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ACR Appropriateness Criteria® on Suspected Osteomyelitis in Patients With Diabetes Mellitus

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Imaging of the diabetic foot is among the most challenging areas of radiology. The authors present a consensus of the suggested tests in several clinical scenarios, such as early neuropathy, soft-tissue swelling, skin ulcer, and suspected osteomyelitis. In most of these situations, magnetic resonance imaging (MRI) with or without contrast is the examination of choice. Most other imaging tests have complementary roles. For soft-tissue swelling or an ulcer, radiography and MRI with or without contrast are suggested. Bone scintigraphy with white blood cell scanning is used when MRI is contraindicated. In patients with diabetes without ulcers, radiography and MRI with or without contrast are suggested; bone scanning may be used when MRI is contraindicated.

Key Words: Appropriateness criteria, infection, diabetes mellitus, osteomyelitis, neuroarthropathy, diagnostic imaging

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SUMMARY OF LITERATURE REVIEW

Over the past 50 years, much has been written about the diabetic foot with little consensus as to whether, when, and what imaging is appropriate. In this overview, we summarize some of the work and draw conclusions on the basis of the available data. We discuss several clinical situations in which osteomyelitis or diabetic pedal disease is suspected but clinical findings differ because of the presence or absence of edema ulceration and neuropathy.

Please note that although several of the variants have similar recommendations, they do present as unique clinical scenarios.

Soft-Tissue Edema Without Ulceration

First, the probability of having osteomyelitis in a diabetic foot without evidence of ulceration is extremely low [1]. Whether there is or is not soft-tissue swelling, these patients have almost no incidence of osteomyelitis and a low incidence of septic arthritis, but some frequency of soft-tissue infections [2]. The only situation in which such a patient can have osteomyelitis is the presence of a "hidden" ulcer that has granulated over and may appear healed. In that situation, the risk for osteomyelitis is still extremely low, because the ulcer would not have granulated over if osteomyelitis were present [3]. Therefore, without a clinically apparent ulcer, the role of imaging might be to diagnose neuropathic disease or to see if there is soft-tissue infection only [3] (see Variant 1).

Neuropathy Without Ulcer

A more difficult question is whether it is neuroarthropathy or soft-tissue infection that is causing soft-tissue swelling

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Variant 1. Soft-tissue edema without ulcer or neuroarthropathy

Radiologic Procedure	Rating	Comments
X-ray foot	9	Initial study. Radiography and MRI are complementary. Both are indicated.
MRI foot with contrast	9	Radiography and MRI are complementary. Both are indicated. Useful for mapping devitalized areas preoperatively. See comments regarding contrast in text under "Anticipated Exceptions."
MRI foot without contrast	9	Radiography and MRI are complementary. Both are indicated.
NUC ^{99m}Tc 3-phase bone scan and ^{111}In WBC scan foot	4	If MRI contraindicated.
NUC ^{99m}Tc 3-phase bone scan foot	1	
NUC ^{111}In WBC scan and ^{99m}Tc sulfur colloid marrow scan foot	1	
NUC ^{99m}Tc 3-phase bone scan and ^{111}In WBC scan and ^{99m}Tc sulfur colloid marrow scan foot	1	
Ultrasound foot	1	
CT foot without contrast	1	
FDG-PET foot	1	

Note: Rating scale: 1 = least appropriate, 9 = most appropriate. CT = computed tomography; FDG-PET = 2-[^{18}F]fluoro-2-deoxyglucose positron emission tomography; MRI = magnetic resonance imaging; NUC = nuclear medicine; WBC = white blood cell.

[4,5]. In a patient who has neuroarthropathy, the risk for infection is usually low without ulceration. Radiography can be used as a screening examination. Computed tomography may pick up neuroarthropathy, which may not be apparent radiographically and may be the cause of the swelling and pain (mimicking infection). Computed tomography can rarely exclude the diagnosis of osteomyelitis definitively if there is no edema in the marrow (fat is visible).

