

## What is the best approach to a solitary pulmonary nodule identified by chest x-ray?

### Evidence-based answer

Your initial risk assessment should include the patient's smoking history, advancing age, cancer history, and chest radiography features (strength of recommendation [SOR]: **A**, based on a validated clinical decision rule). You'll also need to review old chest radiographs (SOR: **C**, based on expert opinion). A solitary pulmonary nodule unchanged for >2 years on chest radiograph or containing benign central calcifications requires no further work-up (SOR: **B**, based on historical cohort studies).

While radiologists' interpretations of a nodule's calcification on chest radiograph

and malignancy on computed tomography (CT) are incorrect in a substantial portion of cases (SOR: **B**, based on limited-quality diagnostic cohort studies), spiral CT with contrast is still diagnostically useful in making decisions regarding watchful waiting, needle biopsy, or surgery (SOR: **B**, based on a decision analysis study).

18-fluorodeoxyglucose positron emission tomography (FDG PET) is useful for assessing malignancy risk (SOR: **B**, based on decision analysis study), but not for solitary pulmonary nodules <1 cm (SOR: **C**, based on expert opinion).

### Clinical commentary

#### Direct more costly, invasive tests to those with higher risk of malignancy

Risk stratification of a solitary pulmonary nodule allows the clinician to direct more costly and invasive testing to patients with a higher probability of malignancy. Historical factors such as previous cancer, advanced age, and smoking increase suspicion for malignancy, but CT is generally warranted in all new solitary pulmonary nodules

found on chest radiographs. It's important to obtain a thorough history regarding symptoms (cough, night sweats, weight loss), occupational exposure (asbestos, bird droppings, decaying wood), travel, and comorbid conditions (especially immunocompromised states); this is likely to prove helpful in the workup.

Parul Harsora, MD and Rhessa Sanni-Thomas, DO  
UT Southwestern Medical Center, Dallas, Tex

### Evidence summary

A solitary pulmonary nodule, or "coin lesion," is an intraparenchymal finding on chest radiograph or CT that is less than 3 to 4 cm in diameter and not associated with atelectasis or adenopathy. Malignancy rates range from 15% to 75%, depending on the population studied.<sup>1</sup> Although early detection of malignancy portends a major improvement in survival (up to 75% at 5 years following surgical resection of stage IA disease), most

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Timothy F. Mott, MD  
Naval Hospital Sigonella,  
Sigonella, Italy

Cheryl Goodwin, MLS  
Mars Hill Graduate School,  
Seattle, Wash

### FAST TRACK

**A nodule unchanged for more than 2 years requires no further workup**

**FAST TRACK****CT is cost-effective when the probability of malignancy is less than 90%**

lung cancers progress asymptotically until quite advanced.<sup>2</sup>

The presumed benign nature of lesions that are either unchanged over 2 years or have central calcifications is based on 3 retrospective studies from the 1950s.<sup>3-6</sup> However, these should not be considered absolutes. A recent study revisiting the original data calculated the predictive value of benign nature based on no growth to be only 65% (95% confidence interval [CI], 47%–83%).<sup>7</sup> Also, a study assessing the accuracy of radiologists' assessment of calcification in solitary pulmonary nodules compared with thin-section CT found that 7% of "definitely calcified" nodules on chest radiograph lacked calcification on thin-section CT.<sup>8</sup>

**Which clinical variables best predict malignancy?**

The best available clinical decision rule was derived and validated from a single split population of patients with solitary pulmonary nodules.<sup>9</sup> The outcome variable was defined as malignancy based on histologic tissue analysis or benignity by radiographic stability or resolution over 2 years. The authors did not report whether those determining outcomes and predictors were appropriately blinded.

The authors found that 3 clinical variables (age, smoking history, and cancer history) plus 3 radiographic variables (diameter, spiculation, and nodule location in the upper lobes) were independent predictors of malignancy. An online calculator using this prediction model is available at [www.chestx-ray.com/SPN/SPNProb.html](http://www.chestx-ray.com/SPN/SPNProb.html).<sup>10</sup>

**CT or PET?**

Three comparative studies observed 8 to 12 radiologists' readings of high-resolution CT images of 28 to 56 patients with solitary pulmonary nodules (established diagnoses by either histology or stability over time).<sup>11-13</sup> Approximately half the nodules represented malignant lesions.

