

Pulmonary Nodules: Common Questions and Answers

Robert C. Langan, MD, St. Luke's Hospital Family Medicine Residency/Sacred Heart Campus, Allentown, Pennsylvania; Temple University School of Medicine, Philadelphia, Pennsylvania

Andrew J. Goodbred, MD, St. Luke's Hospital Family Medicine Residency/Anderson Campus, Easton, Pennsylvania; Temple University School of Medicine, Philadelphia, Pennsylvania

Pulmonary nodules are often incidentally discovered on chest imaging or from dedicated lung cancer screening. Screening adults 50 to 80 years of age who have a 20-pack-year smoking history and currently smoke or have quit smoking within the past 15 years with low-dose computed tomography is associated with a decrease in cancer-associated mortality. Once a nodule is detected, specific radiographic and clinical features can be used in validated risk stratification models to assess the probability of malignancy and guide management. Solid pulmonary nodules less than 6 mm warrant surveillance imaging in patients at high risk, and nodules between 6 and 8 mm should be reassessed within 12 months, with the recommended interval varying by the risk of malignancy and an allowance for patient-physician decision-making. A functional assessment with positron emission tomography/computed tomography, nonsurgical biopsy, and resection should be considered for solid nodules 8 mm or greater and a high risk of malignancy. Subsolid nodules have a higher risk of cancer and should be followed with surveillance imaging for longer. Direct physician-patient communication, clinical decision support within electronic health records, and guideline-based management algorithms included in radiology reports are associated with increased compliance with existing guidelines. (*Am Fam Physician*. 2023;107(3):282-291. Copyright © 2023 American Academy of Family Physicians.)

The incidental discovery of pulmonary nodules on imaging studies of the chest or through dedicated screening programs for the detection of lung cancer is common. It is estimated that 1.57 million nodules are detected incidentally every year, 5% of which are malignant.¹ The incidence of pulmonary nodules in lung cancer screening programs has been reported at approximately 27%, with 1.1% of patients diagnosed with lung cancer.² Guidelines have been published to aid physicians in managing these nodules.³⁻⁵ Examples of benign causes of pulmonary nodules are listed in Table 1.⁶ All patients with a pulmonary nodule and a history of malignancy, with multiple nodules but no dominant nodule, with any pulmonary mass (i.e., lung opacity of greater

than 3 cm in diameter), or who are immunocompromised should be referred to a pulmonologist for further workup.⁷

What Nodule and Patient Characteristics Suggest a Malignant Cause?

The risk of malignancy is higher in solid nodules that are large, have irregular borders, have asymmetric calcifications, have a volume doubling time between one month and one year, or are in the upper lung lobes. Subsolid nodules are more likely to be cancerous than solid nodules. Increasing age and history of cigarette smoking are associated with a higher risk of lung cancer.

EVIDENCE SUMMARY

Malignancy is more common in solid nodules that are 6 mm or greater in diameter.³ Other nodule characteristics associated with cancer include location in the upper lung lobes, irregular or spiculated borders, ground-glass appearance, or punctate or eccentric calcifications⁷ (Figure 1⁸). Nodules with a volume doubling time of more than 30 days to less than 400 days are

CME This clinical content conforms to AAFP criteria for CME. See CME Quiz on page 226.

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Patient information: A handout on this topic, written by the authors of this article, is available with the online version of this article.

also associated with malignancy because nodules that grow rapidly over days to weeks are more likely to be infectious or inflammatory, and aggressive cancers can double in volume every three to four months (*Table 2*).⁷ Significant growth found on follow-up imaging is presumptive evidence of malignancy and requires consultation with a pulmonary subspecialist or more frequent monitoring. Subsolid nodules include pure ground-glass and part-solid nodules. Although

less common than solid nodules (21% vs. 79% in one lung cancer screening study), part-solid nodules are associated with a higher risk of slow-growing cancer.⁹ Increasing age, greater than 20-pack-year smoking history among current smokers or those who have quit within the past 15 years, a family history of lung cancer, and exposure to asbestos, uranium, or radium are associated with an increased risk of pulmonary malignancy.³

TABLE 1

Benign Causes of Pulmonary Nodules

| Category | Examples |
|-------------------------|-----------------------------------|
| Benign tumor | Chondroma |
| | Hamartoma |
| | Lipoma |
| Congenital | Arteriovenous malformation |
| | Bronchogenic cyst |
| Immune-mediated disease | Rheumatoid arthritis |
| | Sarcoidosis |
| Infectious | Infectious granuloma* |
| | <i>Coccidioidomycosis</i> |
| | <i>Histoplasmosis</i> |
| | <i>Mycobacterium tuberculosis</i> |
| | Lung abscess |
| Other | Amyloidosis |
| | Endoparenchymal lymph node |

*—Healed infectious granulomas are the most common type of benign pulmonary nodule.

