



An Official American Thoracic Society/European Respiratory Society Statement: The Role of the Pulmonologist in the Diagnosis and Management of Lung Cancer

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Background: Lung cancer is a common problem seen by pulmonologists. The American Thoracic Society (ATS) and European Respiratory Society (ERS) are professional organizations whose memberships are composed of large numbers of pulmonologists.

Purpose: This document describes the key role of pulmonologists in the prevention, early diagnosis, and management of lung cancer.

Methods: A committee of ATS and ERS leaders and their oncology groups discussed the activities of pulmonologists in relation to lung cancer in various settings and reviewed available literature on the topic. The content of this statement was approved by the board of directors of both the ATS and ERS.

Results: Optimal lung cancer care requires a multidisciplinary team of specialists who care for a significant number of patients on a regular basis. Pulmonologists are responsible for and involved with patients from their initial diagnosis and staging through treatment and restaging. They are often involved with complications, palliative care, and end-of-life care, and thus have an important role in team leadership.

Conclusions: Lung cancer is a disease with high mortality, profound effects on the quality of the lives of patients and their families, and an enormous cost and impact on society. To treat lung cancer optimally, care must be prompt, multidisciplinary, and patient-centered. In the entire process, pulmonologists have a key role. Pulmonologists and their professional societies should also enhance lung cancer research and education to provide better treatment options and patient care.

EXECUTIVE SUMMARY

This document describes the pivotal role of the pulmonologist in the prevention, early diagnosis, and management of lung cancer. The key points are as follows:

- Lung cancer has the highest mortality rate of any cancer in the world. Although the incidence and mortality are now decreasing in men, they are increasing in women, a trend attributable to the changing pattern of cigarette smoking over the past 30 years.
- Pulmonologists are effective leaders of smoking cessation programs and public health efforts to reduce the prevalence of smoking, which is the most important risk factor for lung cancer.
- Pulmonologists play a key role in the prompt diagnosis, staging, and treatment of patients with lung cancer; early intervention improves survival.
- Pulmonologists lead and participate in multidisciplinary efforts to diagnose and treat patients with lung cancer. Close collaborations with thoracic surgeons, medical oncologists, radiation oncologists, radiologists, and palliative medicine specialists should be encouraged by the European Respiratory Society (ERS) and American Thoracic Society (ATS).
- Pulmonologists can have pivotal roles in the development and implementation of algorithms for lung cancer diagnosis and treatment. Specifically, they are involved in the interpretation of clinical and radiographic findings, as well as the performance of interventional procedures, such as bronchoscopy, endobronchial ultrasound (EBUS), thoracentesis, and medical thoracoscopy. These forms of tissue sampling are essential for establishing diagnosis and staging and for providing adequate tissue specimens that can guide targeted and personalized therapies.
- Increasingly, pulmonologists play an important role in clinical trial development and implementation for novel agents directed toward chemoprevention and treatment of lung cancer.
- Pulmonologists often manage comorbidities, such as dyspnea and respiratory failure, and side effects from both the cancer and treatment. In certain countries and settings, they provide medical treatment for the cancer (e.g., chemotherapy and biologics), endobronchial treatment (e.g., brachytherapy), general supportive care, and terminal care.
- There are many differences across countries and settings. For example, in many European countries, chemotherapy and biologics are frequently administered by pulmonologists,

while in the United States these treatments are typically provided by medical oncologists.

- Pulmonologists should be familiar with advances in molecular testing and they should adapt diagnostic procedures, such as EBUS and transthoracic biopsies, to ensure that specimens are sufficient for molecular and immunohistochemical testing.
- Multidisciplinary lung cancer tumor boards create an opportunity for key specialists from all lung cancer-related disciplines to provide specific expertise on important issues in each case. Data suggest that lung cancer care is enhanced by the presence of these boards, which should be in operation in every center that routinely cares for patients with lung cancer. Lung cancer tumor boards should include a support team to discuss patient management on a case-by-case basis.
- Specific training for pulmonologists and oncologists in thoracic oncology will optimize the management of patients with thoracic malignancies.
- ATS and ERS should support research projects that are focused on understanding lung cancer biology and on applying new information to improve diagnosis, staging, and treatment of lung cancer.