Radiologists assigned a level of confidence to their assessment of each case as

benign or malignant. At a minimum, they were informed of each patient's age and gender, and in 2 studies they also knew other information, such as the patient's smoking and cancer histories. The study showed that the radiologists would have correctly diagnosed a pair of solitary pulmonary nodule cases, one malignant and one benign, between 75% and 83% of the time. Conversely, 17% to 25% of the time they would have diagnosed the case pair incorrectly.

A meta-analysis of 40 studies of FDG PET scanning for solitary pulmonary nodules yielded a maximum joint sensitivity and specificity of 90% (95% CI, 86.4%–92.7%).<sup>14</sup> The methodological quality of studies included in the meta-analysis was fair, with small sample sizes (inclusion criteria were for a minimum of 10 patients with pulmonary nodules and malignant prevalence of at least 0.5); masking was frequently incomplete.

**Sensitivity of histologic/cytologic tests varies**

A recent systematic review of studies evaluating patients with suspected lung cancer looked into the diagnostic sensitivity of various methods of histologic and cytologic tests.<sup>15</sup> Researchers compared the evaluated test results to a reference standard of pathology/histology, definitive cytology, or at least 1-year radiographic follow-up.

Transbronchial needle aspiration showed a sensitivity of 67% (95% CI, 64%–70%) for peripheral lung malignancy of any size; however, only 5 studies met study criteria and their sample sizes varied greatly (n=20 to n=480). Eight studies looking at bronchoscopy (including brush or biopsy) for peripheral lung lesions <2 cm in diameter yielded a sensitivity of only 33% (95% CI, 28%–38%). In the same systematic review, 61 studies of trans-thoracic needle aspiration for localized pulmonary lesions of any size had a pooled sensitivity of 90% (95% CI, 88%–92%). The prevalence of malignancy in the studies ranged from

0.58 to 0.93.<sup>15</sup> Factors affecting heterogeneity between studies included the wide range in study dates, imaging technology used, and study sizes.

#### What test is most cost-effective?

CT appears cost-effective when the pretest probability of malignancy is <90%; therefore, consider it on virtually all new cases of solitary pulmonary nodules.<sup>1</sup> Also, when CT and pretest risk-assessments are discordant (eg, a patient has a low pretest probability of malignancy but his CT is suggestive of malignancy), the FDG PET scan is the most economically feasible at less than \$20,000 per quality-adjusted life year.

#### Recommendations from others

The American College of Chest Physicians (ACCP)<sup>2</sup> suggests pursuing no further evaluation if a nodule is unchanged for >2 years or has benign central calcifications. They recommend that physicians perform CT on every patient with a new nodule to characterize the nodule, its location, and the mediastinum. They do not recommend PET scans for nodules <1 cm. Patients who are marginal surgical candidates and have a negative PET scan should have a repeat CT scan in 3 months; serial CTs at 3, 6, 12, and 24 months are suggested, too, if prior chest radiographs are negative.

The ACCP states that transthoracic needle aspiration is not indicated in surgical candidates unless they decline surgery; then transthoracic needle aspiration or a transbronchial approach are the preferred procedure. Transthoracic needle aspiration may also be useful in establishing a diagnosis for patients who are not surgical candidates or who have a high surgical risk.

ACCP expert consensus favors the reference standard of video-assisted thoracoscopic surgery with wedge resection as the ideal method for obtaining tissue diagnosis in consenting, operable patients with solitary pulmonary nodules. Objective evidence is lacking on follow-up

monitoring methods for patients with a nodule who do not have a tissue diagnosis and observation alone is chosen. ACCP expert consensus favors a 2-year follow-up with CT scanning at 3, 6, 12, and 24 months to monitor for nodule growth.<sup>2</sup> ■

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#### FAST TRACK

**A PET scan is useful for assessing risk if the nodule is larger than 1 cm**