Appropriateness Criteria Review

ACR Appropriateness Criteria® Radiographically Detected Solitary Pulmonary Nodule

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Abstract: The solitary pulmonary nodule (SPN) is a common medical problem for which management can be quite complex. Imaging remains at the center of management of SPNs, and computed tomography is the primary modality by which SPNs are characterized and followed up for stability. This manuscript summarizes the American College of Radiology Appropriateness Criteria® for radiographically detected solitary pulmonary nodules and briefly reviews the various imaging techniques available. The American College of Radiology Appropriateness Criteria® are evidence-based guidelines for specific clinical conditions that are reviewed every 2 years by a multidisciplinary expert panel. The guideline development and review include an extensive analysis of current medical literature from peer reviewed journals and the application of a well-established consensus methodology (modified Delphi) to rate the appropriateness of imaging and treatment procedures by the panel. In those instances in which evidence is lacking or not definitive, expert opinion may be used to recommend imaging or treatment.

Key Words: appropriateness criteria, pulmonary nodule, computerized tomography, positron emission tomography, biopsy

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This article is a revised version of the American College of Radiology Appropriateness Criteria® Radiographically Detected Solitary Pulmonary Nodule. Practitioners are encouraged to refer to the complete version at http://www.acr.org/ac.

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The American College of Radiology (ACR) 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.

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SUMMARY OF LITERATURE REVIEW

The solitary pulmonary nodule is defined as a rounded opacity ≤ 3 cm in diameter surrounded by lung parenchyma.[1] There should be no associated abnormality, including atelectasis or hilar lymphadenopathy. This definition is based on information obtained from chest radiographs. On computed tomography (CT), nodules are described as being solid, semisolid (mixed attenuation), or ground-glass attenuation. Pure ground-glass attenuation nodules are areas of increased lung attenuation through which normal structures such as vessels or septa remain discernible.

The incidence of solitary nodules detected by chest radiography was previously estimated to be approximately 150,000 per year in the United States.[2] However, this figure did not include the multitude of smaller nodules detected with CT. There are few reliable characteristics to distinguish benign from malignant nodules. The only findings sufficient to preclude further evaluation are a benign pattern of calcification or stability of nodule size for over 2 years for solid pulmonary nodules. Recently, the radiologic-pathologic correlation of pure ground-glass attenuation nodules and mixed attenuation nodules with the histologic spectrum of pulmonary adenocarcinoma was described.[3] Although not all ground-glass attenuation nodules are malignant, they are more likely to be multiple and may demonstrate an indolent growth pattern, rendering 2-year stability inadequate to establish benignity. The likelihood of malignancy increases with nodule size, which may influence management strategy. Other nodule features such as shape, edge characteristics, cavitation, and location have not yet been found to be accurate clues for distinguishing benign from malignant nodules.[4]

OVERVIEW OF DIAGNOSTIC TESTS

A host of diagnostic tests are available to evaluate patients with solitary pulmonary nodules (Table 1). It should be noted that for all of these tests accuracy tends to decrease with decreasing nodule size. It is often the role of the radiologist to suggest an appropriate management strategy.

Theoretical approaches for decision-making include the use of Bayes theorem, logistic regression models, and neural network analysis.[5–8] These approaches are useful primarily in estimating the probability of malignancy for a

TABLE 1. Variant Table Ratings

	Radiologic Procedures							
Variants	CT Chest Without Contrast	FDG-PET/CT Whole Body	TNB	CT Chest With Contrast	CT Chest Without and With Contrast	Watchful Waiting With CT Follow-up	MRI Chest Without Contrast	MRI Chest Without and With Contrast
Variant 1: Solid nodule ≥ 1 cm, low clinical suspicion for cancer	8*	8†	8‡	6§	6‖	4¶	2#	2#
Variant 2: Solid nodule ≥ 1 cm, moderate to high clinical suspicion for cancer	8*	8†	8‡	6§	6‖	2	2#	2#
Variant 3: Solid nodule < 1 cm, low clinical suspicion for cancer	7	3	2	3	5**	8	2#	2#
Variant 4: Solid nodule < 1 cm, moderate to high clinical suspicion for cancer	8	2	6	4	5**	5	2#	2#