INTRODUCTION

Lung cancer is the leading cause of cancer mortality in the world. It greatly affects the patients' quality of life through debilitating symptoms, such as breathlessness and hemoptysis, and through common comorbidities, such as chronic obstructive pulmonary disease (COPD), that further diminish performance status. Despite its large death toll, developments in diagnosis and treatment suggest a future with fewer lung cancer deaths. Research confirms that early detection of lung cancer in high-risk smokers reduces lung cancer mortality (1). For advanced-stage lung cancer, clinical trials using agents targeted to histology and molecular alterations have demonstrated improvements in survival (2). These targeted therapies are a promising new approach that requires meticulous attention by pulmonologists to provide adequate tissue sampling through the competent use of endoscopic procedures. At all stages of lung cancer diagnosis, staging, treatment, and palliation, pulmonologists can have a key role.

The purpose of this document is to describe the pivotal role of the pulmonologist in the prevention, early diagnosis, and management of lung cancer.

METHODS

The scope of this statement originated with the European Respiratory Society (ERS) and American Thoracic Society (ATS) leadership. A committee representing the oncology groups and the leadership of the ATS and ERS identified key points and reviewed the literature on the key topic areas. A working draft was prepared and reviewed by the full writing group and the board of directors of each organization. The content was based on the systematic review performed by the ERS task force, entitled "European Initiative for Quality Management in Lung Cancer Care," which included a literature search using the Medline database.

The present document is a position paper regarding the role of the pulmonologist in the diagnosis and management of patients with lung cancer. Committee members' conflicts of interest were disclosed and vetted according to procedures agreed on by the ATS and ERS. The content was agreed on by all members.

EPIDEMIOLOGY, RISK FACTORS, AND SCREENING

Lung cancer remains the leading cause of cancer mortality in the world, with approximately 1.4 million deaths per year (3). The number of estimated lung cancer deaths among men in Europe

in 2011 is about 180,000, which is much higher than deaths due to any other cancer (4). Among women in Europe, the estimated number of deaths by lung cancer is about 70,000, which is exceeded only by breast cancer. In the United States, lung cancer is the leading cause of cancer death in both sexes and kills more people than the next four leading cancers combined (prostate for men, breast for women, colon, and pancreas). It is estimated that more than 160,000 people died of lung cancer in 2012. In the United States, death rates from all cancers have been declining by about 1% per year over the last 10 years. The decline in lung cancer, which follows the decrease in tobacco smoking, accounts for almost 40% of the decline of all cancer deaths (5). Because the incidence and death rates of lung cancer follow trends of smoking prevalence over the past 30 years (6), the importance of antismoking campaigns and smoking cessation programs cannot be stressed enough, and pulmonologists should dedicate time and effort to lead these efforts. Studies and data from the World Health Organization show that although all-cancer mortality has decreased in both sexes from 1980 to 2007, mortality due to smoking-related cancers in women rose significantly, which underscores the importance of providing concerted action to address smoking cessation and prevention efforts to women. Other risk factors for lung cancer include exposure to asbestos, radon, diesel exhaust and air pollution, COPD, pulmonary fibrosis, and immune suppression. These risk factors are common in patients seen in a pulmonary practice, and thus pulmonary physicians have a unique opportunity and responsibility to mitigate risk factors and to facilitate early diagnosis and treatment in these patients.

