American College of Radiology
ACR Appropriateness Criteria®

Clinical Condition: **Radiographically Detected Solitary Pulmonary Nodule**

Variant 1: **Solid nodule ≥1 cm, low clinical suspicion for cancer.**

Radiologic Procedure	Rating	Comments	RRL*
CT chest without IV contrast	8	To detect occult calcifications, fat, bronchus sign, etc.	☢☢☢
FDG-PET/CT whole body	8	If nodule is indeterminate on HRCT.	☢☢☢☢
Transthoracic needle biopsy	8	If nodule shows contrast enhancement or PET scan is positive.	Varies
CT chest with IV contrast	6	Probably not indicated if PET is performed.	☢☢☢
CT chest without and with IV contrast	6	Can look at washout.	☢☢☢
Watchful waiting with CT follow-up	4	Reasonable at short interval.	Varies
MRI chest without IV contrast	2	Limited data.	O
MRI chest without and with IV contrast	2	Limited data.	O
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

Variant 2: **Solid nodule ≥1 cm, moderate to high clinical suspicion for cancer.**

Radiologic Procedure	Rating	Comments	RRL*
CT chest without IV contrast	8	To detect occult calcifications, fat, bronchus sign, etc.	☢☢☢
FDG-PET/CT whole body	8	If nodule is indeterminate on HRCT.	☢☢☢☢
Transthoracic needle biopsy	8	If nodule shows contrast enhancement or PET scan is positive.	Varies
CT chest with IV contrast	6	Probably not indicated if PET is performed.	☢☢☢
CT chest without and with IV contrast	6	Can look at washout.	☢☢☢
Watchful waiting with CT follow-up	2		Varies
MRI chest without IV contrast	2	Limited data.	O
MRI chest without and with IV contrast	2	Limited data.	O
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

Clinical Condition: **Radiographically Detected Solitary Pulmonary Nodule**

Variant 3: **Solid nodule <1 cm, low clinical suspicion for cancer.**

Radiologic Procedure	Rating	Comments	RRL*
Watchful waiting with CT follow-up	8		Varies
CT chest without IV contrast	7		☢☢☢
CT chest without and with IV contrast	5	Depends on size (washout study).	☢☢☢
CT chest with IV contrast	3		☢☢☢
FDG-PET/CT whole body	3		☢☢☢☢
Transthoracic needle biopsy	2		Varies
MRI chest without IV contrast	2	Limited data.	O
MRI chest without and with IV contrast	2	Limited data.	O
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

Variant 4: **Solid nodule <1 cm, moderate to high clinical suspicion for cancer.**

Radiologic Procedure	Rating	Comments	RRL*
CT chest without IV contrast	8		☢☢☢
Transthoracic needle biopsy	6		Varies
Watchful waiting with CT follow-up	5		Varies
CT chest without and with IV contrast	5	Depends on size (washout study).	☢☢☢
CT chest with IV contrast	4		☢☢☢
FDG-PET/CT whole body	2		☢☢☢☢
MRI chest without IV contrast	2	Limited data.	O
MRI chest without and with IV contrast	2	Limited data.	O
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

RADIOGRAPHICALLY DETECTED SOLITARY PULMONARY NODULE

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Summary of Literature Review

Introduction/Background

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 the chest radiograph. 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. When these are included, the incidence of pulmonary nodules in the general population dramatically increases, though precise estimates are not available. Although what constitutes a small nodule is not formally established, nodules with diameters <1 cm are generally considered small. As with radiographically detected nodules, the primary aim in evaluating these smaller nodules is the ability to confirm or exclude malignancy.

Although pulmonary nodules have been studied for decades, 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. Both of these criteria have been known since the early 1950s. Recently, the radiologic-pathologic correlation of pure ground-glass attenuation nodules and mixed attenuation nodules with the histologic spectrum of pulmonary adenocarcinoma has been described [3]. While 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]. As a result, the majority of nodules are indeterminate.

Overview of Diagnostic Tests

A host of diagnostic tests are available to evaluate patients with solitary pulmonary nodules. It should be noted that for all of these tests, the accuracy tends to decrease with smaller nodule size. Diagnostic tests range from noninvasive decision-theoretic approaches to major surgery. It is often the role of the radiologist to suggest an appropriate management strategy.

Theoretic 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 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

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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. One area of investigation includes the ability to use 3-dimensional nodule characteristics. Volumetric analysis measures growth of nodules in short time intervals, allowing for assessment of doubling time, a biologic 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].