Information from reference 6.

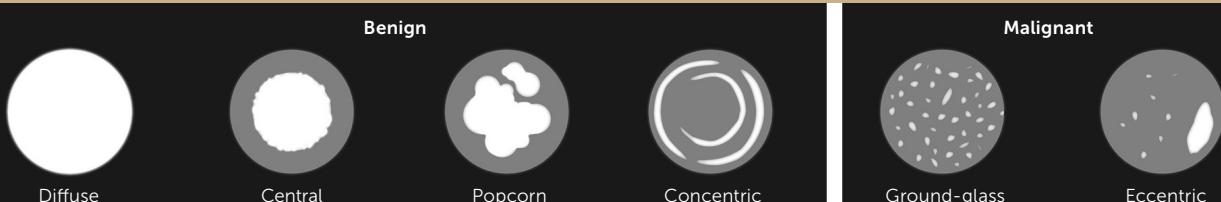
What Is the Evidence for Screening Asymptomatic People for Lung Cancer?

The U.S. Preventive Services Task Force (USPSTF) recommends annual screening for lung cancer with low-dose computed tomography (CT) in adults 50 to 80 years of age who have a 20-pack-year smoking history and currently smoke or quit smoking within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or a willingness to have curative lung surgery (USPSTF Grade B recommendation).¹⁰

EVIDENCE SUMMARY

The National Lung Screening Trial compared annual low-dose CT to chest radiography for three consecutive years in patients at high risk (defined as 55 to 74 years of age with at least a 30-pack-year smoking history who were current smokers or had quit within the previous 15 years). After 6.5 years of follow-up, there was a 20% reduction in lung cancer-related mortality and a 6.7% decrease in overall mortality in the low-dose CT group.¹¹ A more recent meta-analysis of more than 96,000 people that included the National Lung Screening Trial data demonstrated that screening people at high risk with low-dose CT decreased lung cancer-related mortality by 1.8% to 2.2% over five to 10 years but did not change overall mortality.¹² In 2014, the USPSTF recommended the use of low-dose CT for lung cancer screening

FIGURE 1



Patterns of appearance that suggest benign or malignant pulmonary nodules.

Illustration by Dave Klemm

Reprinted with permission from Kikano GE, Fabien A, Schilz R. Evaluation of the solitary pulmonary nodule. *Am Fam Physician*. 2015;92(12):1085.

in people at high risk¹³; this recommendation was updated in 2021 based on data from additional studies and screening models showing benefits for a larger age range (50 to 80 years of age) and shorter smoking history (20-pack-year smoking history) and is endorsed by the American Academy of Family Physicians.^{10,14} Screening patients at high risk of lung cancer with low-dose CT is also recommended by the American College of Chest Physicians (CHEST) and the American Cancer Society, with screening starting at 55 years of age for patients with a 30-pack-year smoking history who currently smoke or have quit within the past 15 years.^{15,16}

What Is the Recommended Management of a Nodule Identified During Lung Cancer Screening?

Repeat low-dose CT is recommended for benign or probably benign nodules; the screening interval depends on the morphology and size of the initial lesion. Additional imaging or referral for biopsy should be considered for patients with very suspicious large solid nodules (15 mm and greater or 8 mm and greater that are new or growing) and subsolid nodules with large solid components (8 mm or greater or 4 mm and greater that are new or growing).

EVIDENCE SUMMARY

The American College of Radiology Lung-RADS score provides management recommendations for pulmonary nodules found during lung cancer screening and is recommended by pulmonary societies^{3,5,15} (Table 3⁵). Patients with a negative screening result or benign-appearing nodules should continue routine annual low-dose CT screening. Probably benign lesions should be reimaged with low-dose CT in six months. Suspicious lesions should be reimaged with low-dose CT in three months.