Rating scale: 1, 2, 3 = usually not appropriate; 4, 5, 6 = may be appropriate; 7, 8, 9 = usually appropriate.
*To detect occult calcifications, fat, bronchus sign, etc.
†If nodule is indeterminate on high-resolution computed tomography.
‡If nodule shows contrast enhancement or PET scan is positive.
§Probably not indicated if PET is performed.
‖Can look at washout.
¶Reasonable at short interval.
#Limited data.
**Depends on size (washout study).

particular nodule. Information from the radiologic appearance of the nodule, such as size, shape, and edge characteristics, can be combined with clinical risk information such as age and smoking history to produce an overall probability for malignancy. If this probability can be set sufficiently low, strategies that include observing nodules for interval change can be advocated.[9] These estimates can be combined with subsequent imaging information to further define the probability of malignancy and guide additional steps in the diagnostic workup.[10]

Extensive work is now being done using advanced image processing techniques to further evaluate nodule attributes and change over time. Volumetric analysis measures growth of nodules in short time intervals, allowing for assessment of doubling time, which is a biological measure of tumor aggressiveness. Changes in nodule morphology and attenuation are also being assessed.[11] Factors that affect the reproducibility of nodule volume measurement on CT include nodule size at detection, examination technique, nodule relationship to adjacent structures, underlying lung disease, and patient factors such as phase of respiration and cardiac motion.[12]

CT

Contrast-enhanced CT of solitary pulmonary nodules has also been used to distinguish benign from malignant nodules. Results from a large multicenter study found that contrast-enhanced CT has a sensitivity of 98% and a specificity of 58% when using a cutoff of 15 Hounsfield units for enhancement. This led the authors to conclude that absence of enhancement is a strong predictor of benignity.[13] An analysis of combined wash-in and washout characteristics on dynamic contrast-enhanced multidetector CT showed 92% accuracy for distinguishing benign from malignant nodules.[14] Limitations of the technique relate to its nonspecific nature for inflammatory disease and measurement error in evaluation of small nodules. Dual-energy CT imaging has also been used in several studies to evaluate nodules with similar diagnostic accuracy.[15,16]

MAGNETIC RESONANCE IMAGING (MRI)

Use of MRI in the evaluation of pulmonary nodules has thus far been limited. Faster imaging sequences and techniques to mitigate artefacts have allowed for detection of smaller nodules (6 to 10 mm) with a sensitivity of almost 95%.[17] For nodules >1 cm, contrast-enhanced dynamic MRI has been shown to be comparable to CT for distinguishing benign from malignant nodules.[18–20] However, further research and validation are required to define a place for MRI in clinical practice.

POSITRON EMISSION TOMOGRAPHY (PET)

PET using fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG) has assumed a major role in the evaluation of patients with solitary pulmonary nodules. Many studies have demonstrated the accuracy of FDG-PET in evaluating solitary pulmonary nodules.[21] The sensitivity and specificity of this technique range from 83% to 97% and from 69% to 100%, respectively. FDG-PET has a higher specificity and only slightly reduced sensitivity compared with nodule-enhancement CT.[22] Limitations of PET scanning include its inability to accurately characterize certain types of lesions, including low-grade adenocarcinoma and typical carcinoid tumors. It is also limited in its ability to characterize nodules < 1 cm in diameter, and it may give false-positive results in patients with active infections and inflammatory diseases.

OTHER DIAGNOSTIC TESTS

The aggressive nature of lung cancer often compels the diagnostic evaluation to be nearly accurate, and consequently tests that provide pathologic material are quite useful. Currently, such diagnostic tests include transthoracic needle biopsy (TNB), bronchoscopy, video-assisted thoracoscopic surgery (VATS), and thoracotomy. The relative roles of these procedures are not well defined in the existing literature. Both TNB[23–26] and bronchoscopy[27] are highly dependent on nodule size and location and on the skill of the person performing the procedure. In general, TNB has a higher sensitivity and specificity compared with bronchoscopy.

Management recommendations for small nodules were revised by the Fleischner Society in 2005 using separate algorithms for high-risk and low-risk patients.[28] The American College of Chest Physicians published a set of 29 recommendations for the evaluation and management of small nodules; these recommendations stress the importance of including patient preference in management decisions.[29]

SUMMARY

In view of the variety of diagnostic tests available and the variable accuracy of the different diagnostic techniques, such as FDG-PET and TNB, no single algorithm for workup is generally accepted.

Practices differ from institution to institution, likely because of the varying prevalence of lung disease in different parts of the country, varying skill levels of operators, and varying availability of equipment.

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