

ACR Appropriateness Criteria[®] Imaging of Possible Tuberculosis

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Abstract

Pulmonary tuberculosis remains a major cause of disease worldwide and an important public health hazard in the United States. The imaging evaluation depends to a large degree on clinical symptoms and whether active disease is suspected or a subject is at high risk for developing active disease.

The American College of Radiology Appropriateness Criteria are evidence-based guidelines for specific clinical conditions that are reviewed annually by a multidisciplinary expert panel. The guideline development and revision include an extensive analysis of current medical literature from peer reviewed journals and the application of well-established methodologies (RAND/UCLA Appropriateness Method and Grading of Recommendations Assessment, Development, and Evaluation or GRADE) to rate the appropriateness of imaging and treatment procedures for specific clinical scenarios. In those instances where evidence is lacking or equivocal, expert opinion may supplement the available evidence to recommend imaging or treatment.

Key Words: Appropriateness Criteria, Appropriate Use Criteria, AUC, CT, chest radiography, pulmonary tuberculosis, tuberculosis

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The American College of Radiology seeks and encourages collaboration with other organizations on the development of the ACR Appropriateness Criteria through society representation on expert panels. Participation by representatives from collaborating societies on the expert panel does not necessarily imply individual or society endorsement of the final document. Reprint requests: publications@acr.org

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Disclaimer: The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). 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 treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent 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 FDA have not been considered in developing these criteria; however, 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.

Variant 1. Suspect active tuberculosis.			
Radiologic Procedure	Rating	Comments	RRL
X-ray chest	9		⊕
CT chest without IV contrast	7	This procedure is recommended if x-ray is equivocal.	⊕⊕⊕
CT chest with IV contrast	6		⊕⊕⊕
CT chest without and with IV contrast	3		⊕⊕⊕
MRI chest without IV contrast	3		○
MRI chest without and with IV contrast	3		○

Note: Rating Scale: 1,2,3 = usually not appropriate; 4,5,6 = may be appropriate; 7,8,9 = usually appropriate. IV = intravenous; RRL = relative radiation level.

Variant 2. Newly positive PPD or IGRA OR positive PPD or IGRA with unknown prior status. No clinical symptoms.			
Radiologic Procedure	Rating	Comments	RRL
X-ray chest	9		⊕
CT chest with IV contrast	4		⊕⊕⊕
CT chest without IV contrast	3		⊕⊕⊕
MRI chest without IV contrast	2		○
MRI chest without and with IV contrast	2		○
CT chest without and with IV contrast	1		⊕⊕⊕

Note: Rating Scale: 1,2,3 = usually not appropriate; 4,5,6 = may be appropriate; 7,8,9 = usually appropriate. IV = intravenous; RRL = relative radiation level.

Variant 3. PPD not available. Placement in group home or skilled nursing facility. No clinical symptoms.			
Radiologic Procedure	Rating	Comments	RRL
X-ray chest	9		⊕
CT chest with IV contrast	2		⊕⊕⊕
CT chest without IV contrast	2		⊕⊕⊕
MRI chest without IV contrast	2		○
CT chest without and with IV contrast	1		⊕⊕⊕
MRI chest without and with IV contrast	1		○

Note: Rating Scale: 1,2,3 = usually not appropriate; 4,5,6 = may be appropriate; 7,8,9 = usually appropriate. IV = intravenous; RRL = relative radiation level.

Table 1. Relative radiation level designations			
RRL	Adult Effective Dose Estimate Range (mSv)	Pediatric Effective Dose Estimate Range (mSv)	
○	0	0	
⊕	<0.1	<0.03	
⊕⊕	0.1-1	0.03-0.3	
⊕⊕⊕	1-10	0.3-3	
⊕⊕⊕⊕	10-30	3-10	
⊕⊕⊕⊕⊕	30-100	10-30	

Note: Relative radiation level (RRL) assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "varies."

SUMMARY OF LITERATURE REVIEW

Introduction/Background

Pulmonary tuberculosis (TB) predominantly results from the transmission of aerosolized mycobacterium TB to susceptible hosts [1]. In the vast majority of cases, this results in subclinical disease with the immune system isolating the organism. In this setting, a person has latent TB and does not pose a risk to the community at large. The development of active infection within 1 year after exposure is termed primary TB and is classically described as a lobar pneumonia and/or mediastinal and hilar adenopathy. This pattern is most often seen in children and severely immunocompromised individuals. If active infection develops later than 1 year after initial exposure, it is considered to be reactivation TB, often presenting with apical posterior upper lobe or superior-segment lower lobe fibrocavitary disease and endobronchial spread through the airways.

