Initial Evaluation of the Patient With Lung Cancer: Symptoms, Signs, Laboratory Tests, and Paraneoplastic Syndromes*

ACCP Evidenced-Based Clinical Practice Guidelines (2nd Edition)

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Background: **This chapter of the guidelines is intended to provide an evidence-based assessment of the initial evaluation of patients recognized as having lung cancer and the recognition of paraneoplastic syndromes.**

Methods: **The current medical literature that is applicable to this issue was identified by a computerized search and was evaluated using standardized methods. Recommendations were framed using the approach described by the Health and Science Policy Committee of the American College of Chest Physicians.**

Results: **Patients with lung cancer usually present with multiple symptoms, both respiratory related and constitutional. There is usually a time delay between symptom recognition by the patient and the ultimate diagnosis of lung cancer by the physician. Whether this time delay impacts prognosis is unclear, but delivering timely and efficient care is an important component in its own right. Lung cancer may be accompanied by a variety of paraneoplastic syndromes. These syndromes may not necessarily preclude treatment with a curative intent.**

Conclusions: **The initial evaluation of the patient with known or suspected lung cancer should include an assessment of symptoms, signs, and laboratory test results in a standardized manner as a screen for identifying those patients with paraneoplastic syndromes and a higher likelihood of metastatic disease.** ***(CHEST 2007; 132:149S–160S)***

Key words: evaluation; laboratory tests; paraneoplastic syndrome; signs; symptoms

Abbreviations: ACTH = adrenocorticotropic hormone; ADH = antidiuretic hormone; HOA = hypertrophic osteoarthropathy; LEMS = Lambert-Eaton myasthenic syndrome; PTH = parathyroid hormone; PTH-rP = parathyroid hormone-related peptide; SIADH = syndrome of inappropriate antidiuretic hormone; SVCO = superior vena cava obstruction; VEGF = vascular endothelial growth factor

Lung cancer, unfortunately, is usually recognized late in its natural history. In large part, this reflects the peculiarities of pulmonary anatomy. A pulmonary nodule could grow for a considerable period of time, and potentially spread outside the lung, before it would cause symptoms. Consequently, at the initial presentation most patients with lung cancer have advanced disease. In general, of 100 newly presenting patients with lung cancer, 80 will be inoperable at presentation and only approximately 20 will proceed to attempted resection.[1] These observations explain why the 5-year mortality rates for lung cancer remain at approximately 85 to 90%. An understanding of how patients with lung cancer initially present will possibly allow the earlier identification of this increasingly common disease.

Materials and Methods

To update previous recommendations on the initial evaluation of the patient with lung cancer, guidelines on lung cancer diagnosis and management published between 2002 and May

2005 were identified by a systematic review of the literature (see "Methodology for Lung Cancer Evidence Review and Guidelines Development" section). Those guidelines including recommendations that are specific to the initial evaluation of the lung cancer patient were identified for possible inclusion in this section. Supplemental material appropriate to this topic was obtained by a literature search of a computerized database (MEDLINE). Recommendations were developed by the writing committee, graded by a standardized method (see "Methodology for Lung Cancer Evidence Review and Guidelines Development" section), and reviewed by all members of the lung cancer panel and the Thoracic Oncology Network prior to approval by the Health and Science Policy Committee, and the Board of Regents of the American College of Chest Physicians.

Presenting Symptoms of Lung Cancer

Initial presenting symptoms in patients with lung cancer may be respiratory related, but are often constitutional and attributable to metastatic disease (Table 1).[2–7] Cough is reported to be the most common presenting symptom of lung cancer; other respiratory symptoms include dyspnea, chest pain, and hemoptysis.[8–10] Patients with lung cancer usually present with multiple symptoms, including both respiratory and constitutional.[8,9] In a series of 678 consecutive lung cancer patients, at presentation 183 patients (27%) had symptoms related to the primary tumor; 232 patients (34%) had nonspecific systemic symptoms suggestive of metastases, including anorexia, weight loss and fatigue; and 219 patients (32%) had symptoms specific to a metastatic site.[11] The percentage of patients found to have lung cancer incidentally through chest radiographs has been consistently low. In the series reported in 1970 by Carbone et al[11] of 678 consecutive newly diagnosed lung cancer patients in the United States, only 44 patients (6%) were asymptomatic. In a community-based survey of lung cancer patients in Sweden who had received new diagnoses between 1997 and 1999, only 24 of 364 patients (7%) were asymptomatic.[12] Buccheri and Ferrigno[8] described the initial presentation of 1,277 consecutive lung cancer patients who received diagnoses at a single center in Italy from 1989 to 2002. Only 154 of these patients (13%) were asymptomatic at diagnosis. Prognosis in lung cancer has been clearly related to the type of presenting symptoms.[11] There was a better 5-year survival rate reported for asymptomatic patients (18%) than for those patients with symptoms related to the primary tumor (12%). Those patients with nonspecific symptoms had a 6% 5-year survival rate, and those patients with symptoms indicating metastatic disease fared the worst, with none alive at 5 years.

Table 1—*Range of Frequencies of Initial Symptoms and Signs of Lung Cancer

Symptoms and Signs	Range of Frequency, %
Cough	8–75
Weight loss	0–68
Dyspnea	3–60
Chest pain	20–49
Hemoptysis	6–35
Bone pain	6–25
Clubbing	0–20
Fever	0–20
Weakness	0–10
Superior vena cava obstruction	0–4
Dysphagia	0–2
Wheezing and stridor	0–2

*Modified from references 2 to 7.

In addition to the time delay between the development of the lung cancer and initial symptoms, there are usually a series of other delays before treatment is eventually initiated. Patients with lung cancer may notice a new symptom or a change in their usual respiratory symptoms but delay in reporting this to their general practitioner. Corner and colleagues[9] interviewed 22 patients with newly diagnosed lung cancer in the United Kingdom. Patients in this study had noted many different symptoms prior to presentation to their general practitioner, with cough and breathing changes being the most common. Of note was that patients described the onset of these symptoms between 4 months and 2 years (median time, 12 months) before they presented to their general practitioner. Koyi et al[13] reviewed the clinical course of 134 patients with lung cancer in whom cancer was newly diagnosed in 1997 and 1998 in Graevleborg, Sweden. The mean delay between symptom onset and first visit to their general practitioner was 43 days (range, 0 to 256 days). The one specific symptom that has been described as prompting more rapid presentation was hemoptysis.[9]

Even when patients present to the general practitioner with a symptom compatible with lung cancer, the general practitioner may not consider lung cancer a possibility. In the review by Koyi et al,[13] the

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The authors have reported to the ACCP that no significant conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.
Manuscript received May 30, 2007; revision accepted June 5, 2007.

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DOI: 10.1378/chest.07-1358