using Montgomery straps.

- There is little clinical evidence to aid in the choice between the different types of wound dressings.
- Consensus opinion supports the following general principles for chronic wound management ,but similar principles may be used for acute wound management:

- Hydrogels for the debridement stage.
- Low-adherent dressings that maintain moisture balance for the granulation stage
- Low-adherent dressings for the epithelialization stage.

- Dressings are typically changed once a day or every other day to avoid disturbing the wound healing environment.
- Because some dressings may impede some aspects of wound healing, they should be used with caution.
- As examples, alginate dressings with high calcium content may impede epithelialization by triggering premature terminal diferentiation of keratinocytes ,and highly silver-containing dressings are potentially cytotoxic and should not be used in the absence of significant infection.

Wound management dressing guide

Type of tissue in the wound	Therapeutic goal	Role of dressing	Treatment options		
			Wound bed preparation	Primary dressing	Secondary dressing
▪ Necrotic, black, dry	▪ Remove devitalized tissue ▪ Do not attempt debridement if vascular insufficiency suspected ▪ Keep dry and refer for vascular assessment	▪ Hydration of wound bed ▪ Promote autolytic debridement	▪ Surgical or mechanical debridement	▪ Hydrogel ▪ Honey	▪ Polyurethane film dressing
▪ Sloughy, yellow, brown, black or grey ▪ Dry to low exudate	▪ Remove slough ▪ Provide clean wound bed for granulation tissue	▪ Rehydrate wound bed ▪ Control moisture balance ▪ Promote autolytic debridement	▪ Surgical or mechanical debridement if appropriate ▪ Wound cleansing (consider antiseptic wound cleansing solution)	▪ Hydrogel ▪ Honey	▪ Polyurethane film dressing ▪ Low adherent (silicone) dressing

Wound management dressing guide

Type of tissue in the wound	Therapeutic goal	Role of dressing	Treatment options		
			Wound bed preparation	Primary dressing	Secondary dressing
▪ Sloughy, ▪ Granulating, clean, red ▪ Moderate to high exudate	▪ Remove slough ▪ Exudate management ▪ Provide healthy wound bed for epithelialization	▪ Absorb excess ▪ Maintain moisture balance ▪ Protect new tissue growth	▪ Surgical or ▪ Wound cleansing ▪ Consider barrier products	▪ Absorbent dressing ▪ Absorbent dressing (alginate/CMC/foam) ▪ Low adherent (silicone) dressing ▪ For deep wounds, use cavity strips, rope or ribbon versions	▪ Retention allergy potential and secondary complications
▪ Epithelializing, red, pink ▪ No to low exudate	▪ Promote epithelialization and wound maturation (contraction)	▪ Protect new tissue growth		▪ Hydrocolloid (thin) ▪ Polyurethane film dressing ▪ Low adherent (silicone) dressing	
▪ Infected ▪ Low to high exudate	▪ Reduce bacterial load ▪ Exudate management ▪ Odor control	▪ Antimicrobial action ▪ Moist wound healing ▪ Odor absorption	▪ Wound cleansing (consider antiseptic wound cleansing solution) ▪ Consider barrier products	▪ Antimicrobial dressing	

Antiseptics and antimicrobial agents

Iodine-based

- Cadexomer iodine (eg, Iodosorb) is an antimicrobial that reduces bacterial load within the wound and stimulates healing by providing a moist wound environment .
- Cadexomer iodine is bacteriocidal to all gram positive and gram-negative bacteria.
- For topical preparations, there is some evidence to suggest that cadexomer iodine generates higher healing rates than standard care but should likely only be considered for use on a short term basis.

Silver-based

- Although silver is toxic to bacteria, silver-containing dressings have not demonstrated significant benefits in comparison with other topical wound dressings .
- A systematic review evaluating topical silver in infected wounds identifed three trials that treated 847 participants with various silver-containing dressings .
- One trial compared silver-containing foam (Contreet) with hydrocellular foam (Allevyn) in patients with leg ulcers. The second compared a silver-containing alginate (Silvercel) with an alginate alone (Algosteril). The third trial compared a silver-containing foam dressing (Contreet) with best local practice in patients with chronic wounds.

Silver-based

- Silver-containing foam dressings were not found to significantly improve ulcer healing at four weeks compared with non-silver-containing dressings for best local practices.
- Nevertheless, silver dressings are used by many clinicians to decrease the heavy bacterial surface contamination.

Honey

- Honey has been used since ancient times for the management of wounds. Honey has broad-spectrum antimicrobial activity due to its high osmolarity and high concentration of hydrogen peroxide .
- Medical-grade honey products are now available as a gel, paste, and impregnated into adhesive, alginate, and colloid dressings .
- Based upon the results of systematic reviews evaluating honey to aid healing in a variety of wounds, there are insuficient data to provide any recommendations for the routine use of honey for all wound types; specific wound types, such as burns, may bene t, whereas others, such as chronic venous ulcers, may not.

Type	Actions	Indications/use	Precautions/contraindications
Alginates/CMC*	▪ Absorb fluid. ▪ Promote autolytic debridement. ▪ Moisture control. Conformability to wound bed.	▪ Moderate to high exuding wounds. ▪ Special cavity presentations in the form of rope or ribbon. ▪ Combined presentation with silver for antimicrobial activity.	▪ Do not use on dry/necrotic wounds. ▪ Use with caution on friable tissue (may cause bleeding). ▪ Do not pack cavity wounds tightly.
Foams	▪ Absorb fluid. ▪ Moisture control. ▪ Conformability to wound bed.	▪ Moderate to high exuding wounds. ▪ Special cavity presentations in the form of strips or ribbon. ▪ Low-adherent versions available for patients with ▪ fragile skin. Combined presentation with silver or PHMB for antimicrobial activity.	▪ Do not use on dry/necrotic wounds or those with minimal exudate.
Honey	▪ Rehydrate wound bed. ▪ Promote autolytic debridement. Antimicrobial action.	▪ Sloughy, low to moderate exuding wounds. ▪ Critically colonized wounds or clinical signs of infection.	▪ May cause "drawing" pain (osmotic effect). ▪ Known sensitivity.
Hydrocolloids	▪ Absorb fluid. ▪ Promote autolytic debridement.	▪ Clean, low to moderate exuding wounds. ▪ Combined presentation with silver for antimicrobial activity.	▪ Do not use on dry/necrotic wounds or high exuding wounds. ▪ May encourage ▪ overgranulation. May cause maceration.

Type	Actions	Indications/use	Precautions/contraindications
Hydrogels	▪ Rehydrate wound bed. ▪ Moisture control. ▪ Promote autolytic debridement. ▪ Cooling.	▪ Dry/low to moderate exuding wounds. ▪ Combined presentation with silver for antimicrobial activity.	▪ Do not use on highly exuding wounds or where anaerobic infection is suspected. ▪ May cause maceration.
Iodine	▪ Antimicrobial action.	▪ Critically colonized wounds or clinical signs of infection. ▪ Low to high exuding wounds.	▪ Do not use on dry necrotic tissue. ▪ Known sensitivity to iodine. ▪ Short-term use recommended (risk of systemic absorption).
Low-adherent wound contact layer (silicone)	▪ Protect new tissue growth. ▪ Atraumatic to periwound skin. ▪ Conformable to body contours.	▪ Low to high exuding wounds. ▪ Use as contact layer on superficial low exuding wounds.	▪ May dry out if left in place for too long. ▪ Known sensitivity to silicone.
PHMB	▪ Antimicrobial action.	▪ Low to high exuding wounds. ▪ Critically colonized wounds or clinical signs of infection. ▪ May require secondary dressing.	▪ Do not use on dry/necrotic wounds. ▪ Known sensitivity.
Odor control (eg, activated charcoal)	▪ Odor absorption.	▪ Malodorous wounds (due to excess exudate). ▪ May require antimicrobial if due to increased bioburden.	▪ Do not use on dry wounds.