Positron emission tomography/CT (PET/CT) imaging is used to assess the metabolic activity of a nodule. Although malignant nodules may be more metabolically active, some inflammatory and infectious nodules also may have high uptake on PET/CT⁷; the reported sensitivity is 89% and specificity is 75% for detecting lung cancer.¹⁷ The Lung-RADS guidelines state that PET/CT may be used in evaluating suspicious or very suspicious lesions with a solid component of 8 mm or greater.⁵ Physicians should be mindful of the cumulative dose of radiation to which a patient is exposed in screening and follow-up studies, which ranges from low-dose CT (1.5 mSv), to CT of the chest (6.1 mSv), to full-body PET/CT (22.7 mSv).¹⁸

Referral to pulmonology, interventional radiology, or thoracic surgery for lung biopsy should be considered for solid nodules 15 mm or greater or new or growing nodules 8 mm or greater. Referral should also be considered for subsolid nodules if the solid component is 8 mm or greater or 4 mm or greater and is new or growing. The presence of additional features of malignancy, such as spiculation, doubling of nodule size in one year, or lymphadenopathy, may also indicate a nodule that requires biopsy.⁵ Lung-RADS scoring may decrease the number of subsequent unnecessary diagnostic procedures when used as part of a lung cancer screening program.¹⁹

What Tools Help Physicians Risk Stratify Incidentally Discovered Pulmonary Nodules?

Validated risk calculators estimate the chance of malignancy for incidentally discovered pulmonary nodules. All calculators use history and nodule characteristics found on low-dose CT; some calculators use the results of PET/CT.

EVIDENCE SUMMARY

Although many incidentally discovered lung nodules are found on CT, nodules may also be found on plain radiography. CHEST recommends that unless nodules can be clearly classified as benign (e.g., due to a benign pattern of calcification), chest CT with thin sections is recommended due to its better sensitivity and specificity for detecting lung

TABLE 2

Radiographic Features of Pulmonary Nodules Suggesting Benign or Malignant Etiology

| Feature | Suggests benign etiology | Suggests malignant etiology |
|----------------------|--|---|
| Appearance | Concentric, central, diffuse, or popcorn-like calcifications | Eccentric calcifications, noncalcified, or ground-glass |
| Border | Smooth | Spiculated (higher risk) or irregular |
| Density | Solid | Subsolid |
| Location | Perifissural, subpleural | Upper lobes |
| Multiple nodules | Dominant nodule present | No dominant nodule present |
| Size | < 6 mm | ≥ 6 mm |
| Volume doubling time | Less than 30 days or greater than 400 days | Between 30 and 400 days |

Information from reference 7.

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malignancy compared with plain radiography, and its ability to provide additional information such as size and attenuation characteristics of any lesions.⁴

Guidelines from the Fleischner Society and CHEST recommend using malignancy risk prediction models for patients with incidentally discovered pulmonary nodules to help determine management.^{3,4} Individual patient risk

of malignancy can be classified as high risk (greater than 65%), intermediate risk (5% to 65%), and low risk (less than 5%).⁴ Validated risk prediction models have been developed and have online tools to help with their implementation into practice (*Table 4*²⁰⁻²⁴). Physicians should choose a calculator that best represents the characteristics of the patient being assessed.⁷ Note that although the accuracy of these tools has

TABLE 3

American College of Radiology Lung-RADS Scoring and Management Recommendations

| Category descriptor | Lung-RADS | Findings | Management |
|--|-----------|---|--|
| Incomplete Estimated population prevalence: ~ 1% | 0 | Prior chest CT examination being located for comparison (see note 9) | Comparison to prior chest CT |
| | | Part or all of lungs cannot be evaluated | Additional lung cancer screening CT imaging needed |
| | | Findings suggestive of an inflammatory or infectious process (see note 10) | 1- to 3-month LDCT |
| Negative Estimated population prevalence: 39% | 1 | No lung nodules OR Nodule with benign features: complete, central, popcorn, or concentric calcifications OR fat-containing | 12-month screening LDCT |
| Benign Based on imaging features or indolent behavior Estimated population prevalence: 45% | 2 | Juxtapleural nodule: < 10 mm mean diameter at baseline or new AND solid, smooth margins; and oval, lentiform, or triangular shape Solid nodule: < 6 mm at baseline OR new < 4 mm Part-solid nodule: < 6 mm total mean diameter at baseline Nonsolid nodule (ground-glass nodule): < 30 mm at baseline, new or growing OR ≥ 30 mm stable or slow-growing (see note 7) Airway nodule, subsegmental at baseline, new, or stable (see note 11) Category 3 nodule that is stable or decreased in size at 6-month follow-up CT, OR category 3 or 4A nodules that resolve on follow-up, OR category 4B findings proven to be benign in etiology following appropriate diagnostic workup | 12-month screening LDCT |
| Probably benign Based on imaging features or behavior Estimated population prevalence: 9% | 3 | Solid nodule: ≥ 6 to < 8 mm at baseline OR new 4 to < 6 mm Part-solid nodule: ≥ 6 mm total mean diameter with solid component < 6 mm at baseline OR new < 6 mm in total mean diameter Nonsolid nodule (ground-glass nodule): ≥ 30 mm at baseline or new Atypical pulmonary cyst: (see note 12) growing cystic component (mean diameter) of a thick-walled cyst Category 4A nodule that is stable or decreased in size at 3-month follow-up CT (excluding airway nodules) | 6-month LDCT |