Variant 2. Ulcer with no exposed bone without neuroarthropathy

Radiologic Procedure	Rating	Comments
X-ray foot	9	Initial study. Radiography and MRI are complementary. Both are indicated.
MRI foot with contrast	9	Radiography and MRI are complementary. Both are indicated. Useful for mapping devitalized areas preoperatively. See comments regarding contrast in text under "Anticipated Exceptions."
MRI foot without contrast	9	Radiography and MRI are complementary. Both are indicated.
NUC ^{99m}Tc 3-phase bone scan and ^{111}In WBC scan foot	4	If MRI contraindicated.
NUC ^{99m}Tc 3-phase bone scan foot	1	
NUC ^{111}In WBC scan and ^{99m}Tc sulfur colloid marrow scan foot	1	
NUC ^{99m}Tc 3-phase bone scan and ^{111}In WBC scan and ^{99m}Tc sulfur colloid marrow scan foot	1	
Ultrasound foot	1	
CT foot without contrast	1	
FDG-PET foot	1	

Note: Rating scale: 1 = least appropriate, 9 = most appropriate. CT = computed tomography; FDG-PET = 2-[^{18}F]fluoro-2-deoxyglucose positron emission tomography; MRI = magnetic resonance imaging; NUC = nuclear medicine; WBC = white blood cell.

Variant 3. Ulcer with exposed bone without neuroarthropathy

Radiologic Procedure	Rating	Comments
X-ray foot	9	Initial study. Radiography and MRI are complementary. Both are indicated.
MRI foot with contrast	9	Radiography and MRI are complementary. Both are indicated. Useful for mapping devitalized areas preoperatively. See comments regarding contrast in text under "Anticipated Exceptions."
MRI foot without contrast	9	Radiography and MRI are complementary. Both are indicated.
NUC ^{99m}Tc 3-phase bone scan and ^{111}In WBC scan foot	4	If MRI contraindicated.
NUC ^{99m}Tc 3-phase bone scan foot	1	
NUC ^{111}In WBC scan and ^{99m}Tc sulfur colloid marrow scan foot	1	
NUC ^{99m}Tc 3-phase bone scan and ^{111}In WBC scan and ^{99m}Tc sulfur colloid marrow scan foot	1	
Ultrasound foot	1	
CT foot without contrast	1	
FDG-PET foot	1	

Note: Rating scale: 1 = least appropriate, 9 = most appropriate. CT = computed tomography; FDG-PET = 2-[^{18}F]fluoro-2-deoxyglucose positron emission tomography; MRI = magnetic resonance imaging; NUC = nuclear medicine; WBC = white blood cell.

Scintigraphy is of indeterminate insensitivity and specificity, whether it is bone scanning, indium or indium with sulfur colloid, or even positron emission tomography [6-9]. Flow images are the best discriminators of infection but remain imperfect. Magnetic resonance imaging (MRI) likely has the best clinical results in this scenario, with or without contrast, but the yield is low in this clinical group of patients, and it is costly [10].

Variant 4. Neuropathy without ulcer

Radiologic Procedure	Rating	Comments
X-ray foot	9	Initial study. Radiography and MRI are complementary. Both are indicated.
MRI foot with contrast	9	Radiography and MRI are complementary. Both are indicated. See comments regarding contrast in text under "Anticipated Exceptions."
MRI foot without contrast	9	Radiography and MRI are complementary. Both are indicated.
CT foot without contrast	5	For neuropathy or if MRI contraindicated.
NUC ^{99m}Tc 3-phase bone scan foot	5	Useful for preradiographic findings of neuropathy. Also if MRI contraindicated.
NUC ^{99m}Tc 3-phase bone scan and ^{111}In WBC scan foot	2	
NUC ^{111}In WBC scan and ^{99m}Tc sulfur colloid marrow scan foot	1	
NUC ^{99m}Tc 3-phase bone scan and ^{111}In WBC scan and ^{99m}Tc sulfur colloid marrow scan foot	1	
Ultrasound foot	1	
FDG-PET foot	1	

Note: Rating scale: 1 = least appropriate, 9 = most appropriate. CT = computed tomography; FDG-PET = 2-[^{18}F]fluoro-2-deoxyglucose positron emission tomography; MRI = magnetic resonance imaging; NUC = nuclear medicine; WBC = white blood cell.