Properties of topical agents and dressing materials

Protease modulating	▪ Active or passive control of wound protease levels.	▪ Clean wounds that are not progressing despite correction of underlying causes, exclusion of infection, and optimal wound care.	▪ Do not use on dry wounds or those with leathery eschar.
Silver	▪ Antimicrobial action.	▪ Critically colonized wounds or clinical signs of infection. ▪ Low to high exuding wounds. ▪ Combined presentation with foam and alginates/CMC for increased absorbency. Also in paste form.	▪ Some may cause discoloration. ▪ Known sensitivity. ▪ Discontinue after 2 weeks if no improvement and reevaluate.
Polyurethane film	▪ Moisture control. ▪ Breathable bacterial barrier. ▪ Transparent (allow visualization of wound).	▪ Primary dressing over superficial low exuding wounds. ▪ Secondary dressing over alginate or hydrogel for rehydration of wound bed.	▪ Do not use on patients with fragile/compromised periwound skin. ▪ Do not use on moderate to high exuding wounds.

Other more advanced dressings (eg, collagen and bioengineered tissue products) may be considered for wounds that are hard to heal [1].

CMC: carboxymethylcellulose; PHMB: polyhexamethylene biguanide.

* Wound dressings may contain alginates or CMC only; alginates may also be combined with CMC.

سایردرمان های کمکی

- We suggest not using the following treatments to address DFIs: (a) adjunctive granulocyte colony-stimulating factor (G-CSF) treatment or (b) topical antiseptics, silver preparations, honey, bacteriophage therapy, or negative- pressure wound therapy (with or without instillation). (Conditional; Low).

- We suggest not using topical (sponge, cream, and cement) **antibiotics** in combination with systemic antibiotics for treating either soft-tissue infections or osteomyelitis of the foot in patients with diabetes. (Conditional; Low).
- We suggest not using Hyperbaric oxygen (HBO) therapy or topical oxygen therapy as an adjunctive treatment for the sole indication of treating a DFI. (Conditional; Low).

- Note: the available data did not allow making a recommendation on the use of rifampicin for the treatment of diabetes- related osteomyelitis of the foot.

Table 12.2—Categories of advanced wound therapies

Negative-pressure wound therapy
Standard electrically powered
Mechanically powered
Oxygen therapies
Hyperbaric oxygen therapy
Topical oxygen therapy
Oxygen-releasing sprays, dressings
Biophysical
Electrical stimulation, diathermy
Pulsed electromagnetic fields, pulsed radiofrequency energy
Low-frequency noncontact ultrasound
Extracorporeal shock wave therapy
Growth factors
Becaplermin: platelet-derived growth factor
Fibroblast growth factor
Epidermal growth factor
Autologous blood products
Platelet-rich plasma
Leukocyte, platelet, fibrin multilayered patches
Whole blood clot

- Acellular matrix tissues
  - Xenograft dermis
    - Bovine dermis
  - Xenograft acellular matrices
    - Small intestine submucosa
    - Porcine urinary bladder matrix
    - Ovine forestomach
    - Equine pericardium
    - Fish skin graft
    - Bovine collagen
      - Bilayered dermal regeneration matrix
    - Human dermis products
    - Human pericardium
    - Placental tissues
      - Amniotic tissues/amniotic fluid
      - Umbilical cord
- Bioengineered allogeneic cellular therapies
  - Bilayered skin equivalent (human keratinocytes and fibroblasts)
  - Dermal replacement therapy (human fibroblasts)
- Stem cell therapies
  - Autogenous: bone marrow–derived stem cells
  - Allogeneic: amniotic matrix with mesenchymal stem cells
- Miscellaneous active dressings
  - Hyaluronic acid, honey dressings, etc.
  - Sucrose octasulfate dressing

- There have been a number of developments in the treatment of ulcerations over the years .These include negative-pressure therapy, growth factors, bioengineered tissue, acellular matrix tissue, stem cell therapy, hyperbaric oxygen therapy, and, most recently, topical oxygentherapy.

- While there is literature to support many modalities currently used to treat diabetic foot wounds, robust RCTs are often lacking.
- However, it is agreed that the initial treatment and evaluation of ulcerations include the following five basic principles of ulcer treatment.

Negative pressure wound therapy

- Based on randomized trials showing improved wound healing ,we suggest NPWT for extensive open wounds following debridement for infection and necrosis, or following partial foot amputation, provided there is no residual necrotic tissue or infected bone (osteomyelitis).

- NPWT, also called vacuum-assisted closure (VAC), involves the application of controlled sub atmospheric pressure to the surface of the ulcer.

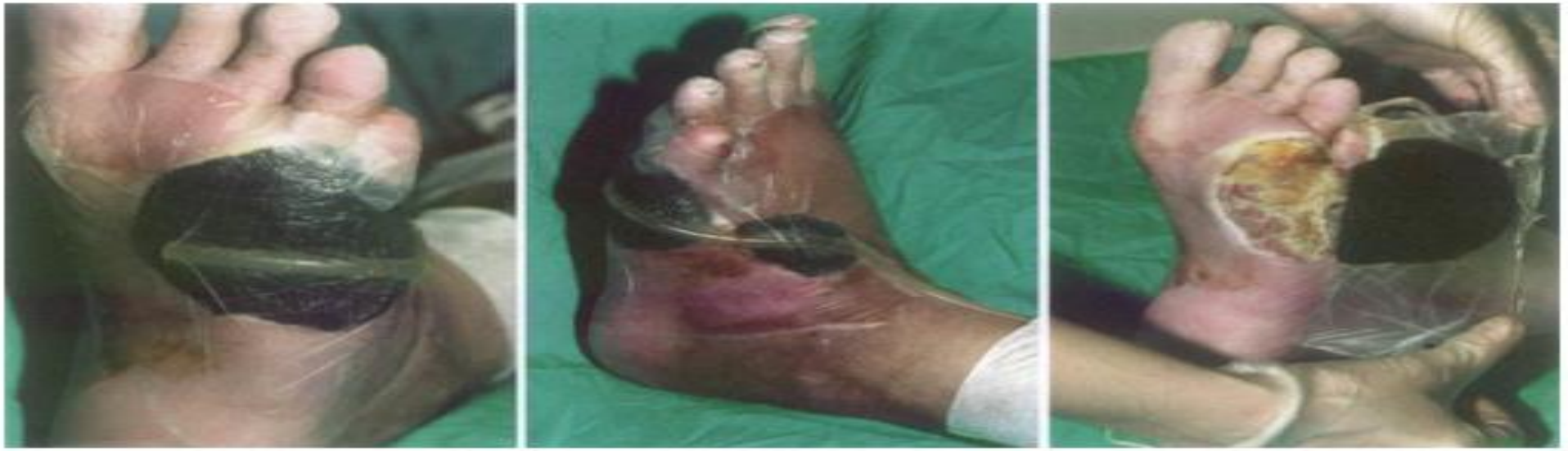
- NPWT enhances healing by increasing wound **perfusion**, **reducing edema**, **reducing the local bacterial** burden, and **increasing the formation of granulation** tissue.

Negative pressure wound therapy

- NPWT appears to improve healing of diabetic foot ulcers, as well as wounds following diabetic foot surgery .
- NPWT also **decreases the length of hospitalization**, **complication rates**, and **costs** .
- Among ve trials in a systematic review, NPWT signifcantly increased the chance of foot ulcer healing compared with dressings (risk ratio [RR] 1.40, 95% CI 1.14-1.72) .