continues

CT = computed tomography; LDCT = low-dose chest CT; PET/CT = positron emission tomography/computed tomography.

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TABLE 3 (continued)

American College of Radiology Lung-RADS Scoring and Management Recommendations

| Category descriptor | Lung-RADS | Findings | Management |
|---|-----------|---|---|
| Suspicious Estimated population prevalence: 4% | 4A | Solid nodule: ≥ 8 to < 15 mm at baseline OR growing < 8 mm OR new 6 to < 8 mm Part-solid nodule: ≥ 6 mm with solid component ≥ 6 to < 8 mm at baseline OR new or growing < 4 mm solid component Airway nodule, segmental or more proximal at baseline or new (see note 11) Atypical pulmonary cyst: (see note 12) thick-walled cyst OR multilocular cyst at baseline OR thin- or thick-walled cyst that becomes multilocular | 3-month LDCT; PET/CT may be considered if there is a ≥ 8 mm solid nodule or solid component |
| Very suspicious Estimated population prevalence 2% | 4B | Airway nodule, segmental or more proximal, and stable or growing (see note 11) Solid nodule: ≥ 15 mm at baseline OR new or growing ≥ 8 mm Part-solid nodule: solid component ≥ 8 mm at baseline OR new or growing ≥ 4 mm solid component Atypical pulmonary cyst: (see note 12) thick-walled cyst with growing wall thickness/nodularity OR growing multilocular cyst (mean diameter) OR multilocular cyst with increased loculation or new/increased-opacity (nodular, ground glass, or consolidation) Slow-growing solid or part-solid nodule that demonstrates growth over multiple screening exams (see note 8) | Referral for further clinical evaluation Diagnostic chest CT with or without contrast; PET/CT may be considered if there is a ≥ 8 mm solid nodule or solid component; tissue sampling; and/or referral for further clinical evaluation Management depends on evaluation, patient preference, and the probability of malignancy (see note 13) |
| Estimated population prevalence < 1% | 4X | Category 3 or 4 nodules with additional features or imaging findings that increase suspicion for lung cancer (see note 14)w | |
| Significant or potentially significant Estimated population prevalence 10% | S | Modifier: may add to category 0-4 for clinically significant or potentially clinically significant findings unrelated to lung cancer (see note 15) | As appropriate to the specific finding |

CT = computed tomography; LDCT = low-dose chest CT; PET/CT = positron emission tomography/computed tomography.

Notes:

1. Lung-RADS Category: Each exam should be coded 0-4 based on the nodule with the highest degree of suspicion.
2. Lung-RADS Management: The timing of follow-up imaging is from the date of the exam being interpreted. For example, 12-month screening LDCT for Lung-RADS 2 is from the date of the current exam. Also note that management of category 3 and 4A nodules follows a stepped approach based on follow-up stability or decrease in size. If nodules resolve on follow-up, reclassify according to the most concerning finding.
3. Practice Audit Definitions: A negative screen is defined as categories 1 and 2; a positive screen is defined as categories 3 and 4. A negative screen does not mean that an individual does not have lung cancer.
4. Nodule Measurement: To calculate nodule mean diameter, measure both the long and short axis to one decimal point in mm, and report mean nodule diameter to one decimal point. The long and short axis measurements may be in any plane to reflect the true size of the nodule. Volumes, if obtained, should be reported to the nearest whole number in mm^3 .
5. Size Thresholds: Apply to nodules at first detection and that enlarge, reaching a higher size category. When a nodule crosses a new size threshold for other Lung-RADS categories, even if not meeting the definition of growth, the nodule should be reclassified based on size and managed accordingly.
6. Growth: An increase in mean diameter size of > 1.5 mm within a 12-month interval.
7. Slow-Growing–Non-Solid (Ground-Glass) Nodules: A ground-glass nodule (GGN) that demonstrates growth over multiple screening exams but does not meet the > 1.5 mm threshold increase in size for any 12-month interval may be classified as Lung-RADS 2 until the nodule meets findings criteria of another category, such as developing a solid component (then manage per part-solid nodule criteria).

