American College of Radiology
ACR Appropriateness Criteria®

Clinical Condition: **Solitary Pulmonary Nodule**

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

Radiologic Procedure	Rating	Comments	RRL*
CT chest without contrast	8	To detect occult calcifications, fat, bronchus sign, etc.	Med
FDG-PET chest	8	If nodule is indeterminate on HRCT.	High
INV fine needle aspiration lung	8	If nodule shows contrast enhancement or PET scan is positive.	IP
CT chest without contrast	8	To detect occult calcifications, fat, bronchus sign, etc.	Med
CT chest with contrast	6	Probably not indicated if PET performed.	Med
CT chest watchful waiting with follow up	4		Med
Rating Scale: 1=Least appropriate, 9=Most appropriate			***Relative Radiation Level***

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

Radiologic Procedure	Rating	Comments	RRL*
CT chest without contrast	8	To detect occult calcifications, fat, bronchus sign, etc.	Med
FDG-PET chest	8	If nodule is indeterminate on HRCT.	High
INV fine needle aspiration lung	8	If nodule shows contrast enhancement or PET scan is positive.	IP
CT chest with contrast	6	Probably not indicated if PET performed.	Med
CT chest watchful waiting with follow up	2		Med
Rating Scale: 1=Least appropriate, 9=Most appropriate			***Relative Radiation Level***

Clinical Condition: **Solitary Pulmonary Nodule**

Variant 3:   **Nodule ≤1 cm, low clinical suspicion for cancer.**

Radiologic Procedure	Rating	Comments	RRL*
CT chest watchful waiting with follow up	8		Med
CT chest without contrast	7		Med
CT chest with contrast	3		Med
FDG-PET chest	3		High
INV fine needle aspiration lung	2		IP
Rating Scale: 1=Least appropriate, 9=Most appropriate			***Relative Radiation Level**

Variant 4:   **Nodule ≤1 cm, moderate to high clinical suspicion for cancer.**

Radiologic Procedure	Rating	Comments	RRL*
CT chest without contrast	8		Med
INV fine needle aspiration lung	6		IP
CT chest watchful waiting with follow up	5		Med
CT chest with contrast	4		Med
FDG-PET chest	2		High
Rating Scale: 1=Least appropriate, 9=Most appropriate			***Relative Radiation Level**

SOLITARY PULMONARY NODULE

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Summary of Literature Review

The solitary pulmonary nodule is traditionally defined as a relatively spherical opacity 3 cm or less in diameter surrounded by lung parenchyma [1]. There should be no associated abnormality, including atelectasis or hilar adenopathy. This definition is based predominantly on information obtained from the chest radiograph.

The ever-expanding role of computed tomography (CT) in medical imaging is leading to additional insights into this definition. The more generic term to describe a nodule is a focal opacity. This term encompasses those abnormalities that are solid, semi-solid and non-solid (ground glass opacity). The incidence of solitary nodules was traditionally believed to be in the range of approximately 150,000 new cases per year in the United States [2]. However, this figure was based on chest radiographic findings and did not include all of the smaller nodules detected with CT. When these are included, the incidence dramatically increases, although precise estimates are not available. In particular, CT has placed us in the domain of finding smaller nodules. Although a precise definition of small has not been standardized, it is generally considered to be in the range of less than 1 cm. As with radiographically detected nodules, the primary concern in evaluating even these smaller nodules is the ability to exclude malignancy.

The radiologist is now in the position of being able to detect many more nodules. In addition there are many more diagnostic tests available. 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 largely the role of the radiologist to help select the appropriate management strategy.

Decision theoretic approaches include the use of Bayes theorem, logistic regression models, and neural network analysis [3-6]. This type of approach is 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 overall probability for malignancy. If this can be set sufficiently low, strategies that include observing nodules for interval change can be advocated. While this policy of watchful waiting has generally not been advocated, it is becoming increasingly clear that under certain circumstances, it is appropriate [7]. Similarly, these estimates can be combined with subsequent imaging information to further define the probability of malignancy and guide additional steps in the diagnostic work-up [8].

