

Lung Cancer FRONTIERS

The Forum for Early Diagnosis and Treatment of Lung Cancer



Thomas L. Petty, M.D.

The purpose of **Lung Cancer Frontiers** is to acquire and disseminate new knowledge about lung cancer and how it can be most quickly and effectively diagnosed and treated.

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New Era Begins for Lung Cancer Frontiers

This issue ushers in a new era for **Lung Cancer Frontiers** and its readership. I am pleased to announce that National Jewish Medical and Research Center will be the new home of **Lung Cancer Frontiers**.

I began **Lung Cancer Frontiers** 12 years ago, when I envisioned the need to stimulate interest in healthcare providers about lung cancer and multidisciplinary approaches to this difficult disease. Since 1996, **Lung Cancer Frontiers** has served as an educational forum for disseminating new knowledge about the prevention, early diagnosis, and effective treatment of lung cancer. We have published 33 issues, with the goal of improving the cure rate for a disease that continues to kill more Americans each year than colon, breast, ovarian, and prostate cancers combined. National Jewish, which has long been at the forefront of pulmonary medicine and research, will carry on this mission as it assumes publication of **Lung Cancer Frontiers**. I will remain as Editor Emeritus, Dr. Esther Langmack will serve as Managing Editor, and, along with our Editorial Board, we will continue to provide a newsletter of key value to all who care about lung cancer.

Over the last decade, the development of CT and PET scanning, novel biopsy techniques, tissue-sparing surgery, and new chemotherapeutic agents have greatly expanded our treatment armamentarium, providing new hope for those suffering from lung cancer. Some time ago, I pointed out that the solution to the problem of tuberculosis required the combined skills of the pulmonologist, radiologist, physiologist, microbiologist and surgeon. Together, this team found ways to treat and cure tuberculosis, using evolving surgical and pharmacologic approaches. Today, we need the pulmonologist, bench researcher, radiologist, radiation oncologist, oncologist, pathologist, pharmacologist and surgeon, all working together, to find the most effective means of lung cancer diagnosis and treatment. **Lung Cancer Frontiers** will continue to highlight new developments and collaborations in this exciting area.

Thomas L. Petty, M.D.

Founder, Lung Cancer Frontiers

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President's Message



Michael Salem, M.D., FACS

Dear Readers,

National Jewish is pleased and honored to be chosen as the new home of *Lung Cancer Frontiers*.

Throughout his outstanding career, Dr. Thomas L. Petty, the founder of *Lung Cancer Frontiers*, has been dedicated to finding new ways to prolong and improve the lives of patients suffering from lung diseases, including lung cancer. He is well known for his pioneering work in the area of early lung cancer diagnosis, which he carried out here in Colorado with collaborators Dr. Geno Saccomanno, Dr. Tim Kennedy, and Dr. Joel Bechtel.

Dr. Petty is admired for his tireless enthusiasm and for his compassionate care of his patients. We are grateful for the opportunity to work with him to educate healthcare professionals about advances in lung cancer research, diagnosis, and treatment. As survival statistics demonstrate, we still have much to do to improve our diagnosis and treatment of this terrible disease.

In January 2007, National Jewish began to develop a personalized, multidisciplinary program in **lung cancer** as part of our Decade of Innovation – 2017 Strategic Plan. This plan also includes additional personalized medicine programs in asthma, COPD, cardiovascular disease, allergy and immunology. The creation of an Institute for Advanced Biomedical Imaging™, an Integrated Bioinformation and Specimen Center, and the Center for Genetics and Therapeutics will support innovation in all of these programs. In addition, National Jewish recently became the site of the first comprehensive interventional pulmonology program in Colorado.

As National Jewish welcomes *Lung Cancer Frontiers*, we look forward to bringing Dr. Petty's spirit of innovation, collaboration, and compassionate care to our patients and the field of lung cancer.