Studies of lung cancer screening, staging, drug development, and molecular diagnostics have demonstrated important advances that promise to decrease death rates over time (1, 7, 8). For example, in the National Lung Screening Trial (NLST), which included more than 50,000 patients at high risk of lung cancer, a relative reduction of 20% in lung cancer mortality was observed with low-dose computed tomography (CT) screening, and the rate of death from any cause was also reduced in the low-dose CT group by 6.7% (1). The results of this rigorous, large, randomized controlled trial have led several organizations such as the International Association for the Study of Lung Cancer (IASLC), National Comprehensive Cancer Network (NCCN), American College of Chest Physicians (ACCP), American Society of Clinical Oncology (ASCO), and American Thoracic Society (ATS) to recommend consideration of screening in high-risk smokers (9). Final results of other randomized studies on screening, such as the Danish Lung Cancer Screening Trial and the Dutch, Belgian (NELSON) trial, are also expected soon (8, 9). Results from these studies will define the future European screening policy. Pulmonologists see patients at risk for developing lung cancer that may benefit from an effective screening program. The increased use of detailed CT imaging has led to the increased identification of lung nodules, and this prevalence will increase in the era of CT-based screening (9, 10). Advances in the evaluation of lung nodules include the use of guided bronchoscopy procedures performed by the pulmonologist, such as electromagnetic navigation, endobronchial ultrasound, and virtual bronchoscopic navigation. Thus, pulmonary physicians have important roles in educating and advising patients about the benefits and risks of screening, and in managing findings in those patients who participate in screening programs.

EARLY AND SPECIFIC DIAGNOSIS

Current standards of care for lung cancer treatment assign therapy on the basis of histology (11). Small cell lung cancer has an established workup and treatment. There has been a paradigm

shift away from homogeneous therapy of non-small cell lung cancer. The treatment and course of adenocarcinoma are based in part on the presence of epidermal growth factor receptor (EGFR) mutation and anaplastic lymphoma kinase (ALK) translocation status (12). This treatment change often requires increased tissue sampling and different bronchoscopic approaches for lung cancer diagnosis and staging, which enhances the importance of pulmonary physicians in lung cancer management. Studies have shown that endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is less invasive and at least as accurate as mediastinoscopy (13). The amount of material collected by EBUS-TBNA, however, is small relative to the specimens obtained by mediastinoscopy. As sample size has gotten smaller, the amount of pathologic and molecular information required of these samples has grown larger. Potentially all treatment decisions, at the time of diagnosis and later, will be based on the information obtained from that specimen. Therefore, it is essential that the specimen collection and processing procedures be optimized to ensure that the quality and quantity of the specimen are adequate to provide answers to all the questions that may be asked (2).

Several studies have shown that cytological specimens obtained by EBUS-TBNA are suitable for molecular testing for EGFR, Kirsten rat sarcoma viral oncogene homolog (K-ras), and ALK status (14–17). Optimal use of EBUS-TBNA for lung cancer diagnosis and staging requires a coordinated effort between the bronchoscopist and the cytopathologist to collect and triage specimens for diagnostic testing. The pulmonologist must understand the rationale for histological and molecular testing of lung cancer diagnostic specimens and ensure that they are acquired and processed in a fashion that provides information from small cytological specimens that is sufficient to guide treatment in this era of targeted therapy.

Pulmonologists have a primary role in the implementation of these advances for the purposes of identifying high-risk individuals who may benefit from screening, managing pulmonary nodules detected on screening CT scans, diagnosing and staging lung cancer by techniques such as bronchoscopy with EBUS-TBNA, and procuring and processing cancer specimens for molecular analysis.

EVALUATION, STAGING, AND TREATMENT

After the diagnosis of lung cancer, therapy is tailored according to stage, performance status, and histological and molecular classification of the disease. Pertinent diagnostic algorithms now recommend the routine use of positron emission tomography in combination with computed tomography (PET-CT), or endobronchial ultrasound (18–21). Such algorithms have been implemented in many but not all countries. Until recently, surgical mediastinoscopy was the preferred initial approach for staging the mediastinum. EBUS-TBNA has gained wide acceptance as an alternative procedure for sampling mediastinal lesions in patients with suspected or known lung cancer, now often supplanting mediastinoscopy as a first-line approach for diagnosis and staging (13).