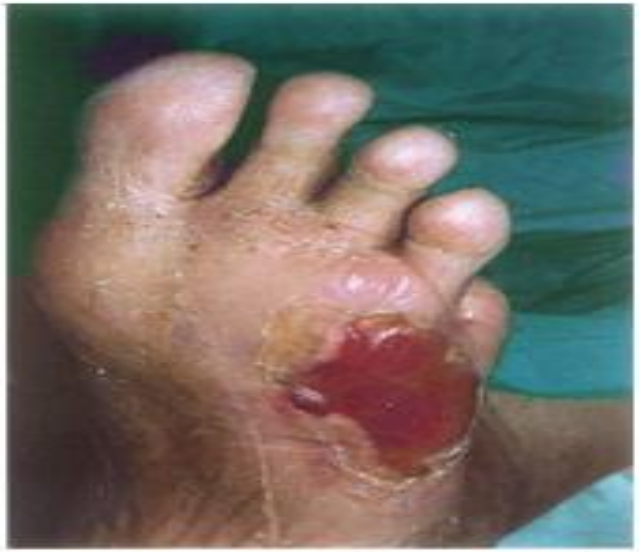
Negative pressure wound therapy

- Among three trials, NPWT reduced the risk of amputation (RR 0.33, 95% CI 0.15-0.70). There was no effect on ulcer recurrence.
- For managing postoperative wounds, a multicenter trial followed 162 diabetic patients for 16 weeks following partial foot amputation [59]. Compared with the control group, the NPWT group had a significantly higher percentage of patients with healed wounds (56 versus 39 percent), and shorter time to complete closure (42 versus 84 days).



(a) (b) (c)

(d)



(e)

Fig. 4.14 (a) VAC pump sponge attached to plantar aspect of foot. (b) VAC pump sponge also attached to dorsolateral aspect of foot. (c) Pump sponge being removed from foot. (d) The VAC pump and drainage tube, canister and sponges. (e) Ulcer healing after 10 days VAC therapy.

Hyperbaric oxygen

- Adjunctive systemic hyperbaric oxygen therapy also

Hyperbaric oxygen therapy (HBOT)

- Hyperbaric oxygen therapy (HBOT) may be associated with improved healing as a component of diabetic ulcer management, but the indications for HBOT in the treatment of nonhealing diabetic foot ulcers remain uncertain.
- Most, but not all meta-analyses of randomized trials suggest that hyperbaric oxygen therapy may a benefit in the treatment of diabetic foot ulcers; however, each meta-analysis noted variability in methodologic quality of the included studies .
- The available trials are limited by small sample size and heterogeneity of the wounds being treated (eg, ulcer size, ulcer depth, microbial environment, presence of ischemia.
- No conclusions could be drawn regarding specfic indications for or timing of therapy.

Hyperbaric oxygen therapy (HBOT)

- A pooled analysis found significantly improved wound healing (OR 9.99, 95% CI 3.97-25.1) and decreased risk of amputation (odds ratio [OR] 0.24, 95% CI 0.14-0.43) for HBOT .
- A later meta-analysis found similar results .As an example of these effects, in one of the larger trials that included 70 patients with severely ischemic foot ulcers, the amputation rate was 9 percent in the treatment group and 33 percent in the control .

Hyperbaric oxygen therapy (HBOT)

- In another trial that included 94 patients, significantly more wounds healed completely in the HBOT group compared with a placebo group (52 versus 29 percent) .
- However, in a later longitudinal cohort of 6259 patients with diabetic foot ulcers, use of HBOT did not result in better wound healing, and amputation rates were similar to those not receiving the therapy.

Topical oxygen therapy

- — Topical oxygen therapy/continuous di ffusion of oxygen appears to be associated with improved healing of diabetic foot ulcers .
- This therapy involves local administration of oxygen and appears to improve **epithelialization** by **upregulating** vascular endothelial growth factor (**VEGF**) expression and **collagen synthesis**, **improving overall matrix deposition**, and altering **microbiome ecology.**

Topical oxygen therapy

- Several sham controlled, double-blind randomized trials support the use of this therapy, including a multinational study that included 220 subjects, which reported a 4.5-fold greater rate of healing in those receiving active topical oxygen therapy at home compared with placebo .
- Other similarly designed studies have reported similar findings .

Shock wave therapy

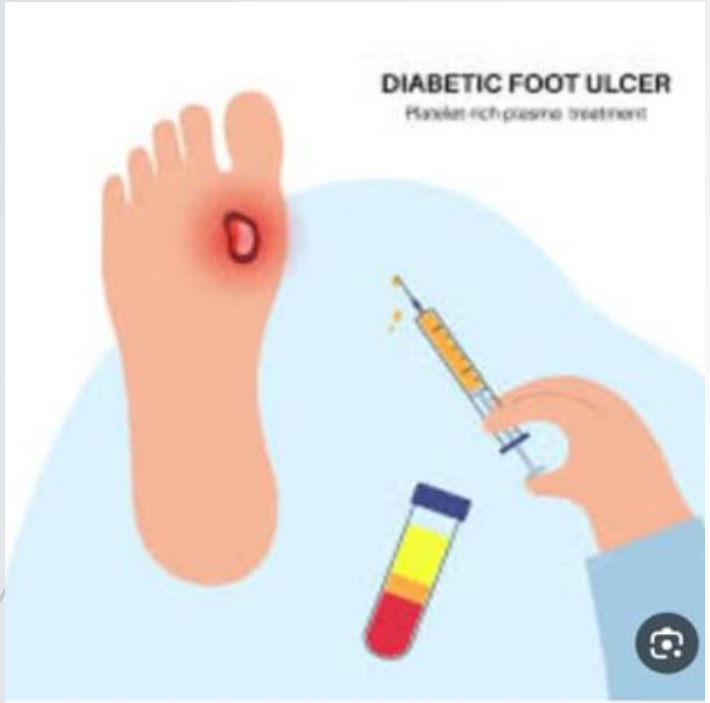
- Shock wave therapy, which consists of treatment using a handheld probe to deliver high-energy pulses locally to the wound, purportedly **increases local perfusion** and a**ngiogenesis**, disrupts biofi lm, and may **upregulate growth factors**.
- Observational and small randomized trials suggest that shock wave therapy may improve healing of chronic diabetic foot ulcers .
- In two proprietary trials, 336 patients were randomly assigned to shock wave therapy (DermaPACE) or usual care consisting of wet-to-dry dressings or debridement. At 24-week follow-up, significantly more patients in the shock wave group achieved complete wound closure compared with usual care (44 versus 30 percent.)