The choice of imaging test to evaluate solitary nodules is extensive. However, only two findings are considered to be sufficient to preclude further evaluation: calcification in a benign pattern and stability in size for over two years. Both of these criteria have been known since the early 1950s [9,10]. However, only a small number of nodules meet these criteria; the majority falls in the category of indeterminate. Other radiographic features—including size, shape, edge characteristics and density—have not yet been found to be sufficiently accurate to characterize nodules. Extensive work is now being done using advanced image processing techniques to further advance this capability. In particular, this includes the ability to utilize information using three-dimensional characteristics. This field is rapidly developing and is now readily available with the newer multi-row CT scanners. Volumetric analysis measures growth of nodules in short time intervals, allowing for assessment of doubling times. This is an extension of the concept of watchful waiting. Factors that affect the reproducibility of nodule volume measurement on CT include nodule size at detection and the presence of patient-induced artifacts [11]. The only current guidelines for management of small nodules in the radiological literature are those that have been developed in the context of lung cancer screening. Based on a retrospective review of 2,897 baseline screening scans, the authors determined that a non-calcified nodule measuring <5 mm should have a follow-up scan in one year [12].

Recently, computed-aided diagnosis (CAD) systems have been developed for lung nodule detection on CT. CAD has the potential to improve radiologists' diagnostic accuracy in distinguishing small benign nodules from malignant ones on high resolution CT (HRCT) [13,14].

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Contrast-enhanced CT of solitary pulmonary nodules has also been used to differentiate benign from malignant nodules. Results from a large multi-center 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 [15]. Recent studies have also shown that analysis of the time-density curve for enhancement may even provide additional information [16]. The extent of enhancement reflects underlying nodule angiogenesis [17]. Limitations of the technique relate to its nonspecific nature for inflammatory disease and an incomplete knowledge base for small nodules. More recently, contrast-enhanced dynamic MR imaging of solitary pulmonary nodules has shown to be comparable to CT for differentiatong between benign and malignant pulmonary nodules with a sensitivity of 96%, specificity of 88% and accuracy of 92% [18,19].

PET scanning using fluorodeoxyglucose (FDG) has gained 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 [20,21]. The sensitivity and specificity for this technique, as reported in the literature, have ranged from 83%-97% and from 69%-100%, respectively. Limitations of PET scanning include its inability to accurately characterize certain types of lesions, including bronchoalveolar carcinoma and typical carcinoid tumors. It is also limited in its ability to characterize nodules less than 1 cm in diameter and it may give false positive results in patients with active infections and inflammatory diseases.

In view of the necessity to approach near certainty with the diagnostic evaluation due to the aggressive nature of lung cancer, tests that provide pathologic material are quite useful. Currently, such diagnostic tests include transthoracic needle biopsy (TNB], bronchoscopy, video-assisted thorascopy (VATS], and thoracotomy. The relative roles of these procedures, is not well defined in existing literature, perhaps because of the lack of a defined sensitivity and specificity for the semi-invasive tests. Both TNB [22-25] and bronchoscopy [26] 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, is usually a more appropriate test in diagnosing solitary nodules. CT fluoroscopy-guided lung biopsy using the new 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% [27]. The role of TNB relative to the surgical approach depends primarily on the ability to make a benign diagnosis. If its only role is to confirm malignancy, then it only adds to the cost of the overall work-up, 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 non-diagnostic 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. In general, for benign nonspecific and nondiagnostic studies, repeat biopsy or resection is necessary [28]. 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 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 thorascopically, 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 thorascopy [29,30].

In view of the variety of diagnostic tests available and the variable accuracy of the different diagnostic techniques, no single algorithm for work-up is generally accepted. It has been found to vary from institution to institution. This is probably appropriate given 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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