continues

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TABLE 3 (continued)

American College of Radiology Lung-RADS Scoring and Management Recommendations

8. Slow-Growing-Solid or Part-Solid Nodules: A solid or part-solid nodule that demonstrates growth over multiple screening exams but does not meet the > 1.5 mm threshold increase in size for any 12-month interval is suspicious and may be classified as a Lung-RADS 4B. Slow-growing nodules may not have increased metabolic activity on PET/CT; therefore, biopsy, if feasible, or surgical evaluation may be the most appropriate management recommendation.
9. Prior Exams: If waiting on prior exams (either a prior screening or diagnostic CT), the Lung-RADS 0 category is temporary until the comparison study is available and a new Lung-RADS category is assigned.
10. Suspected Infectious or Inflammatory Findings:
 - a. Lung-RADS 0 with 1-3 month follow-up LDCT may be recommended for pulmonary findings suggesting an indeterminate infectious or inflammatory process. Such findings may include segmental or lobar consolidation, multiple new nodules (more than six), large solid nodules (≥ 8 mm) appearing in a short interval, and new nodules in certain clinical contexts (e.g., immunocompromised patient). At 1-3 month follow-up, a new Lung-RADS classification and management recommendation should be provided based on the most suspicious nodule.
 - b. New solid or part-solid nodules with imaging features more concerning for malignancy than an infectious or inflammatory process meeting Lung-RADS 4B size criteria may be classified as such with appropriate diagnostic and/or clinical evaluation.
 - c. Some findings indicative of an infection or infectious process may not warrant short-term follow-up (e.g., tree-in-bud nodules or new < 3 cm ground glass nodules). These nodules may be evaluated using existing size criteria with a Lung-RADS classification and management recommendation based on the most suspicious finding.
11. Airway Nodules:
 - a. Endotracheal or endobronchial abnormalities that are segmental or more proximal are classified as Lung-RADS 4A.
 - b. Subsegmental and/or multiple tubular endobronchial abnormalities favor an infectious process; if no underlying obstructive nodule is identified, these findings may be classified as Lung-RADS 0 (likely infectious or inflammatory) or 2 (benign).
 - c. The presence of air in segmental or more proximal airway abnormalities often favors secretions; if no underlying soft tissue nodule is identified, these findings may be classified as Lung-RADS 2.
 - d. Segmental or more proximal airway nodules that are stable or growing on 3-month follow-up CT are upgraded to Lung-RADS 4B with management recommendation for further clinical evaluation (typically bronchoscopy).
12. Atypical Pulmonary Cysts:
 - a. Thin-walled Cyst: Unilocular with uniform wall thickness < 2 mm. Thin-walled cysts are considered benign and are not classified or managed in Lung-RADS.
 - b. Thick-walled Cyst: Unilocular with uniform wall thickness, asymmetric wall thickening, or nodular wall thickening ≥ 2 mm (cystic component is the dominant feature); manage as an atypical pulmonary cyst.
 - c. Multilocular Cyst: Thick- or thin-walled cyst with internal septations. Manage as an atypical pulmonary cyst.
 - d. Cavitary Nodule: Wall thickening is the dominant feature; manage as a solid nodule (total mean diameter).
 - e. Cyst with an Associated Nodule: Any cyst with adjacent internal (endophytic) or external (exophytic) nodule (solid, part-solid, or ground-glass). Management is based upon Lung-RADS criteria for the most concerning feature.
 - f. Growth: > 1.5 mm increase in nodule size (mean diameter), wall thickness, and/or size of the cystic component (mean diameter) occurring within a 12-month interval.
 - g. Fluid-containing cysts may represent an infectious process and are not classified in Lung-RADS unless other concerning features are identified.
 - h. Multiple cysts may indicate an alternative diagnosis such as Langerhans cell histiocytosis (LCH) or lymphangioleiomyomatosis (LAM) and are not classified in Lung-RADS unless other concerning features are identified. (Reference: Seaman DM, Meyer CA, Gilman MD, McCormack FX. Diffuse Cystic Lung Disease at High-Resolution CT. AJR 2011;196: 1305-1311)
13. Category 4B: Management is predicated on clinical evaluation (comorbidities), patient preference, and risk of malignancy. Radiologists are encouraged to use the McWilliams, et. al. Assessment Tool when making recommendations (<https://brocku.ca/lungcancer-screening-and-risk-prediction/risk-calculators/>).
14. Category 4X: Category 3 or 4 nodules with additional imaging findings that increase the suspicion of lung cancer, such as spiculation, lymphadenopathy, frank metastatic disease, a GGN that doubles in size in 1 year, etc. 4X is a distinct Lung-RADS category; X should not be used as a modifier.
15. Exam Modifier: An S modifier may be added to Lung-RADS categories 0-4 for clinically significant or potentially clinically significant findings unrelated to lung cancer.
 - a. Management should adhere to available ACR Incidental Findings management recommendations (<https://www.acr.org/Clinical-Resources/Incidental-Findings>). The ACR Lung Cancer Screening CT Incidental Findings Quick Reference Guide summarizes common findings and management (<https://www.acr.org/-/media/ACR/Files/Lung-Cancer-Screening-Resources/LCS-Incidental-Findings-Quick-Guide.pdf>).
 - b. Findings that are already known, and have been or are in the process of clinical evaluation DO NOT require an S modifier. Any evidence of a concerning change in a known significant or potentially significant finding that is unexpected warrants renewed use of the S modifier.
16. Lung Cancer Diagnosis: Once a patient is diagnosed with lung cancer, further management (including additional imaging, such as PET/CT) may be performed for purposes of lung cancer staging; this is no longer considered screening.