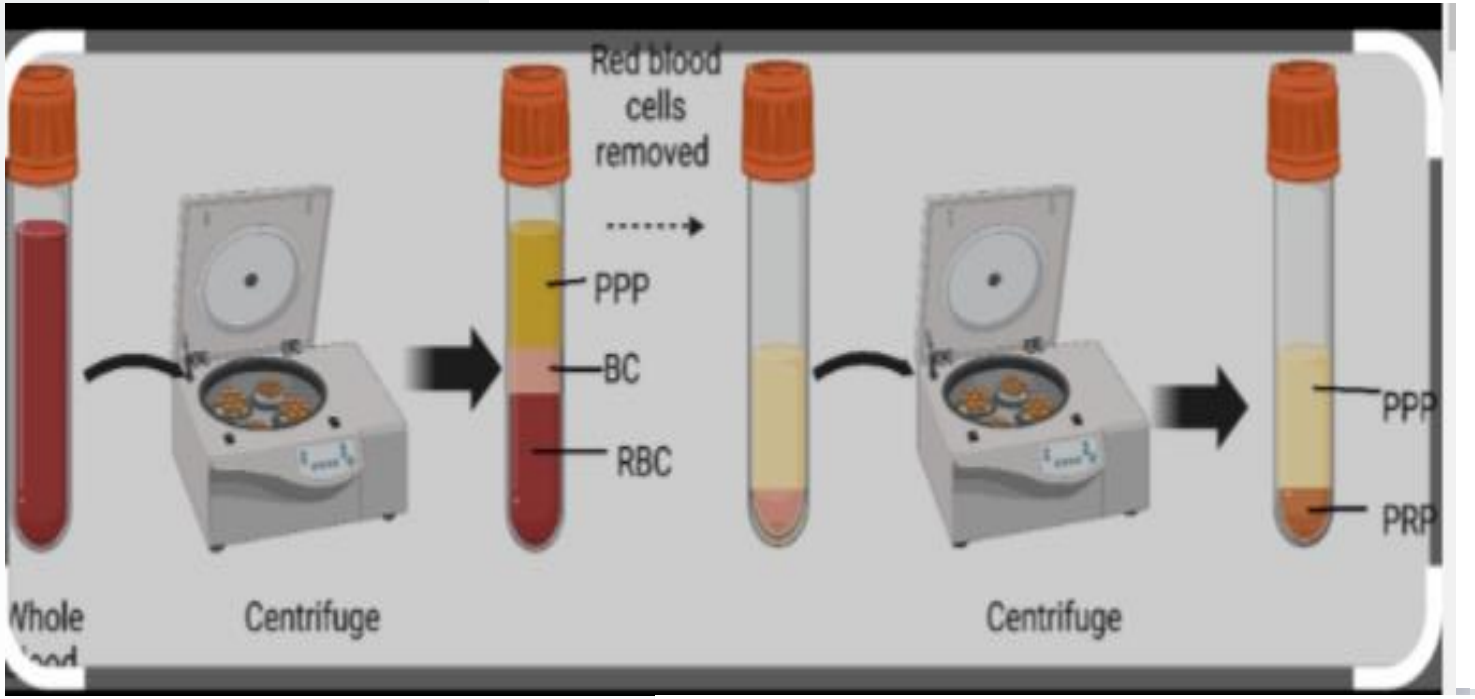
Growth factors

- Platelet-derived growth factor – Becaplermin is a PDGF gel preparation that promotes cellular proliferation and angiogenesis and thereby improves wound healing .
- It is approved for use in the United States as an adjuvant therapy for the treatment of diabetic foot ulcers and is the only pharmacological agent approved for the treatment of chronic wounds.
- The growth factor is delivered in a topical aqueous-based sodium carboxymethylcellulose gel. It is indicated for noninfected diabetic foot ulcers that extend into the subcutaneous tissue and have an adequate vascular supply

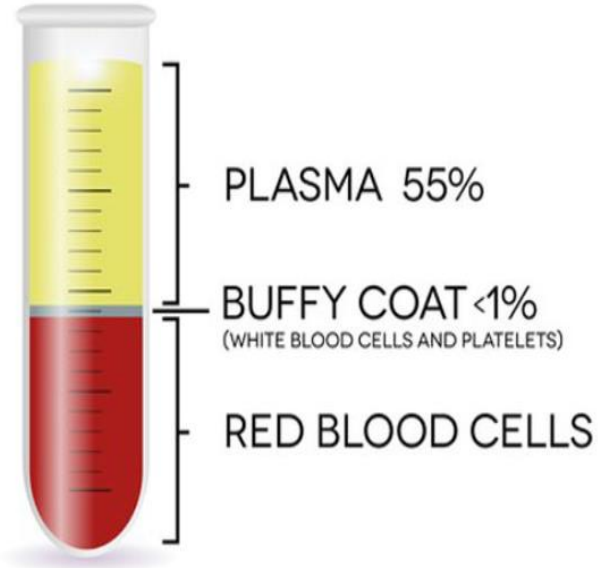
- A black box warning mentions a concern for malignancy; however, the overall malignancy risk is believed to be low.
- Malignancy complications of this therapy may reflect usage of the agent in multiple courses of treatment, and possible selective transformation of wounds already at risk .
- A post-marketing study found an increased rate of mortality secondary to malignancy in patients treated with three or more tubes of becaplermin (3.9 versus 0.9 per 1000 person years) compared with controls .

Platelet-Rich plasma


DIABETIC FOOT ULCER


Red blood cells removed
PPP
BC
RBC
Whole
Centrifuge
Centrifuge
PPP
PRP


CEN-SWING PRP BAG
Centrifuge
PRP
START
STOP
DOWN
UP
TIME
DOWN
UP
RPM & RCF


PLASMA 55%
BUFFY COAT <1%
(WHITE BLOOD CELLS AND PLATELETS)
RED BLOOD CELLS 45%

Review > Front Endocrinol (Lausanne). 2023 Nov 18:14:1256081.
doi: 10.3389/fendo.2023.1256081. eCollection 2023.

Platelet-rich plasma for the treatment of diabetic foot ulcer: a systematic review

Hong OuYang [1], Yi Tang [# 1], Fan Yang [# 1], Xin Ren [1], Jing Yang [1], Hongyi Cao [1], Yifan Yin [2]

- Twenty studies were evaluated, and nineteen measures for the evaluation of the efficacy of PRP in DFU treatment were introduced by eliminating relevant duplicate measures. The meta-analysis found that PRP was significantly improve the healing rate(OR = 4.37, 95%CI 3.02-6.33, P < 0.001) and shorten the healing time(MD =-3.21, 95% CI-3.83 to-2.59,P < 0.001)of patients with DFU when compared to the conventional treatment, but there was no significant difference in reducing the of ulcer area(MD = 5.67, 95% CI-0.77 to 12.11, P =0.08>0.05).

Epidermal growth factor

- Epidermal growth factor – In a study of chronic venous ulcers, topical application of human recombinant epidermal growth factor was associated with a greater reduction in ulcer size (7 versus 3 percent reduction) and higher ulcer healing rate (35 versus 11 percent) compared with placebo, but these diferences were not statistically significant .Epithelialization was not significantly affected.

Granulocyte-macrophage colony stimulating factor

- Granulocyte-macrophage colony stimulating factor – Intradermal injections of GM-CSF promote healing of chronic leg ulcers, including venous ulcers .
- A trial that randomly assigned 60 patients with venous ulcers to four weekly injections with GM-CSF 200 mcg, 400 mcg, or placebo found significantly higher rates of healing at 13 weeks in the GM-CSF group (57, 61, and 19 percent, respectively) .GM-CSF has been used in various types of chronic wounds to promote healing .

Skin grafts and substitutes

- — Human skin grafts and bioengineered skin substitutes (eg, **Dermagraft**, **Apligraf**, **TheraSkin**, Graftskin, **EpiFix**, **Zelen**, **Graftjacket**, **Hyalograft 3D**, **Kaloderm**, **OrCel**) have been studied in individuals with noninfected, nonischemic chronic plantar diabetic foot ulcers .
- A systematic review identifed 17 trials using skin grafts or substitutes for the treatment of diabetic foot ulcers. The incidence of completed closure of diabetic foot ulcers was significantly improved for the skin grafts or substitutes compared with standard care (RR 1.55, 95% CI 1.30-1.85).