A handwritten signature in black ink that reads "Michael Salem". The signature is fluid and cursive.

Michael Salem, M.D., FACS
President and CEO

National Jewish Medical
and Research Center
main health campus in
Denver, Colorado.



ACCP 2007 Lung Cancer Recommendations: A Commentary

In September 2007, the American College of Chest Physicians published the 2nd edition of Evidence-Based Clinical Practice Guidelines for the Diagnosis and Management of Lung Cancer (*CHEST* 2007; 132:1S-422S). The review panel that updated and expanded the previous guidelines contained representatives from all of the relevant medical disciplines. The resulting comprehensive review comments on topics that range from screening for lung cancer, to follow-up and surveillance. The guidelines are evidence-based and focus on literature published since the 1st set of guidelines were released in 2003 (*CHEST* 2003; 123:1S-337S).

Recommendations are classified as strong (grade 1) or weak (grade 2), and the accompanying evidence is graded for quality (A – high, B – moderate, C – low). For example, to receive a rating of A on evidence quality, randomized, controlled trials (RCTs) without important limitations, or overwhelming evidence from observational studies, must be present. A rating of B indicates RCTs with important limitations or extremely strong evidence from observational studies. A rating of C indicates some evidence from observational studies or case series is present.

For this commentary, I have chosen to focus on new guidelines that are of particular interest to pulmonologists and primary care providers. I will address them by subject area and provide the level of supporting evidence.

1. **Chemoprevention:** No pharmacologic agents have been proven to prevent lung cancer (1A), and subjects at risk (> 20 pack year smoking history) and those with a history of lung cancer should take agents only as part of a well-designed clinical trial (2C). Smoking prevention and cessation remain the single best preventive measures, as 90% of all lung cancer is related to cigarette smoking.
2. **Screening:** Serial chest radiographs or sputum cytology should not be used to screen for the presence of lung cancer (1A), and low-dose spiral CT should be used only in the context of a well-designed clinical trial (2C). Results from the National Lung Screening Trial (an RCT comparing serial chest radiograph to spiral chest CT in 50,000 subjects, www.cancer.gov/nlst) should become available in the next couple of years and should provide more information about screening.
3. **Solitary pulmonary nodules (SPNs):** For all patients with an SPN (defined as a nodule up to 3 cm in size surrounded by aerated lung and not associated with mediastinal widening, adenopathy, or a pleural effusion), clinicians should estimate the pretest probability of malignancy with clinical judgment or with a validated model (1C). SPNs calcified in a clearly benign pattern (diffuse, central, laminated and popcorn patterns) (1C) and those that have stable imaging for 2 years (2C) do not need additional diagnostic evaluation. Pure ground glass opacities, such as those found on low-dose helical CT, should be followed for a longer period of time because of the slower growth rate of bronchioloalveolar cell carcinoma (BAC). In patients with a low to moderate pretest probability of cancer, and SPNs measuring 8-10 mm, a PET scan should be performed to better characterize the nodule (2C). The ACCP guidelines contain extensive recommendations regarding nodule size and management, including suggested intervals for follow-up imaging. Additional guidelines for the management of pulmonary nodules have been published by the Fleischner Society (*Radiology* 2005; 237:395-400).
4. **Physiologic evaluation:** Patients with lung cancer being assessed for curative surgical resection should be evaluated by a multi-disciplinary team (1C). If the FEV₁ is > 80% of predicted or > 2L and there is no evidence of severe dyspnea or interstitial lung disease, the patient is suitable for resection without further physiologic testing (1C). A predicted postoperative FEV₁ < 40% or D_{LCO} < 40% is associated with a greater risk of perioperative complications, and these patients should undergo preoperative exercise testing (1C). A P_{aCO2} > 45 mm Hg is not an independent risk factor for complications, but these patients should also have additional testing (1C).
5. **Endobronchial carcinoma *in situ* (intraepithelial neoplasia):** Patients with severe dysplasia, carcinoma *in situ*, or carcinoma on sputum cytology should have white light bronchoscopy, with autofluorescence, if possible (1B). For non-surgical candidates with carcinoma *in situ*, photodynamic therapy, electrocautery, cryotherapy and brachytherapy are acceptable treatment options (1C).