Variant 5. Neuroarthropathy with ulcer without exposed bone

Radiologic Procedure	Rating	Comments
X-ray foot	9	Initial study. Radiography and MRI are complementary. Both are indicated.
MRI foot with contrast	9	Radiography and MRI are complementary. Both are indicated. See comments regarding contrast in text under "Anticipated Exceptions."
MRI foot without contrast	9	Radiography and MRI are complementary. Both are indicated.
NUC ^{99m}Tc 3-phase bone scan and ^{111}In WBC scan foot	4	If MRI contraindicated.
NUC ^{99m}Tc 3-phase bone scan	1	
NUC ^{111}In WBC scan and ^{99m}Tc sulfur colloid marrow scan foot	1	
NUC ^{99m}Tc 3-phase bone scan and ^{111}In WBC scan and ^{99m}Tc sulfur colloid marrow scan foot	1	
CT foot without contrast	1	
Ultrasound foot	1	
FDG-PET foot	1	

Note: Rating scale: 1 = least appropriate, 9 = most appropriate. CT = computed tomography; FDG-PET = 2-[^{18}F]fluoro-2-deoxyglucose positron emission tomography; MRI = magnetic resonance imaging; NUC = nuclear medicine; WBC = white blood cell.

There is some importance in diagnosing neuropathic disease before radiographic changes, because these patients will be treated with altered footwear and orthotics to prevent the progression to deformity. However, scintigraphy is extremely sensitive to early neuropathic disease, long before radiographic changes are present. Magnetic resonance imaging is less sensitive but is a better test if there is a possibility of soft-tissue infection (see Variant 4).

Variant 6. Neuroarthopathy with ulcer with exposed bone

Radiologic Procedure	Rating	Comments
X-ray foot	9	Initial study. Radiography and MRI are complementary. Both are indicated.
MRI foot with contrast	9	Radiography and MRI are complementary. Both are indicated. See comments regarding contrast in text under "Anticipated Exceptions."
MRI foot without contrast	9	Radiography and MRI are complementary. Both are indicated.
NUC ^{99m}Tc 3-phase bone scan and ^{111}In WBC scan foot	4	If MRI contraindicated.
NUC ^{99m}Tc 3-phase bone scan	1	
NUC ^{111}In WBC scan and ^{99m}Tc sulfur colloid marrow scan foot	1	
NUC ^{99m}Tc 3-phase bone scan and ^{111}In WBC scan and ^{99m}Tc sulfur colloid marrow scan foot	1	
CT foot without contrast	1	
Ultrasound foot	1	
FDG-PET foot	1	

Note: Rating scale: 1 = least appropriate, 9 = most appropriate. CT = computed tomography; FDG-PET = 2-[^{18}F]fluoro-2-deoxyglucose positron emission tomography; MRI = magnetic resonance imaging; NUC = nuclear medicine; WBC = white blood cell.

Ulcer With Exposed Bone

If an ulcer is present, the risk for infection is quite high and almost invariable if the ulcer reaches bone. The role of imaging would be to confirm the infection and show its extent. Radiography will show the infection, however late. Bone scanning is quite nonspecific [7,11]. Surprisingly, indium scanning, even when combined with sulfur colloid marrow imaging, has low specificity [12-14], although if the ulcer is away from the joint, these techniques are better. Magnetic resonance imaging has high specificity and sensitivity both with and without contrast [15]. Ultrasound may have promise in long bones, but to date, data about its utility in diagnosing the diabetic foot are quite limited. Positron emission tomographic results are similarly poor, because this technique primarily shows metabolic activity and therefore is not specific [16] (see Variants 2-3).