روش درمانی	مکانیسم عملکرد	مزایا	محدودیت‌ها	کاربردها
تحریک الکتریکی (Electrical Stimulation)	ایجاد جریان الکتریکی برای تحریک مهاجرت سلول‌های ترمیمی و افزایش جریان خون به ناحیه زخم.	- تسریع بازسازی بافت - افزایش جریان خون - بهبود اکسیژن‌رسانی	- نیاز به تجهیزات خاص - مطالعات محدود با کیفیت پایین	زخم‌های مزمن و دیابتی
انرژی رادیوفرکانس پالسی (Pulsed Radiofrequency Energy)	ارسال امواج رادیویی پالسی برای تحریک متابولیسم سلولی و افزایش تولید فاکتورهای رشد.	- کاهش التهاب - تحریک بازسازی بافت - بهبود جریان خون	- شواهد علمی محدود - نیاز به تجهیزات پیشرفته	زخم‌های التهابی و مزمن
شوک‌ویو خارجی (Extracorporeal Shock Wave Therapy)	ارسال امواج شوک به ناحیه زخم برای تحریک تولید فاکتورهای رشد و افزایش جریان خون.	- تحریک تولید فاکتورهای رشد - کاهش درد - تسریع التیام	- ممکن است دردناک باشد - نیاز به جلسات مکرر	زخم‌های مزمن، دردناک یا مقاوم به درمان
اولتراسوند غیرتماسی با فرکانس پایین (Low-Frequency Noncontact Ultrasound)	ایجاد امواج صوتی غیرتماسی برای تمیز کردن زخم و حذف بافت مرده (دبریدمان).	- حذف بافت مرده - کاهش بار میکروبی - تسهیل فرآیند	- هزینه بالا - نیاز به اپراتور ماهر	دبریدمان زخم‌های عفونی یا دارای بافت نکروتیک

Effect of Cold Atmospheric Plasma Therapy vs Standard Therapy Placebo on Wound Healing in Patients With Diabetic Foot Ulcers

A Randomized Clinical Trial

Bernd Stratmann [1], Tania-Cristina Costea [1], Catharina Nolte [1], Jonas Hiller [1], Jörn Schmidt [2], Jörg Reindel [2], Kai Masur [3,4], Wolfgang Motz [2], Jürgen Timm [5], Wolfgang Kerner [2], Diethelm Tschoepe [1,✉]

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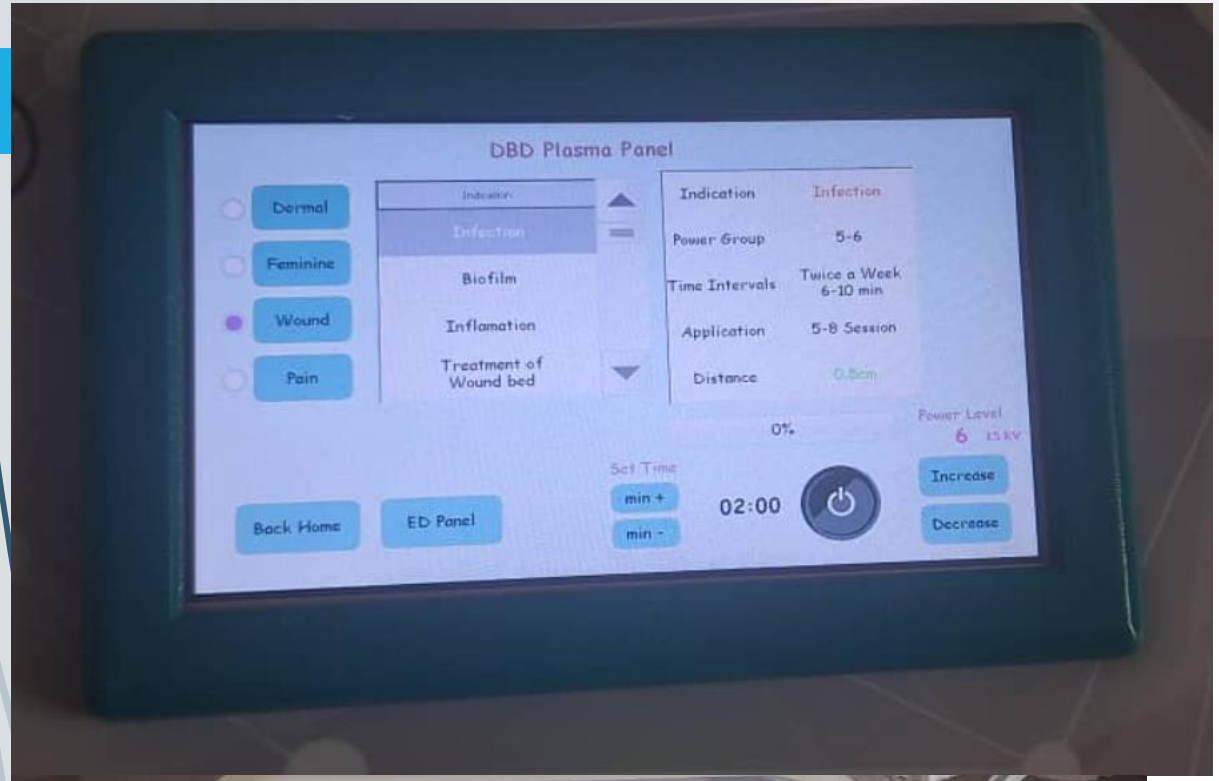
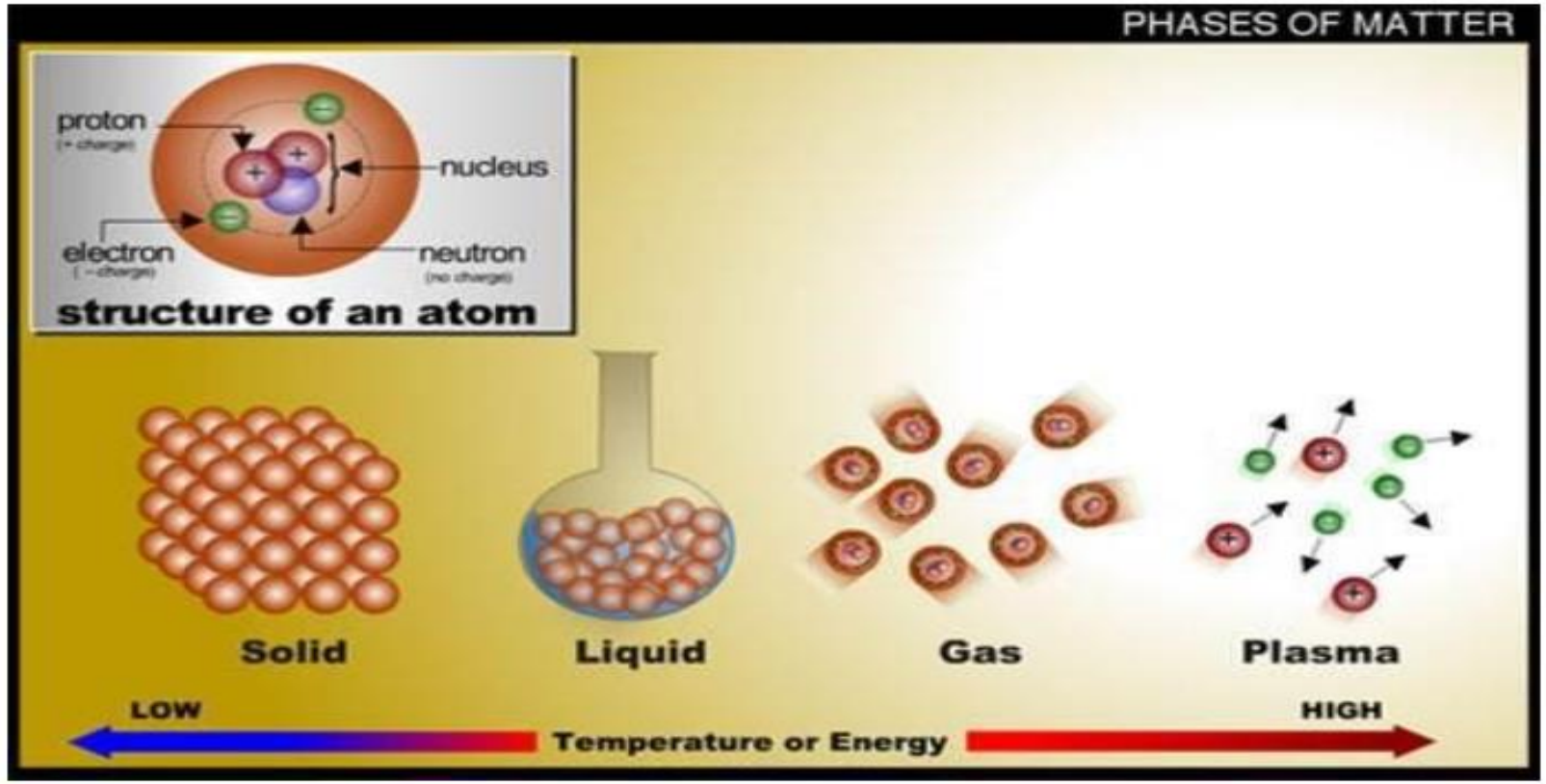
Of 65 diabetic foot ulcer wounds from 45 patients assessed for study, 33 wounds from 29 patients were randomized to CAP and 32 wounds from 28 to placebo, with 62 wounds from 43 patients (31 wounds per group) included for final evaluation (mean [SD] age, 68.5 [9.1] years for full sample). Four patients with 5 wounds of 31 (16.1%) wounds in the CAP group and 3 patients with 4 wounds of 31 (13%) wounds in the placebo group were active smokers. CAP therapy yielded a significant increase in wound healing, both in total mean (SD) area reduction (CAP vs placebo relative units, −26.31 [11.72]; $P = .03$) and mean (SD) time to relevant wound area reduction (CAP vs placebo relative units, 10% from baseline, 1.60 [0.58]; $P = .009$). Reduction of infection and microbial load was not significantly different between CAP and placebo. No therapy-related adverse events occurred during therapy; patient's perceptions during therapy were comparable.