Pulmonologists are pivotal in lung cancer staging as they interpret the imaging tests and provide tissue for pathological examination. They also perform the preoperative physiological evaluation, provide postresection surveillance, and treat the patients' most common comorbidities, such as COPD, pleural effusions, lung infections, and respiratory failure. These comorbidities also affect the performance status of patients and their ability to undergo surgery (22, 23). Moreover, pulmonologists can provide treatment by local and endoscopic approaches, such as laser and cauterization, and they can treat early-stage central lung cancer by

established endobronchial techniques such as photodynamic therapy. Pulmonologists can alleviate inoperable endobronchial obstruction through the use of stents or other techniques and, in many European countries, pulmonologists administer systemic chemotherapy or other targeted therapies. Pulmonologists manage disease-related complications, using methods such as medical thoracoscopy or the interventional treatment of endobronchial obstruction (24, 25). Pulmonologists also may manage treatment-related side effects, such as postradiation pneumonitis and other systemic side effects, and they provide general supportive and palliative care (26).

Of course, lung cancer care does not involve pulmonologists alone. Data show that multidisciplinary teams provide improved adherence to evidence-based guidelines, better treatment decisions, and better clinical outcomes with longer survival for oncologic patients (27, 28), and specifically for patients with lung cancer (23, 29). Pulmonologists participate in and often lead multidisciplinary efforts to provide prompt, state of the art, and cost-effective care to patients with lung cancer. The ERS and ATS should encourage and facilitate the roles of pulmonologists in these multidisciplinary collaborations.

IMPORTANCE OF HIGH-VOLUME SPECIALIZED CENTERS AND MULTIDISCIPLINARY TEAMS

Medical, structural, and even historical reasons support a leading role for pulmonologists in multidisciplinary efforts to treat patients with lung cancer. The European Respiratory Society/European Society of Thoracic Surgeons (ERS/ESTS) guidelines for fitness for radical therapy of lung cancer (22) recommend that the management of patients with lung cancer be performed by multidisciplinary teams (pulmonologists, thoracic surgeons specialized in lung cancer, medical oncologists, and radiation oncologists). The American College of Chest Physicians (ACCP) has proposed similar recommendations for patients with potentially respectable lung cancer (29).

Since the 1970s, centers for thoracic diseases that emerged from former tuberculosis hospitals, particularly in Europe, have focused on the diagnosis and treatment of patients with primary thoracic malignancies and especially lung cancer (30). Traditionally, these centers were staffed by pulmonologists and thoracic surgeons, but now include an extended range of health care workers including the relatively new disciplines of palliative care and rehabilitation medicine. These high-volume centers treat all aspects of problems affecting patients with lung cancer. Evidence in favor of the multidisciplinary management concept comes from a number of publications on cancer management in general and fewer studies in lung cancer in particular. A report, from a single center study in Scotland (31) shows that median survival of patients with inoperable non-small cell lung cancer was 3.2 months in 1997 and 6.6 months in 2001, before and after the introduction of a multidisciplinary team ($P < 0.001$). The difference was not accounted for by differences in age, sex, or extent of disease between the two years. However, in 2001, 23% of patients received chemotherapy treatment compared with 7% in 1997 ($P < 0.001$). Certification of lung cancer centers was initiated in Germany under the guidance of pulmonologists, in close cooperation with thoracic surgeons, radiation oncologists, and medical oncologists (26). This process is still being evaluated but may serve as a model for other societies, countries, and regions, although specific adaptations will be required to accommodate local competences as well as disparate health care structures. Lung cancer prognosis and outcomes depend not only on histological characteristics and staging of the cancer but also on the presence and proper management of comorbidities, local symptoms, treatment-related

morbidity, and quality of life (32–34). Data show that high-volume centers and multidisciplinary teams are more efficient at managing patients with lung cancer than low-volume or nonmultidisciplinary centers by providing more complete staging, better adherence to guidelines, and increased survival (23, 26, 31). These data supporting multidisciplinary teams are included in national guidelines for lung cancer centers under the coordination of chest physicians (35). These multidisciplinary teams must be flexible to account for differences in practice patterns. For example, in European multidisciplinary centers, pulmonologists often administer chemotherapeutic drugs to patients with lung cancer. In the United States, most chemotherapy treatment is given by medical oncologists who have prominent roles in these centers.

