CHEST Special Features

A Practical Algorithmic Approach to the Diagnosis and Management of Solitary Pulmonary Nodules

Part 2: Pretest Probability and Algorithm

Vishal K. Patel, MBBS; Sagar K. Naik, MBBS; David P. Naidich, MD, FCCP; William D. Travis, MD, FCCP; Jeremy A. Weingarten, MD, FCCP; Richard Lazzaro, MD; David D. Gutterman, MD, FCCP; Catherine Wentowski, MD; Horiana B. Grosu, MD; and Suhail Raoof, MBBS, FCCP

In this second part of a two-part series, we describe an algorithmic approach to the diagnosis of the solitary pulmonary nodule (SPN). An essential aspect of the evaluation of SPN is determining the pretest probability of malignancy, taking into account the significant medical history and social habits of the individual patient, as well as morphologic characteristics of the nodule. Because pretest probability plays an important role in determining the next step in the evaluation, we describe various methods the physician may use to make this determination. Subsequently, we outline a simple yet comprehensive algorithm for diagnosing a SPN, with distinct pathways for the solid and subsolid SPN. ***CHEST 2013; 143(3):840–846***

Abbreviations: GGN = ground glass nodule; FDG = ^{18}F-2-deoxy-2-fluoro-D-glucose; SPN = solitary pulmonary nodule

A practical diagnostic algorithm for approaching the solitary pulmonary nodule (SPN), stratifying clinical risk factors in a standardized manner and blending this information with radiologic clues, would point the physician toward a benign or malignant cause.[1-7] Such an approach would be expected to spare patients with benign causes the morbidity and cost associated with invasive tissue sampling and, at the same time, guide the physician toward recommending invasive tests for the nodules likely to be malignant.

Calculation of Pretest Probability

The clinical and radiologic features described in Part 1 (see page 825)[8] can individually provide clues as to whether a given SPN is benign or malignant.[9-16] However, assimilating all these factors and assigning the "weight" of probability of malignancy to each factor, and coming up with the approximate probability of malignancy, is an onerous task. Let us take, for example, a 65-year-old patient with a 20-pack-year smoking history who is found to have a 3-cm noncalcified SPN with lobulated borders in the right upper lobe (Fig 1). The physician is faced with the task of calculating the probability of malignancy in this nodule. If the probability is low, the physician is likely to recommend follow-up of this SPN with serial CT scans. On the other hand, if the probability of malignancy is moderate or high, the patient should be referred for further testing or tissue sampling. How consistent are physicians in stratifying the malignant potential of a SPN? In the instance cited, the range of pretest probability was calculated by showing the same image on the same computer screen to 44 physicians (internists and pulmonologists in academic and private practice

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Affiliations: From the New York Methodist Hospital (Drs Patel, Naik, Weingarten, Lazzaro, Wentowski, Grosu, and Raoof), Brooklyn, NY; New York University Langone Medical Center (Dr Naidich), New York, NY; Memorial Sloan-Kettering Cancer Center (Dr Travis), New York, NY; and Medical College of Wisconsin (Dr Gutterman), Milwaukee, WI.
Correspondence to: Suhail Raoof, MBBS, FCCP, New York Methodist Hospital, Department of Pulmonary and Critical Care, 506 Sixth St, Brooklyn, NY 11215; e-mail: suhailraoof@gmail.com

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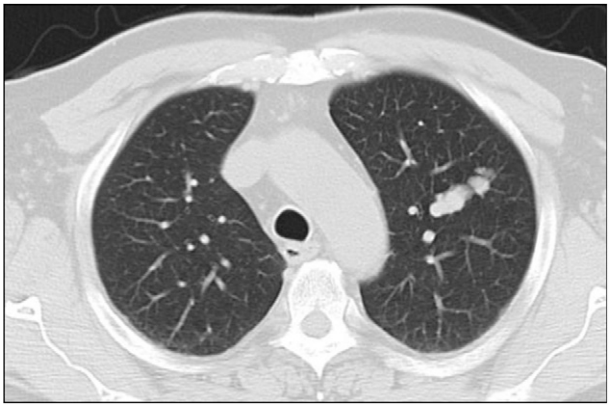

