American College Of Radiology
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WORK-UP OF THE 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 x-ray.

The ever-expanding role of computed tomography 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 not necessarily solid in appearance and not entirely spherical. 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 was based on the chest x-ray 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 known. 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 chest x-ray-detected nodules, the primary concern in evaluation of 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 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.

The choice of imaging test to evaluate solitary nodules is extensive. However, there remain only two findings that are considered to be sufficient to preclude further evaluation. This includes calcification in a benign pattern and stability in size for over two years. Both of these have been known since the early 1950s (8,9). However, only a small number of nodules meet these criteria; the majority fall into 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

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particular, this includes the ability to utilize information using three-dimensional characteristics (10). This field is rapidly developing and will greatly benefit from the improved resolution of the newer multi-row CT scanners. A new image processing technique currently being evaluated measures growth of nodules in short time intervals, allowing for assessment of doubling times (11). This is an extension of the concept of watchful waiting.

Two relatively new imaging techniques that have gained popularity in recent years are contrast-enhanced CT scanning and PET scanning. 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 (12). There have also been some recent studies showing that analysis of the time density curve for enhancement may even provide additional information (13). Limitations of the technique relate to its nonspecific nature for inflammatory disease and an incomplete knowledge base for small nodules.

PET scanning using fluorodeoxyglucose (FDG) represents the first in what may eventually prove to be a highly useful diagnostic paradigm. This technique relies on measuring glucose metabolism, which has been shown to be different between benign and malignant nodules. Newer, more specific receptor-based compounds are currently under development and may eventually be even more useful. Currently, PET scanning has been reported to have a sensitivity ranging from 82% to 95% and a specificity from 85% to 100% (14,15). Limitations of PET scanning include its inability to accurately detect certain types of lesions including bronchoalveolar carcinoma and carcinoid tumors. It is also limited in its ability to detect nodules less than 1 cm in diameter, and it can give false positive results with active inflammatory disease.

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. The exact role of the various invasive and semi-invasive tests is not fully defined. Tests primarily considered include transthoracic needle biopsy (TNB), bronchoscopy, thoracoscopy and thoracotomy. The medical literature is somewhat confusing in regard to the relative role of each of these procedures. This primarily relates to lack of a defined sensitivity and specificity for the semi-invasive tests. Both TNB and bronchoscopy are highly dependent on size and location, and the skill of the person performing the procedure (16,17). In general, TNB has a higher sensitivity and specificity than bronchoscopy and, therefore, is usually a more appropriate test in diagnosis of solitary nodules. 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 two broad categories: specific benign and nonspecific. 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 (18). In general, nonspecific diagnosis cannot be accepted as definitive and, at a minimum, require long-term follow up if more definitive surgical procedures are to be avoided.

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 disease in different parts of the country and the varying skill levels and availability of equipment (19).

Anticipated Exceptions

None.

Review Information

This guideline was originally developed in 1995. A complete review and revision of this document was approved in 2000. The next review will be completed in 2002.

Clinical Condition: **Solitary Pulmonary Nodule, Noncalcified.**

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

Radiologic Exam Procedure	Appropriateness Rating	Comments
High-resolution CT	8	
Fine needle aspiration	8	
Watchful waiting with CT follow-up	8	
Contrast-enhanced CT	6	
PET scan	6	If available. Appropriateness depends on results of other tests such as HRCT, contrast enhanced CT, and results, availability and local expertise in the performance of needle biopsy.
Bronchoscopy	4	
Thoracoscopy	3	Not as the preferred initial approach.
Surgical resection (for diagnosis)	2	
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1=Least appropriate** **9=Most appropriate**		

Clinical Condition: **Solitary Pulmonary Nodule, Noncalcified.**

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

Radiologic Exam Procedure	Appropriateness Rating	Comments
High-resolution CT	8	
Contrast-enhanced CT	8	
Fine needle aspiration	8	
PET scan	6	If available. Appropriateness depends on results of other tests such as HRCT, contrast enhanced CT, and results, availability and local expertise in the performance of needle biopsy.
Surgical resection (for diagnosis)	5	Depends on institution, accuracy and results of needle biopsy, availability of PET, etc.
Bronchoscopy	4	
Thoracoscopy	3	Not as the preferred initial approach.
Watchful waiting with CT follow-up	2	

Appropriateness Criteria Scale

1 2 3 4 5 6 7 8 9

1=Least appropriate **9=Most appropriate**

Clinical Condition: **Solitary Pulmonary Nodule, Noncalcified.**

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

Radiologic Exam Procedure	Appropriateness Rating	Comments
High-resolution CT	8	
Watchful waiting with CT follow-up	8	
Contrast-enhanced CT	4	
PET scan	4	If available. Appropriateness depends on results of other tests such as HRCT, contrast enhanced CT, and results, availability and local expertise in the performance of needle biopsy.
Fine needle aspiration	4	Depends on operator experience and size and accessibility of nodule.
Bronchoscopy	2	
Thoracoscopy	***2***	
Surgical resection (for diagnosis)	2	
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1=Least appropriate** **9=Most appropriate**		

Clinical Condition: **Solitary Pulmonary Nodule, Noncalcified.**

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

Radiologic Exam Procedure	Appropriateness Rating	Comments
High-resolution CT	8	
Fine needle aspiration	8	
PET scan	6	If available. Appropriateness depends on results of other tests such as HRCT, contrast enhanced CT, and results, availability and local expertise in the performance of needle biopsy.
Thoracoscopy	5	If needle biopsy is not available, not technically feasible, or is nondiagnostic.
Contrast-enhanced CT	4	Limited data available.
Surgical resection (for diagnosis)	4	
Watchful waiting with CT follow-up	3	To be considered only when nodules are very small and biopsy is not technically feasible, and in patients who are poor surgical risks.
Bronchoscopy	2	

Appropriateness Criteria Scale

1 2 3 4 5 6 7 8 9

1=Least appropriate **9=Most appropriate**

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