Additional resources available at: <https://www.acr.org/Clinical-Resources/Reporting-and-Data-Systems/Lung-RADS>

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been established, their clinical usefulness has not been verified and may not add much beyond the clinical expertise and interpretation provided by specialists or radiologists.⁷

What Is the Recommended Management of an Incidentally Detected Solid Pulmonary Nodule?

The Fleischner Society and CHEST recommend no follow-up for small, low-risk nodules and scheduled follow-up with CT for medium-sized nodules. The Fleischner Society recommends short-term CT follow-up, PET/CT, or tissue sampling for large nodules, whereas CHEST recommends management based on the risk of malignancy.

EVIDENCE SUMMARY

Management of solid pulmonary nodules varies among guidelines (*Table 5*).^{3,4} The Fleischner Society recommends follow-up be performed based on nodule size (less than 6 mm, 6 to 8 mm, greater than 8 mm) and risk assessment

(high, which combines the intermediate- and high-risk groups; or low).³ High-risk factors include older age, significant smoking history, larger nodule size, irregular or spiculated borders, or upper lobe location. Low-risk factors include young age, less smoking, smaller nodule size, regular margins, and location not in the upper lobes. Patients at low risk with small nodules (less than 6 mm) do not require further surveillance. Repeat CT at 12 months may be considered in patients at high risk. Short-interval imaging with CT in six to 12 months is recommended for medium-sized nodules (6 to 8 mm) regardless of the risk category, followed by more frequent surveillance. For large nodules (greater than 8 mm), physicians should consider CT in three months, PET/CT, or referral for tissue sampling.

The CHEST guideline makes similar recommendations for small and medium-sized nodules.⁴ However, for large nodules, management differs based on the risk of malignancy, which includes the use of risk prediction models. Patients at low risk (less than 5%) may be followed with low-dose

TABLE 4

Validated Risk Prediction Models for Pulmonary Nodules

| Characteristic | Mayo Clinic | U.S. Department of Veterans Affairs | Herder | Cleveland Clinic | PanCan (Brock University) |
|---------------------------|---|---|---|---|---|
| Population characteristic | Incidental nodule on chest radiography | Incidental nodule on chest radiography confirmed with CT | Incidental nodule on chest radiography with PET/CT performed | Incidental nodules referred for biopsy or lung resection | Nodules detected during lung cancer screening |
| Components of model | Age Extrathoracic cancer \geq 5 years ago Nodule diameter Smoking history Spiculation Upper lobe location | Age Nodule diameter Smoking history Time since quitting smoking | Age Extrathoracic cancer \geq 5 years ago PET/CT results | Age Presence of emphysema PET/CT results History of nonlung cancer | Age Presence of emphysema Family history of lung cancer Location Nodule count Nodule size Nodule type Patient sex |
| Website | https://reference.medscape.com/calculator/solitary-pulmonary-nodule-risk | Available in original article ²³ : https://journal.chestnet.org/article/S0012-3692(15)48320-5/fulltext | http://www.nucmed.com/nucmed/spn_risk_calculator.aspx | Available in original article ²⁴ : https://journal.chestnet.org/article/S0012-3692(19)30689-0/fulltext | https://www.uptodate.com/contents/calculator-solitary-pulmonary-nodule-malignancy-risk-in-adults-brock-university-cancer-prediction-equation |

CT = computed tomography; PET/CT = positron emission tomography/computed tomography.