Computed-aided detection (CAD) systems have been developed for lung nodule detection on CT. CAD has the potential to improve radiologists' diagnostic confidence in detection and accuracy in distinguishing small benign nodules from malignant ones on high-resolution CT (HRCT) [13-15]. At this point, studies have shown that CAD information can be helpful in clinical practice by providing radiologists a "second opinion" [16].

Computed Tomography

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 [17]. An analysis of combined wash-in and washout characteristics at dynamic contrast-enhanced multidetector CT showed 92% accuracy for distinguishing benign from malignant nodules [18]. The extent of enhancement reflects underlying nodule angiogenesis [19]. 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 [20,21]. Through postprocessing techniques, contrast-enhanced and virtual-noncontrast images are generated from a single acquisition, which may reduce patient radiation dose.

Magnetic Resonance Imaging

Use of magnetic resonance imaging (MRI) in evaluation of pulmonary nodules has thus far been limited. Faster imaging sequences and techniques to mitigate artifact have allowed for detection of smaller nodules (6-10 mm) with sensitivity near 95% [22]. For nodules >1 cm, contrast-enhanced dynamic MRI has shown to be comparable to CT for distinguishing benign from malignant nodules with a sensitivity of 96%, specificity of 88%, and accuracy of 92% [23-25]. The possibility of a nonionizing assessment method for nodules is attractive, especially for younger patients. However, further research and validation are required to define a place for MR in clinical practice.

Positron Emission Tomography

Positron emission tomography (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. This technique relies on measuring glucose metabolism, which has been shown to be different between benign and malignant nodules. Many studies have demonstrated the accuracy of FDG-PET in evaluating solitary pulmonary nodules [26]. The sensitivity and specificity for this technique, as reported in the literature, have ranged from 83%-97% and from 69%-100%, respectively. FDG-PET has a higher specificity and only slightly reduced sensitivity compared to nodule-enhancement CT [27]. 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 near certainty, 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 existing literature, perhaps because of the lack of a defined sensitivity and specificity for the semi-invasive tests. Both TNB [28-31] and bronchoscopy

[32] 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 than bronchoscopy, and therefore it is usually a more appropriate test in diagnosing solitary nodules. CT fluoroscopy-guided lung biopsy using an automated cutting needle provides a high degree of diagnostic accuracy, allows for the specific characterization of lung nodules, and can be performed safely with a sensitivity of 95.1%, specificity of 100%, and accuracy of 96.2% [33]. The role of TNB relative to the surgical approach depends primarily on the ability to make a benign diagnosis. If the only role of TNB is to confirm malignancy, then it only adds to the cost of the overall workup, although there can be some use in confirming malignancy before surgery, such as diagnosing small-cell carcinoma. The diagnosis of benign disease using TNB is generally divided into three broad categories: specific benign diagnosis, nonspecific benign diagnosis, and nondiagnostic biopsy.

Recent reports suggest that the number of specific benign diagnoses can be increased using core needles, although this occurs at the cost of increasing complication rates when large-caliber needles are used. In general, for benign nonspecific and nondiagnostic studies, repeat biopsy or resection is necessary [34]. Compared to thoracotomy, VATS offers the benefit of lower perioperative morbidity and decreased length of hospital stay. VATS is most successful for peripheral lesions and some central lesions in the lower lobe, and it is the surgical method of choice for diagnosis and resection of pulmonary nodules. If the nodules are too small or located too deeply to be detected thoracoscopically, preoperative CT-guided placement of a pulmonary nodule-marker system like methylene blue or wires is a safe and accurate method of localizing pulmonary nodules at thoracoscopy [35,36].

Much of the information on which guidelines are based for management of small nodules is derived from lung cancer screening. Based on a retrospective review of 2,897 baseline screening scans, initial recommendations for noncalcified nodules measuring <5 mm were to have a follow-up scan in 1 year [37]. Management recommendations for small nodules were revised by the Fleischner Society in 2005, using separate algorithms for high- and low-risk patients [38]. Subsequently, The American College of Chest Physicians published a set of 29 recommendations for the evaluation and management of small nodules, which stress inclusion of patient preference in management decisions [39].

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 vary 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.

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 exposures 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 below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document.

Relative Radiation Level Designations		
Relative Radiation Level*	**Adult Effective Dose Estimate Range**	**Pediatric Effective Dose Estimate Range**
O	0 mSv	0 mSv
☢	<0.1 mSv	<0.03 mSv
☢☢	0.1-1 mSv	0.03-0.3 mSv
☢☢☢	1-10 mSv	0.3-3 mSv
☢☢☢☢	10-30 mSv	3-10 mSv
☢☢☢☢☢	30-100 mSv	10-30 mSv
*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".		

Supporting Documents

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

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