With modern molecular techniques it has been shown that radiographic patterns of primary and reactivation TB overlap, and thus the preferred terminology for TB infection is “active TB” [2]. The important public health issue is that both primary and reactivation TB present a risk for exposing the general population to TB infection.

A high level of suspicion should be maintained in immunocompromised hosts, particularly those with AIDS, as imaging manifestations may not fit a classic primary or reactivation pattern; instead, these patients may present with mediastinal lymphadenopathy alone or a deceptively normal chest radiograph.

Overview of Imaging Modalities

Chest Radiography. Chest radiography is usually the first study performed in patients suspected of having TB. Although frontal and lateral radiographs are often performed in this setting, it has been shown that lateral radiography does not improve the detection of findings related to TB [3]. In those with signs or symptoms of disease, the radiographic pattern of upper lobe or superior-segment lower lobe fibrocavitary disease in the appropriate clinical setting is sufficient to warrant respiratory isolation and sputum culture for definitive diagnosis. Using radiography in combination with clinical evaluation results in high sensitivity for the diagnosis but relatively low specificity for both latent [4] and active [5] TB. In addition, radiography may reveal ancillary findings of TB such as pleural effusion or spondylitis. For immunocompromised hosts, particularly those with a low CD4 count, CT should be considered.

CT. The major advantage of CT is increasing the specificity of the diagnosis of TB; therefore, CT is often not necessary in the acute setting, particularly when the disease is already suspected and appropriate precautions and testing are already under way. CT may be able to better show distinct findings such as cavitation or endobronchial spread with tree-in-bud nodules and may be helpful in cases in which chest radiography does not show “classic” findings of TB [6]. CT findings can also be helpful in predicting acid-fast bacilli smear positivity [7-9]. Even in acid-fast bacilli smear-negative patients, CT may suggest the risk that a patient will be TB culture positive when findings consistent with active TB are present [10]. CT may be of value in a severely immunocompromised patient with a normal or near normal radiograph by revealing abnormal lymph nodes or subtle parenchymal disease. Finally, CT may also have a role in identifying patients with latent TB who will be at risk for reactivation disease [4,11].

MRI. Only one study has been performed evaluating MRI for suspected TB. In this study the accuracy of MRI was similar to CT in describing findings related to culture-positive patients [12]. Inferential data regarding the value of MRI can also be derived from its role in cystic fibrosis and the observation in other settings that MRI correlates well with CT for parenchymal findings including bronchiectasis, cavitation, and tree-in-bud nodules [13]. Although MRI is technically feasible and described in the literature, MRI has not been specifically evaluated as a primary imaging modality for patients with suspected or proven TB.

Nuclear Scintigraphy. Several nuclear radiopharmaceuticals have been used for the purpose of evaluating possible TB, particularly for differentiating active from inactive tuberculomas and distinguishing tuberculomas from neoplasms. In small studies, Tc-99m methoxyisobutylisonitrile has shown higher activity over background in active tuberculomas compared with inactive tuberculomas [14,15]. Similarly, metabolic activity measured by fluorine-18-2-fluoro-2-deoxy-D-glucose PET (FDG-PET) is higher in active tuberculomas. Dual-time-point FDG-PET imaging (1 and 2 hours postinjection) can also help differentiate active tuberculomas from neoplasms because of the longer retention of FDG in benign lesions [16]. Gallium-67 has been used to follow patients for disease activity and correlates with the number of organisms on sputum smears [17]. Evidence for the use of nuclear imaging to diagnose active TB is limited to either small single-site studies or

several small studies, and the impact on clinical practice and patient care at this time is minimal.

Discussion of the Imaging Modalities by Variant

Variant 1: Suspect Active Tuberculosis. The initial suspicion of active TB should be made on the basis of clinical symptoms and demographics. Those at particular risk include those in close contact with patients having active TB, spending time in a TB-endemic country, or working or spending time in sites where TB is more prevalent, such as prisons, homeless shelters, and long-term care facilities. Those who are immunocompromised are at particular risk. Included in this category are also individuals with a newly positive purified protein derivative (PPD) skin test or a positive interferon-gamma release assay (IGRA) and who have symptoms that could be related to active TB. Clinical symptoms of active TB may include unexplained weight loss, night sweats, fever, prolonged cough, hemoptysis, and fatigue.

Chest Radiography. Identified individuals should undergo chest radiography as the initial test. Chest radiography has been shown to have high sensitivity for detecting manifestations of active TB [5]. Chest radiography has high sensitivity but relatively poor specificity because of the overlap of findings with nontuberculous pulmonary infection. The yield of chest radiography in high-risk patients ranges from 1% to 7%, although it is not clear how many of these cases would have been suspected on the basis of clinical symptoms alone [18,19].