DBD Plasma Panel
Dermal
Feminine
Wound
Pain
Indication
Infection
Biofilm
Inflamation
Treatment of Wound bed
Indication Infection
Power Group 5-6
Time Intervals Twice a Week 6-10 min
Application 5-8 Session
Distance
0%
Power Level
6
Set Time
min +
min -
02:00
Increase
Decrease
Back Home
ED Panel


Plasma Surgical Unit
ED Plasma
DBD Plasma

پلاسماکلد سه حالت اول ماده عبارت است از جامد ، مایع و گاز که ماده از یک حالت به حالت بعد با اضافه کردن انرژی (اغلب به صورت گرما) تبدیل میشود . به عنوان مثال ، حالت "جامد" آب یخ است و با افزودن گرما (انرژی) به آب تبدیل و آب با افزودن گرمای بیشتری تبخیر می شود . پلاسما بعد از حالت گاز با اضافه کردن انرژی بیشتر بوجود می آید. هنگامی که به مولکول های گاز به بیش از پتانسیل یونیزاسیون خود انرژی داده می شوند ، الکترون ها قادر به فرار از ابر الکترون می شوند . این کار به ایجاد جفت یونهای با بار مثبت و الکترونهای با بار منفی منجر می شود.



پیگیری

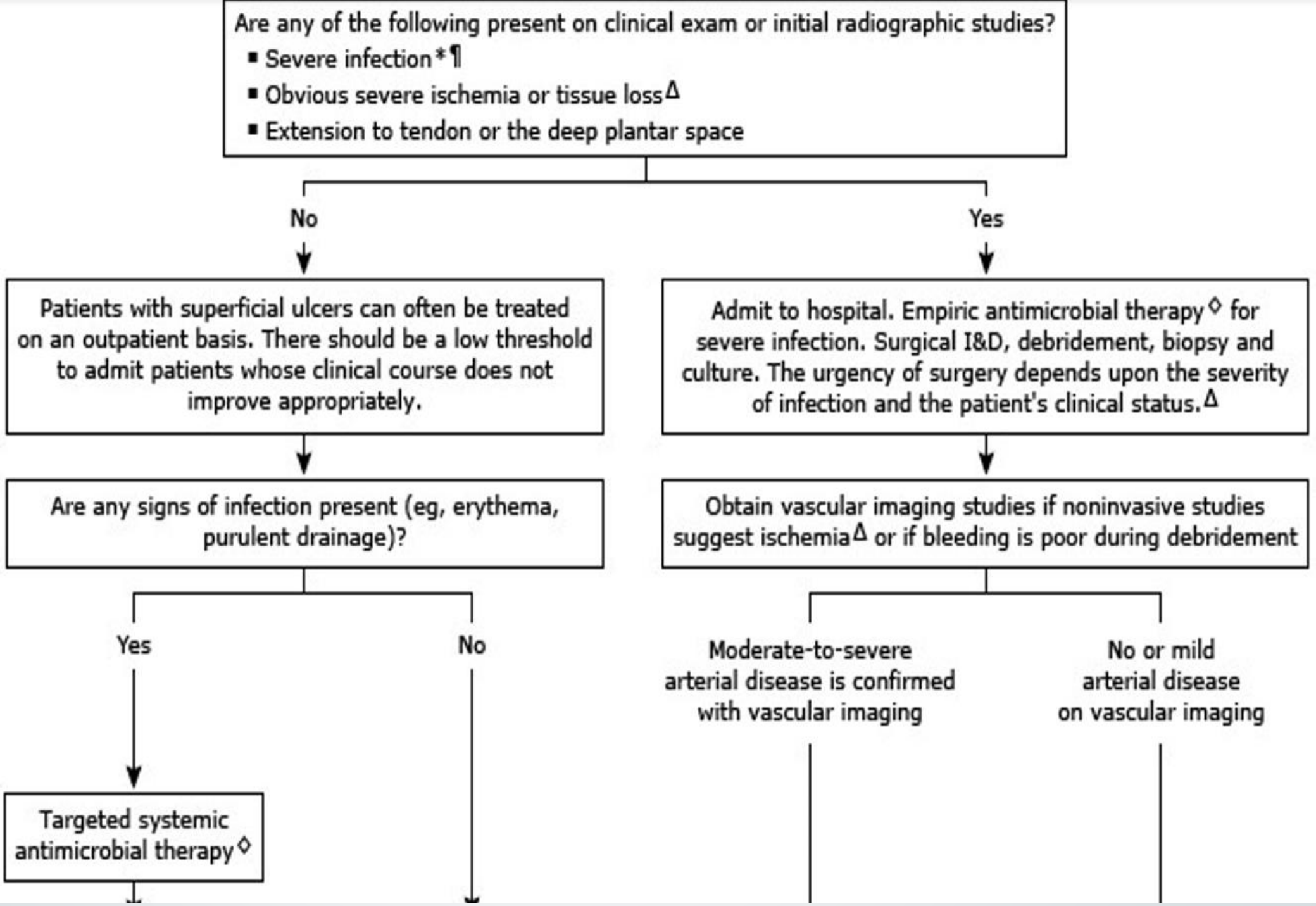
follow-up

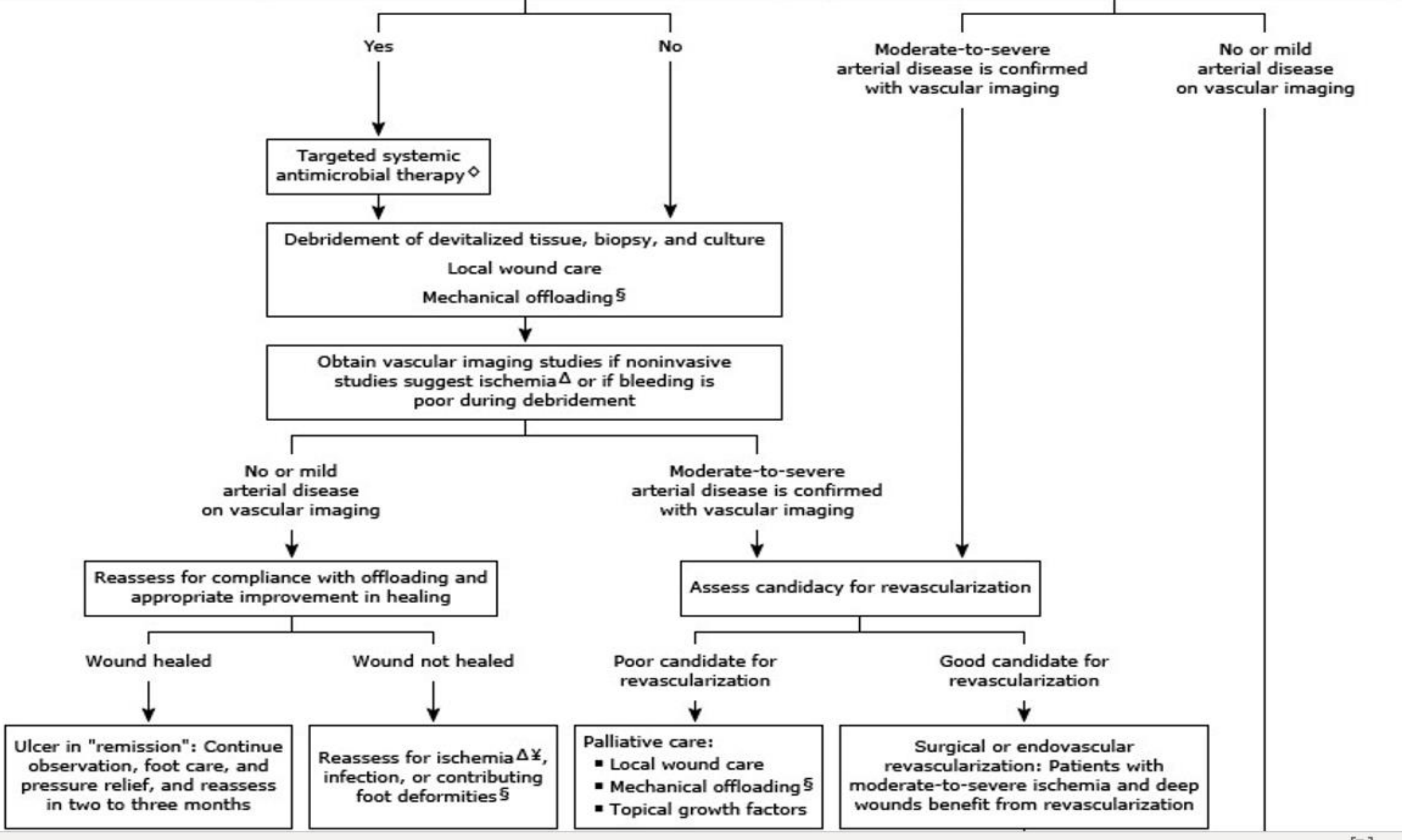
— Close follow-up is important to ensure continued improvement and to evaluate the need for modifcation of antimicrobial therapy, further imaging, or additional surgical intervention.

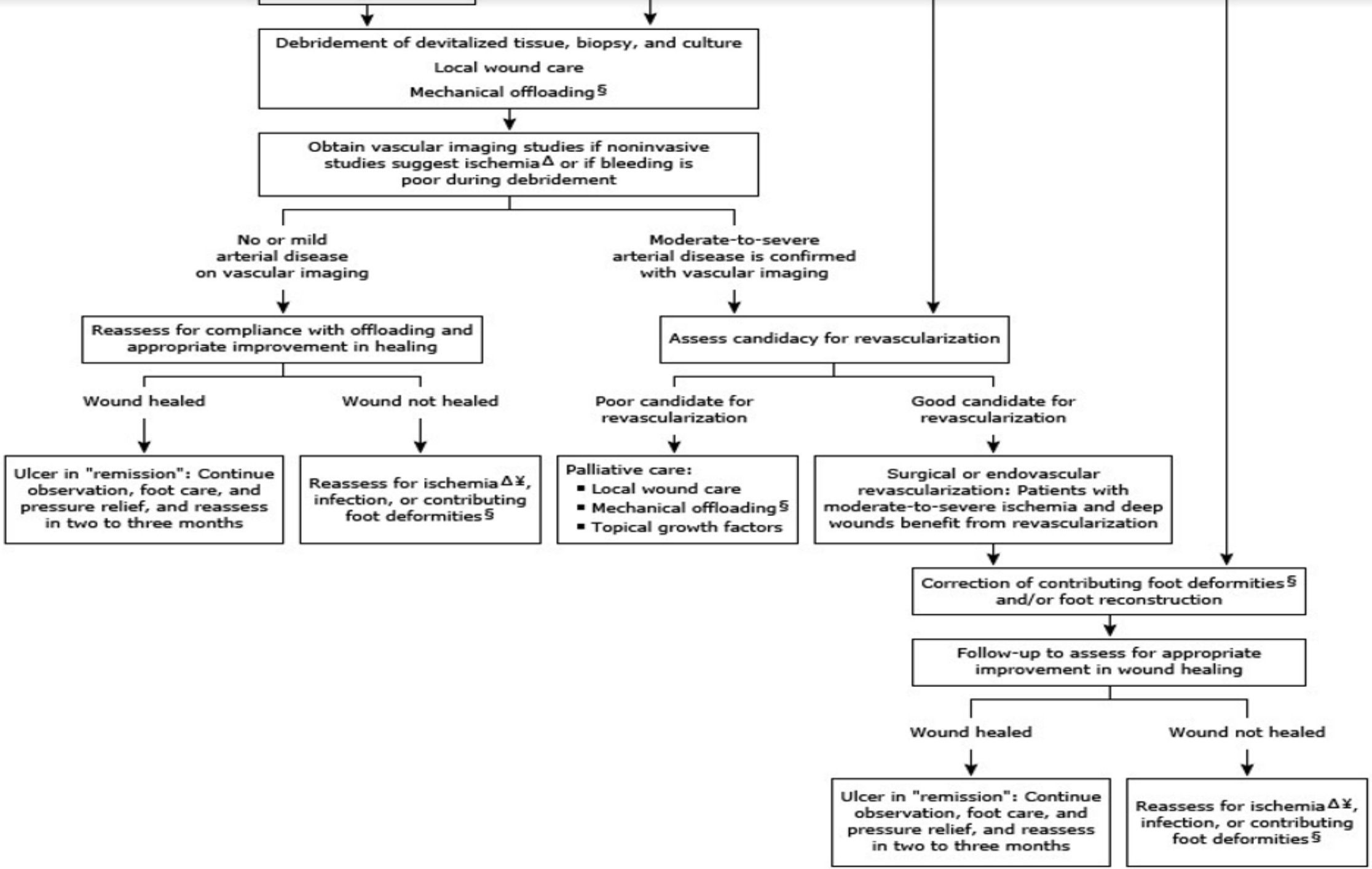
Wound healing and a decrease in previously elevated inflammatory markers can be signs of clinical resolution and may be particularly helpful in cases of osteomyelitis.