ACCP 2007 Lung Cancer Recommendations: A Commentary (continued)

6. **Treatment of stage I/II non-small cell lung cancer (NSCLC):** Surgical resection is recommended in appropriate patients (1A), preferably by a thoracic surgical oncologist (1B). For those medically fit for resection, lobectomy is preferable to wedge or segmentectomy (1A). Video-assisted thoracic surgery (VATS) by an experienced surgeon is an acceptable alternative to open thoracotomy (1B). Systematic mediastinal lymph node sampling should be performed in all patients having a surgical resection (1B). Adjuvant chemotherapy for completely resected Stage IA or IB disease is not recommended, unless it is part of a clinical trial (1A). While platinum-based adjuvant chemotherapy is recommended for patients with completely resected Stage II disease and good performance status (1A), postoperative radiotherapy is not recommended (1B).

7. **Special treatment issues:** In patients with a suspected or biopsy-proven lung cancer and a satellite nodule in the same lobe, no further diagnostic workup of the satellite nodule is indicated and the patient should proceed to definitive treatment (1B). For those with a completely resected NSCLC and an isolated brain metastasis, resection or radiosurgical ablation is recommended (1B).

8. **Bronchioloalveolar cell carcinoma:** For patients with CT scans suggestive of BAC (ground glass opacities or consolidation), PET scans can be falsely negative and additional diagnostic testing is needed to exclude the presence of cancer (1C).

9. **Small cell lung cancer:** Routine staging should include CT of chest and abdomen (including entire liver and adrenal glands), brain CT or MRI, and bone scan (1B). Patients with limited-stage disease should be treated with concurrent chemoradiotherapy (1A). Elderly patients with a good performance status (PS 0 or 1) should be treated with platinum-based chemotherapy (1A).

10. **Follow-up and surveillance of lung cancer patients:** In those treated with curative intent, surveillance with a history/physical and CT imaging is recommended every 6 months for the first 2 years and then yearly thereafter (1C). The use of routine blood tests, PET scanning, sputum cytology, and fluorescence bronchoscopy is not recommended (2C). Smoking cessation should be strongly encouraged (1A).

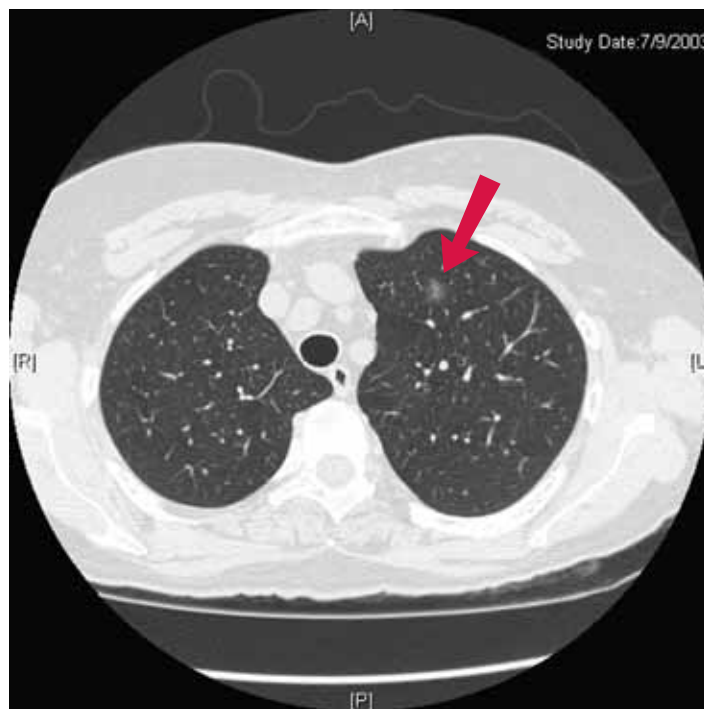
11. Additional chapters in the guidelines discuss integrative oncology, complementary therapies and palliative care.