Ulcer With Neuropathy and Exposed Bone

In patients with diabetes and secondary neuroarthropathy, the infection is usually over an osseous abnormality with an ulcer. If the ulcer tracks down to bone, the risk for osteomyelitis is extremely high, perhaps even higher than in the preceding situation, in which there is an ulcer without neuropathic deformity. The overall role of imaging, therefore, is more to determine the extent of the disease than to definitively diagnose it [17]. Therefore, most authors do not advocate scintigraphy in this situation because of its relative poor spatial resolution for extent of disease; similar conclusions apply to positron emission tomography [11] (see Variant 6).

Similarly, indium-labeled white blood cell scanning with or without bone marrow scanning has only mixed sensitivity and specificity for osteomyelitis with neuropathy and yields poor anatomic extent of infection. Radiography has high specificity but low sensitivity. Ultrasound is unproven. Computed tomography will show the neuroarthropathic disease but not much else. Magnetic resonance imaging should be performed to determine the extent of disease [1]. T_1-weighted and fat-suppressed sequences are complementary, and contrast may or may not be used. The use of contrast is more to see the extent of the disease as well as the extent of vascularity than to diagnose infections [10]. Contrast may also help identify necrotic or poorly perfused regions and to aid in surgical planning [18,19] (see Variant 5).

SUMMARY AND RECOMMENDATIONS

If a patient has an ulcer that extends to bone, there is quite likely, but not invariably, osteomyelitis. The best way to confirm this diagnosis and determine the extent of disease is with MRI. If there is no ulcer and there is still a clinical suspicion of infection, MRI is the test of choice. However, conventional radiography should be done simultaneously in both situations. In indeterminate cases, aspiration and biopsy would be the next step.

If there is soft-tissue swelling, the question is whether early neuropathic disease or infection is present. Radiography should be performed first. If the radiographic results are normal, another test should be performed. If the suspicion of infection is low, the next test should probably be a 3-phase bone scan. If there is a modest risk for infection, MRI is probably indicated.

ANTICIPATED EXCEPTIONS

Nephrogenic systemic fibrosis (NSF; also known as nephrogenic fibrosing dermopathy) was first identified in 1997 and has recently generated substantial concern among radiologists, referring doctors, and laypeople. Until the last few years, gadolinium-based magnetic resonance contrast agents were widely believed to be almost universally well tolerated, extremely safe, and not nephrotoxic, even when used in patients with impaired renal function. All available experience suggests that these agents remain generally very safe, but recently, some patients with renal failure who have been exposed to gadolinium contrast agents (the percentage is unclear) have developed NSF [20-22], a syndrome that can be fatal. Further studies are necessary to determine what the exact relationships are between gadolinium-containing contrast agents, their specific components and stoichiometry, patient renal function, and NSF. Current theory links the development of NSF to the administration of relatively high doses (eg, >0.2 mmol/kg) and to agents in which the gadolinium is least strongly chelated. The US Food and Drug Administration [23] has recently issued a "black box" warning concerning these contrast agents.

This warning recommends that until further information is available, gadolinium contrast agents should not be administered to patients with either acute or significant chronic kidney disease (estimated glomerular filtration rate < 30 mL/min/1.73 m^2), recent liver or kidney transplantation, or hepatorenal syndrome, unless a risk-benefit assessment suggests that the benefit of administration in the particular patient clearly outweighs the potential risk(s) [21].

Disclaimer: *The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for the diagnosis and treatment of specified medical conditions. These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treat-*

ments. Only those examinations generally used for the evaluation of a patient's condition are ranked. Other imaging studies necessary to evaluate other coexistent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the US Food and Drug Administration have not been considered in developing these criteria, but the study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

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