In particular, lobar pneumonia with associated hilar and/or mediastinal adenopathy or cavitary air space disease involving the apical posterior segments of the upper lobe or superior segment of the lower lobe should raise particular concern [20]. When chest radiography confirms the clinical suspicion of active TB, it is sufficient to warrant respiratory isolation pending sputum cultures. However, in patients who are immunocompromised, particularly those with AIDS and very low CD4 counts, chest radiographs may be deceptively normal.

CT. The role of CT remains less clear, but it should be considered for those with equivocal chest radiographic findings and may be efficacious in excluding active TB because of its higher specificity. High-risk acid-fast bacilli smear-negative patients may also benefit from CT. AIDS patients with low CD4 counts and those taking anti-tumor necrosis factor medications have sufficient risk to warrant CT in the setting of high clinical suspicion for active TB and an unrevealing chest radiograph.

MRI. MRI is a reasonable consideration for use in select patients for whom there is a desire to avoid ionizing radiation.

Variant 2: Newly Positive PPD or IGRA or Positive PPD or IGRA With Unknown Prior Status. No Clinical Symptoms. *Chest Radiography.* One key principal of PPD testing is application in those at high risk for developing latent TB infection. This may include those who work in settings where contact with active TB is possible and those coming from regions where TB is endemic. Although screening of low-risk individuals is discouraged, it is recommended for those whose future activity will place them at high risk for exposure or reactivation. The rationale behind performing chest radiography after a positive PPD is to distinguish latent TB from active TB, as these are managed differently. However, in patients without clinical symptoms, the yield of radiography for active TB (that would change management) is negligible [21]. Furthermore, parenchymal findings of latent TB are relatively poor predictors of future reactivation. If a chest radiography is performed, a frontal view is sufficient [3].

CT. CT should be reserved for the rare case in which chest radiography may be equivocal for active TB and cases for which knowledge of latent TB abnormalities may inform future care, such as patients undergoing solid organ transplantation and biologic therapy for rheumatologic disease [4,11].

MRI. Like CT, there is a very limited role for MRI, although it may be considered when cross-sectional imaging is deemed necessary in a patient for whom there is a desire to avoid ionizing radiation.

Variant 3: PPD Not Available. Placement in Group Home or skilled Nursing Facility. No Clinical Symptoms. *Chest Radiography.* Low-risk screening also frequently occurs in patients being transferred to correctional institutions, group homes, and skilled nursing facilities. Because of time constraints related to placing and interpreting a PPD, chest radiography has emerged as a surrogate measure. A meta-analysis of homeless populations suggests that using chest radiography as a screening measure is sufficient and can lead in some cases to a decline in the incidence of TB over time [19]. This study, however, did not compare chest radiographic screening to other screening strategies in terms of efficacy. Screening procedures vary from one prison site to another. There does not appear to be a large discrepancy in TB incidence regardless of

screening technique (symptom survey, PPD, or chest radiography) [22]. There is no evidence regarding the performance of routine radiography in low-risk patients who did not receive other TB screening before transfer to a group home or nursing facility.

CT. CT should be reserved for the rare case in which chest radiography is equivocal for active TB and more definitive testing such as sputum culture is impractical.

MRI. Like CT, there is a very limited role for MRI, although it might be considered when cross-sectional imaging is deemed necessary in a patient for whom there is a desire to avoid ionizing radiation.

SUMMARY OF RECOMMENDATIONS

- Chest radiography is the first recommended test in patients with suspected tuberculosis.
- Chest radiography is generally appropriate for patients with new evidence of exposure or at high risk for development of tuberculosis, although it may be of low yield in patients who have no clinical symptoms.
- Chest CT is appropriate when tuberculosis is suspected and radiography is nonrevealing or nondiagnostic.

SUMMARY OF EVIDENCE

Of the 23 references cited in the ACR Appropriateness Criteria® Imaging of Possible Tuberculosis document, all are categorized as diagnostic references, including 1 well-designed study, 10 good-quality studies, and 2 quality studies that may have design limitations. There are 9 references that may not be useful as primary evidence. There is 1 reference that is a meta-analysis study.

The 23 references cited in the ACR Appropriateness Criteria® Imaging of Possible Tuberculosis document were published from 2004 to 2015.

While there are references that report on studies with design limitations, 11 well-designed or good-quality studies provide good evidence.

RELATIVE RADIATION LEVEL INFORMATION

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposure associated with different diagnostic procedures, a relative radiation level

(RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared to those specified for adults (see Table 1). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document [23].

SUPPORTING DOCUMENTS

For additional information on the Appropriateness Criteria methodology and other supporting documents go to www.acr.org/ac.

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