Despite being the number one cause of cancer death in men and women in the United States, it is striking that a large number of recommendations are based on evidence rated at the 2C level. It is clear that we must continue to promote successful smoking cessation and tobacco control. Lung cancer research will advance more quickly as the number of patients involved in clinical trials increases. Critical advances are being made in lung cancer, and multi-disciplinary treatment approaches hold considerable promise.

Robert L. Keith, M.D., FCCP

Associate Professor of Medicine
Denver VA Medical Center/UCDHSC

Disclosure of potential conflicts of interest: Dr. Keith holds a patent on the use of prostacyclin analogues for the chemoprevention of lung cancer



An 11 mm ground-glass nodule (arrow) in the left upper lobe of a former smoker, suspicious for bronchioloalveolar carcinoma.

Selections from the Peer-Reviewed Literature

By Thomas L. Petty, M.D.

1. Overstating the evidence for lung cancer screening: the International Early Lung Cancer Action Program (I-ELCAP) study.

Arch Intern Med. 2007;167:2289-95.

Welch HG, Woloshin S, Schwartz LM, et al.

VA Outcomes Group, White River Junction VA Medical Center, White River Junction, VT, USA.

Last year, the New England Journal of Medicine ran a lead article reporting that patients with lung cancer had a 10-year survival approaching 90% if detected by screening spiral computed tomography. The publication garnered considerable media attention, and some felt that its findings provided a persuasive case for the immediate initiation of lung cancer screening. We strongly disagree. In this article, we highlight 4 reasons why the publication does not make a persuasive case for screening: the study had no control group, it lacked an unbiased outcome measure, it did not consider what is already known about this topic from previous studies, and it did not address the harms of screening. We conclude with 2 fundamental principles that physicians should remember when thinking about screening: (1) survival is always prolonged by early detection, even when deaths are not delayed nor any lives saved, and (2) randomized trials are the only way to reliably determine whether screening does more good than harm.

Editorial Comment: Lung cancer screening continues to be highly controversial with enthusiastic proponents and those who are irrevocably glued to the necessity of randomized trials as the only way to reliably determine whether the screening does more good than harm. Let's turn back the clock a bit and ask ourselves what evidence exists that the pelvic PAP smear alters the outcome of cervical carcinoma treatment? This might make dealing with the current controversy a bit easier. It seems to this editor that finding cancer early in order to improve survival, is one of the goals of early detection.

2. Computed tomographic screening for lung cancer: individualizing the benefit of screening.

Eur Respir J. 2007;30:843-7.

International Early Lung Cancer Action Program Investigators.

Dept of Radiology, New York Presbyterian Hospital-Weill Cornell Medical Center, New York, NY.

Individuals concerned about their risk of lung cancer are recommended to talk with their physicians about computed tomographic screening for lung cancer. To provide the necessary information, the survival benefit of the screening, specific to a particular person for a particular round of screening, is needed. The probability of survival gain from the first, baseline, round of screening was addressed as the product of: 1) the screening resulting in a diagnosis of lung cancer; 2) not dying from some other cause for a sufficiently long period of time; and 3) cure resulting from pre-symptomatic treatment of lung cancer. These probabilities were estimated using the International Early Lung Cancer Action Program data on individuals aged 40-85 yrs with a cigarette smoking history of 0-150 pack-yrs. The estimated probability of survival gain ranged from 0.4% for a 60-yr-old with a 10-pack-yr smoking history who quit smoking 20 yrs ago, to 3.1% for a 70-yr-old current smoker with a 100 pack-yr history and 2.0% for an 85-yr-old current smoker with a 150-pack-yr history. When seeking counsel about initiation of screening for lung cancer, an estimate of the probability of survival gain from the first round of computed tomographic screening, specific to the person's age and history of smoking, can be provided.