Information from references 20-24.

TABLE 5

Comparison of Guidelines for the Management of Incidental Solid Pulmonary Nodules

| Nodule size* | Assigned risk† | American College of Chest Physicians | Fleischner Society |
|-----------------------|----------------|--|--|
| Small (< 6 mm) | High risk | ≤ 4 mm: CT at 12 months (if stable, no further follow-up) > 4 to 6 mm: CT at six to 12 months (if stable, repeat CT at 18 to 24 months) | Optional: follow-up CT in 12 months |
| | Low risk | ≤ 4 mm: patient discussion, with option for follow-up > 4 to 6 mm: follow-up CT at 12 months (if stable, no further follow-up) | No follow-up |
| Medium (6 to 8 mm) | High risk | CT at three to six months (if stable, then nine to 12 months and 24 months) | CT in six to 12 months, then repeat CT in 18 to 24 months |
| | Low risk | CT at six to 12 months (if stable, follow-up at 18 to 24 months) | CT in six to 12 months, then consider repeat CT at 18 to 24 months |
| Large (> 8 mm) | High/low risk | ≥ 8 mm: calculate probability of malignancy: Pretest probability < 5%: surveillance CT in three months Pretest probability 5% to 65%: PET/CT with plan for continued surveillance, nonsurgical biopsy, or surgical biopsy/resection Pretest probability > 65%: surgical biopsy or resection after staging | Consider follow-up CT at three months, PET/CT, or tissue sampling |

CT = computed tomography; PET/CT = positron emission tomography/computed tomography.

*—The Fleischner Society adds volume criteria for nodule size: small < 100 mm³; medium = 100 to 250 mm³; large > 250 mm³.

†—The American College of Chest Physicians recommends the use of clinical judgement or a validated risk prediction model (Table 4) to assign the personal risk of malignancy as high (> 65%), intermediate (5% to 65%), or low (< 5%). The Fleischner Society recommends characterizing personal risk of malignancy as high risk using any of the following: older age, significant smoking history, larger nodule size, irregular or spiculated borders, or upper lobe location; vs. low risk using any of the following: young age, less smoking, smaller nodule size, regular margins, and location not in the upper lobes.

Information from references 3 and 4.

CT in three months. Patients with an intermediate risk of malignancy (5% to 65%) may be offered PET/CT to define the risk of malignancy further or determine the need for a biopsy. Peripherally located nodules are often more accessible by CT-guided transthoracic needle biopsies, whereas bronchoscopy may more easily reach nodules nearer to an airway.⁷ In one meta-analysis, transthoracic needle biopsies had a higher diagnostic yield than bronchoscopy (93% vs. 75%) but were also associated with a higher risk of bleeding and pneumothorax.²⁵ Technological advances in bronchoscopy have improved diagnostic yield with similarly low complication rates.²⁶

When the risk of malignancy is high (greater than 65%), surgical resection is recommended for patients who can tolerate the procedure.⁷ Nonsurgical options, including biopsy, stereotactic radiotherapy, or ablative therapies, may be considered for patients at very high risk of death from the resection procedure.

What Is the Recommended Management for Incidentally Detected Subsolid Nodules?

Small subsolid nodules (5 mm or less per CHEST, less than 6 mm per the Fleischner Society) do not require further imaging. Regular surveillance imaging with CT is recommended for

intermediate-sized (6 to 8 mm) subsolid nodules, and larger (greater than 8 mm) subsolid nodules are managed similarly to large solid nodules.

EVIDENCE SUMMARY

CHEST and Fleischner Society guidelines do not recommend further imaging for small subsolid pulmonary nodules. Larger ground-glass nodules should be followed with repeat CT at six to 12 months, then periodically for the next few years (Table 6).^{3,4} CHEST recommends that part-solid, 6 to 8 mm nodules be reimaged with CT at three, 12, and 24 months, then annually for five years. Nodules greater than 8 mm should have follow-up CT at three months with PET/CT, biopsy, or resection if the nodule persists. The Fleischner Society recommends repeat CT in three to six months for part-solid nodules 6 mm or greater, then annually for five years.