FIGURE 1. Pulmonary varix.

in a community hospital in New York). The range was found to be 2% to 95% (unpublished data). Although experienced physicians routinely make these judgments by gestalt in day-to-day practice, standardized methods have been developed to calculate the probability of the malignancy of a SPN.[17]

Bayesian analysis is one such approach. Likelihood ratios for malignancy are assigned to each clinical and radiologic feature by dividing the probability of finding a particular feature in patients with malignant nodules by the probability of finding the same feature in patients with benign nodules. The odds of malignancy can then be calculated by multiplying the likelihood ratios for each individual clinical and radiologic feature by the prior odds of malignancy. Probability of malignancy can then be calculated easily from the odds. A number of authors developed this approach during the 1970s and 1980s,[18-23] but Gurney et al[24,25] provided the most rigorous test. They derived likelihood ratios from a database of 3,858 patients and then validated the model by comparing it with subjective clinical assessments. Following a review of the literature current at that time, they calculated likelihood ratios for age, smoking history, history of previous malignancy, hemoptysis, size of the SPN, location, edge characteristics, calcification, growth rate, and cavity wall thickness. Needless to say, these calculations were only as accurate as the studies that were used to glean the data. Subsequently, a total of 66 patients with SPNs were evaluated for the probability of malignancy by four radiologists with an average experience of 16 years, yielding an accuracy of 62.5% and an error rate of 37%. When the previously determined Bayesian analysis was employed by a separate set of radiologists with far less experience, the accuracy and error rates were much better, at 77.5% and 15.5% respectively, with fewer false-negative results.

A convenient and reliable way of performing this assessment is by using a calculator available online at www.chestx-ray.com under the tab "Practice." This calculator takes into account the likelihood ratios from a list of clinical and radiologic factors (Table 1) and generates a percentage probability of malignancy. Based on this calculator, the pretest probability of malignancy in the lesion described in the previous paragraph is 95%. Interestingly, only 66% of the respondents in our survey correctly identified the pretest probability of malignancy as ≥ 60%.

Swensen et al[26] employed multivariate regression analysis in an attempt to account for the correlation and interaction among various clinical and radiologic risk factors. They derived their model from a cohort of 419 patients with SPNs detected on chest radiograph and identified risk factors as delineated in Table 1. This prediction model is described by the following equation:

$$\text{Probability of malignancy} = e^x / (1 + e^x)$$

$$x = -6.8272 + (0.0391 \times \text{age}) + (0.7917 \times \text{smoke}) + (1.3388 \times \text{cancer}) + (0.1274 \times \text{diameter}) + (1.0407 \times \text{spiculation}) + (0.7838 \times \text{location})$$

where e = the natural logarithm, age is the patient's age in years, smoke = 1 if the patient is a current or former smoker (otherwise, smoke = 0), diameter is the diameter of the nodule in millimeters, spiculation = 1 if the edge of the nodule has spicules (otherwise, spiculation = 0), and location = 1 if the nodule is located in an upper lobe (otherwise, location = 0). The model

Table 1—*Calculation of Probability of Malignancy*

Source/Reference	Factors Taken Into Consideration to Determine the Probability of Malignancy
www.chestx-ray.com	1. Age
	2. Smoking (ever vs never and pack-y)
	3. Hemoptysis
	4. History of prior malignancy
	5. Nodule diameter
	6. Location
	7. Edge characteristics
	8. Growth rate
	9. Cavity wall thickness
	10. Calcification
	11. Contrast enhancement on CT scan > 15 HU
	12. PET scan
Swensen et al[26]	1. Age
	2. Smoking history (ever vs never)
	3. History of previous malignancy > 5 y ago
	4. Presence of spiculation
	5. Upper lobe location
Gould et al[27]	1. Age
	2. Smoking history (ever vs never)
	3. Nodule diameter
	4. Time since quitting smoking

HU = Hounsfield unit.

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