If clinical evidence of infection persists beyond the expected duration, issues of patient adherence to therapy, development of antibiotic resistance, an undiagnosed deeper infection (eg, abscess or osteomyelitis), or ischemia should be evaluated.

الگوریتم کلی مدیریت زخم دیابتی


Are any of the following present on clinical exam or initial radiographic studies?
Severe infection*¶
Obvious severe ischemia or tissue loss△
Extension to tendon or the deep plantar space
No
Yes
Patients with superficial ulcers can often be treated on an outpatient basis. There should be a low threshold to admit patients whose clinical course does not improve appropriately.
Admit to hospital. Empiric antimicrobial therapy◊ for severe infection. Surgical I&D, debridement, biopsy and culture. The urgency of surgery depends upon the severity of infection and the patient's clinical status.△
Are any signs of infection present (eg, erythema, purulent drainage)?
Obtain vascular imaging studies if noninvasive studies suggest ischemia△ or if bleeding is poor during debridement
Yes
No
Moderate-to-severe arterial disease is confirmed with vascular imaging
No or mild arterial disease on vascular imaging
Targeted systemic antimicrobial therapy◊


Yes
No
Moderate-to-severe arterial disease is confirmed with vascular imaging
No or mild arterial disease on vascular imaging
Targeted systemic antimicrobial therapy◇
Debridement of devitalized tissue, biopsy, and culture
Local wound care
Mechanical offloading§
Obtain vascular imaging studies if noninvasive studies suggest ischemiaΔ or if bleeding is poor during debridement
No or mild arterial disease on vascular imaging
Moderate-to-severe arterial disease is confirmed with vascular imaging
Reassess for compliance with offloading and appropriate improvement in healing
Assess candidacy for revascularization
Wound healed
Wound not healed
Poor candidate for revascularization
Good candidate for revascularization
Ulcer in "remission": Continue observation, foot care, and pressure relief, and reassess in two to three months
Reassess for ischemiaΔ¥, infection, or contributing foot deformities§
Palliative care:
Local wound care
Mechanical offloading§
Topical growth factors
Surgical or endovascular revascularization: Patients with moderate-to-severe ischemia and deep wounds benefit from revascularization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Local wound care
Mechanical offloading§
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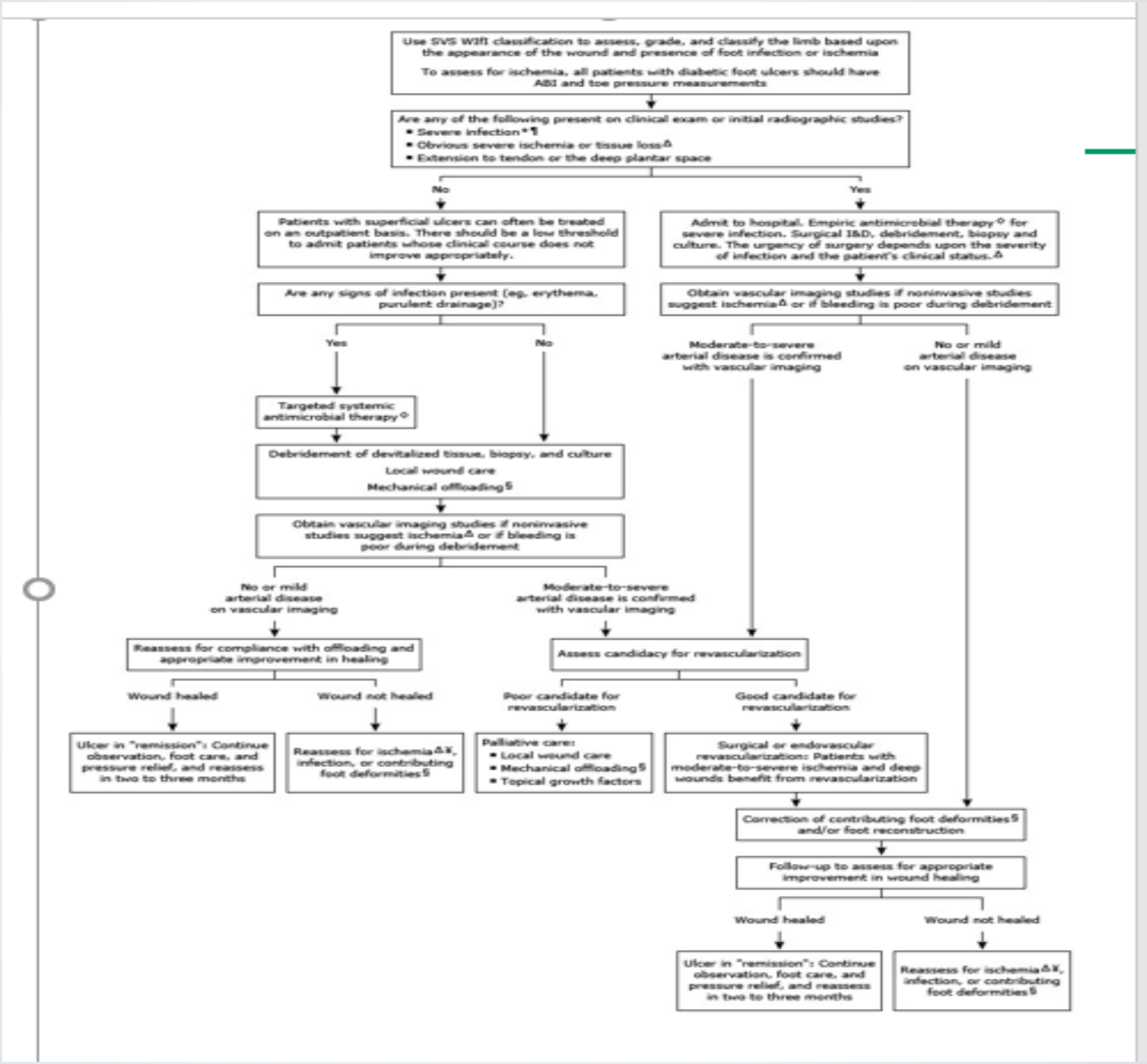
Palliative care:
Local wound care
Mechanical offloading§
Topical growth factors
Surgical or endovascular revascularization: Patients with moderate-to-severe ischemia and deep wounds benefit from revascularization
Correction of contributing foot deformities§ and/or foot reconstruction
Follow-up to assess for appropriate improvement in wound healing
Wound healed
Wound not healed
Ulcer in "remission": Continue observation, foot care, and pressure relief, and reassess in two to three months
Reassess for ischemiaΔ¥, infection, or contributing foot deformities§


Use SVS WIfI classification to assess, grade, and classify the limb based upon the appearance of the wound and presence of foot infection or ischemia
To assess for ischemia, all patients with diabetic foot ulcers should have ABI and toe pressure measurements
Are any of the following present on clinical exam or initial radiographic studies?
Severe infection*¶
Obvious severe ischemia or tissue loss△
Extension to tendon or the deep plantar space
No
Yes
Patients with superficial ulcers can often be treated on an outpatient basis. There should be a low threshold to admit patients whose clinical course does not improve appropriately.
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