This shift toward incorporation of multidisciplinary teams for cancer management is also reflected in the elaboration of guidelines or recommendations for diagnosis and treatment of patients with other thoracic malignancies. For example, in Europe the ERS and ESTS made recommendations together for patients suffering from malignant mesothelioma (36). Both of these disciplines, with radiation oncologists, created evidence-based recommendations that favor conservative treatment. A Europe-wide, systematic investigation of national health care structures, medical resources, quality assurance and management, and the circumstances for the constitution of national guidelines is expected to deliver a widely applicable framework for comprehensive multidisciplinary lung cancer care (37, 38). Such a framework, however, must be open to evolving changes in practice, especially of targeted treatment for these patients. Also, the economic and social disparities within regions and between countries should not limit the options for care of patients with thoracic malignancies.

Although recommended by scientific societies, multidisciplinary management is not yet available everywhere. The ERS task force for quality management is currently assessing this practice in the countries of the European Union and in those represented at the national level in the ERS (37). Ideally, centers managing patients with thoracic malignancies should have multidisciplinary clinics with a thoracic oncology board prescribing individualized management based on evidence-based data. Formal connections should also be established with intensive care and palliative care specialists, who in most countries are pulmonologists. In many countries in Europe and in the United States, tumor boards are required for cancer program accreditation.

IMPORTANCE OF RESEARCH

The progress in lung cancer diagnosis, staging, and targeted therapies convincingly shows that investments in research have an impact on reducing lung cancer deaths. On the basis of these advances, future discoveries of the basic mechanisms of neoplasia will further accelerate progress in the field. Expansion of research efforts directed toward applying new molecular techniques and comparative effectiveness will reduce the enormous burden of this disease. Research in lung cancer, by far the leading cause of cancer-related deaths, must command research funding that is proportional to its impact on public health. In Europe and the United States, pulmonologists design and conduct clinical trials of novel agents to prevent and treat lung cancer, including chemoprevention and tumor immunotherapy. The ATS and ERS must continue to strongly support research projects and the career development of investigators focused on understanding lung cancer biology and on translating molecular and clinical research advances to reduce lung cancer deaths. These societies must also continue to advocate for more research funding so that these advances are applied promptly to the diagnosis, treatment, and prevention of lung cancer.

CONCLUSIONS

Optimal treatment of patients with lung cancer requires a thoracic oncology center and specialists who care for a significant number of patients on a regular basis. The multidisciplinary team should include representatives of all specialties concerned in the management of thoracic malignancies: pulmonologists, thoracic surgeons, medical oncologists, radiation oncologists, pathologists, radiologists, and nuclear medicine specialists, as well as nurses, pharmacists, physiologists, and palliation specialists. Treatment plans using surgical, radiotherapeutic, and pharmacologic approaches should be reviewed by the team.

As a key member of these multidisciplinary teams, pulmonologists are responsible for and involved with the lung cancer patient from initial diagnosis and staging through treatment, restaging, support, and often palliative care. Diagnosis and management of lung cancer require the competent use of endoscopic procedures to acquire specimens that can stage and guide targeted therapy while minimizing respiratory side effects and complications.

Pulmonology fellowship programs should offer extensive training and experience with lung cancer so that pulmonologists will be well qualified to manage all aspects of the care of these patients. Lung cancer needs to be dealt with effectively and promptly because of its high mortality, its effects on the quality of the lives of patients and their families, and the enormous cost and impact on society.

This official statement was prepared by an *ad hoc* subcommittee of the Section on Thoracic Oncology of the Clinical Problems and the Respiratory Cell and Molecular Biology assemblies.

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