Editorial Comment: This article stresses individualized screening, factoring in age. It wisely advises consideration of survival gain, which must also factor in comorbidities when one considers screening for lung cancer.

3. A risk model for prediction of lung cancer.

J Natl Cancer Inst. 2007;99:715-26.

Spitz MR, Hong WK, Amos CI, et al.

Department of Epidemiology, The University of Texas M. D. Anderson Cancer Center, Houston, USA.

BACKGROUND: Reliable risk prediction tools for estimating individual probability of lung cancer have important public health implications. We constructed and validated a comprehensive clinical tool for lung cancer risk prediction by smoking status. **METHODS:** Epidemiologic data from 1851 lung cancer patients and 2001 matched control subjects were

Selections from the Peer-Reviewed Literature (continued)

randomly divided into separate training (75% of the data) and validation (25% of the data) sets for never, former, and current smokers, and multivariable models were constructed from the training sets. The discriminatory ability of the models was assessed in the validation sets by examining the areas under the receiver operating characteristic curves and with concordance statistics. Absolute 1-year risks of lung cancer were computed using national incidence and mortality data. An ordinal risk index was constructed for each smoking status category by summing the odds ratios from the multivariable regression analyses for each risk factor. **RESULTS:** All variables that had a statistically significant association with lung cancer (environmental tobacco smoke, family history of cancer, dust exposure, prior respiratory disease, and smoking history variables) have strong biologically plausible etiologic roles in the disease. The concordance statistics in the validation sets for the never, former, and current smoker models were 0.57, 0.63, and 0.58, respectively. The computed 1-year absolute risk of

lung cancer for a hypothetical male current smoker with an estimated relative risk close to 9 was 8.68%. The ordinal risk index performed well in that true-positive rates in the designated high-risk categories were 69% and 70% for current and former smokers, respectively. **CONCLUSIONS:** If confirmed in other studies, this risk assessment procedure could use easily obtained clinical information to identify individuals who may benefit from increased screening surveillance for lung cancer. Although the concordance statistics were modest, they are consistent with those from other risk prediction models.

Editorial Comment: A number of models have been introduced to predict high risk for lung cancer screening. This study confirms our findings in the Grand Junction Study (Bechtel JJ, Kelley WA, Coons TA, Klein MG, Slagel DD, Petty TL: Lung cancer detection in patients with airflow obstruction identified in a primary care outpatient practice. *Chest* 2005;127:1140-5), where heavy smoking, family history of lung cancer, and occupational exposures increased risk.

Lung Cancer Meetings and Symposia

National Lung Cancer Partnership Annual Meeting

Lung Cancer 2008: Progress and Promise

May 30, 2008

Chicago, IL

Contact: Alice@NationalLungCancerPartnership.org

9th Annual International Lung Cancer Congress

June 18-21, 2008

Koloa, HI

Contact: CME@pergrouppl.com

International Lung Cancer Conference

July 9-12, 2008

Liverpool, England

Contact: jaime@happen.co.uk

Chicago/IASCL/ASCO/ASTRO: Malignancies of the Chest and Head and Neck Symposium

November 13-15, 2008

Chicago, IL

Contact: evokes@medicine.bsd.uchicago.edu

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Obesity: Impact on Heart and Lung Disease

Featuring: Robert Eckel, MD and E. Rand Sutherland, MD

May 3, 2008

Rheumatologic Lung Disease Symposium: Focus on ILD and Pulmonary Hypertension

Featuring: Aryeh Ficher, MD and Kevin Brown, MD

September 8, 2008

The Denver TB Course

Featuring: Michael Iseman, MD

October 22 – 25, 2008

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