What Factors Are Associated With Improved Adherence to These Guidelines?

Adherence to guidelines is improved with high-quality physician-patient communication, clinical decision support tools, and radiology reports that include guideline templates.

| Clinical recommendation | Evidence rating | Comment |
|--|-----------------|--|
| Annual lung cancer screening with low-dose computed tomography is recommended in adults 50 to 80 years of age who have a 20-pack-year smoking history and currently smoke or have quit within the past 15 years. ¹⁰ | B | U.S. Preventive Services Task Force recommendation based on reduction in cancer-associated mortality |
| Chest computed tomography with thin sections should be ordered for patients with pulmonary nodules detected on chest radiography that cannot be clearly classified as benign. ⁴ | C | Guideline recommendations from the American College of Chest Physicians |
| A validated clinical decision tool should be used in patients with pulmonary nodules to determine the probability of malignancy (high risk, greater than 65%; intermediate risk, 5% to 65%; and low risk, less than 5%) and guide management. ^{3,4} | C | Guideline recommendations from the American College of Chest Physicians and Fleischner Society |
| Direct communication with patients, clinical decision support within electronic health records, and guideline-based management algorithms included in radiology reports improve compliance with guidelines for the management of pulmonary nodules. ²⁸⁻³⁰ | C | Several small studies demonstrated improved adherence to guidelines but did not discuss improvements in specific patient-oriented outcomes |

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <https://www.aafp.org/afpsort>.

TABLE 6

Comparison of Guidelines for the Management of Incidental Subsolid Pulmonary Nodules

| Nodule size | American College of Chest Physicians | Fleischner Society |
|-------------|---|--|
| Small | ≤ 5 mm: no follow-up | < 6 mm: no routine follow-up for ground-glass or part-solid nodules |
| Large | > 5 mm Ground-glass: CT at 12 months, then annual CT for three years Part-solid nodule: ≤ 8 mm solid component: CT at three, 12, and 24 months, then annually for five years > 8 mm solid component: CT at three months, further evaluation with PET/CT, biopsy, or resection if nodule persists | ≥ 6 mm Ground-glass: CT at six to 12 months, then every two to five years Subsolid nodule: CT at three to six months, then annually for five years |

CT = computed tomography; PET/CT = positron emission tomography/computed tomography.

Information from references 3 and 4.

EVIDENCE SUMMARY

In one study, only 55% of patients with pulmonary nodules of any type diagnosed outside of a lung cancer screening program received appropriate, guideline-based care.²⁷ Direct physician-patient communication, clinical decision support within electronic health records, and guideline-based management algorithms included in radiology reports are all associated with increased compliance with guidelines.²⁸⁻³⁰ Conversely, inappropriate or incomplete radiology reports, receiving care at multiple facilities, and incidental detection

during inpatient care or preoperative visits are associated with subsequent nonadherence to published guidelines.²⁷

This article updates previous articles on this topic by Kikano, et al.,⁸ and Albert and Russell.³¹

Data Sources: A PubMed search was completed using the key terms solitary pulmonary nodule, diagnosis, management, and lung cancer screening. Also searched were the Agency for Healthcare Research and Quality evidence reports, Clinical Evidence, the Cochrane database, Essential Evidence Plus, U.S. Preventive Services Task Force, and the Institute for Clinical Systems

Improvement. Search dates: March 4, 2022 to July 15, 2022, August 20, 2022, and January 23, 2023.

The Authors

ROBERT C. LANGAN, MD, FAAFP, is the program director at St. Luke's Hospital Family Medicine Residency/Sacred Heart Campus, Allentown, Pa., and an adjunct professor in the Department of Family and Community Medicine at Temple University School of Medicine, Philadelphia, Pa.

ANDREW J. GOODBRED, MD, FAAFP, is the associate program director at St. Luke's Hospital Family Medicine Residency/Anderson Campus, Easton, Pa., and an adjunct associate professor in the Department of Family and Community Medicine at Temple University School of Medicine.

Address correspondence to Robert C. Langan, MD, FAAFP, St. Luke's Family Medicine Residency/Sacred Heart Campus, 450 Chew St., Ste. 101, Allentown, PA 18102 (email: robert.langan@sluhn.org). Reprints are not available from the authors.

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