The American Association for Thoracic Surgery guidelines for lung cancer screening using low-dose computed tomography scans for lung cancer survivors and other high-risk groups

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Objective: Lung cancer is the leading cause of cancer death in North America. Low-dose computed tomography screening can reduce lung cancer–specific mortality by 20%.

Method: The American Association for Thoracic Surgery created a multispecialty task force to create screening guidelines for groups at high risk of developing lung cancer and survivors of previous lung cancer.

Results: The American Association for Thoracic Surgery guidelines call for annual lung cancer screening with low-dose computed tomography screening for North Americans from age 55 to 79 years with a 30 pack-year history of smoking. Long-term lung cancer survivors should have annual low-dose computed tomography to detect second primary lung cancer until the age of 79 years. Annual low-dose computed tomography lung cancer screening should be offered starting at age 50 years with a 20 pack-year history if there is an additional cumulative risk of developing lung cancer of 5% or greater over the following 5 years. Lung cancer screening requires participation by a subspecialty-qualified team. The American Association for Thoracic Surgery will continue engagement with other specialty societies to refine future screening guidelines.

Conclusions: The American Association for Thoracic Surgery provides specific guidelines for lung cancer screening in North America. (J Thorac Cardiovasc Surg 2012;144:33-8)

Lung cancer remains the most common cause of cancer death in the United States and Canada. This year there will be more lung cancer deaths alone than the combined deaths from breast, prostate, and colon cancer. Effective screening programs have identified early cases of the other 3 cancers, but until recently lung cancer has lacked an effective screening tool.

Changes in disease demographics have witnessed a doubling of lung cancer incidence and a decline in tuberculosis over the past 30 years. Minimally invasive techniques have dramatically improved the safety and expected recovery of surgical resections. Most important, the publication of the National Lung Screening Trial (NLST) has established the ability of low-dose computed tomography (LDCT) scans to decrease lung cancer–specific mortality by 20% in a screened high-risk population.[1]

As a result of the International Association for the Study of Lung Cancer (IASLC) Screening Workshop 2011, the IASLC created a Strategic Screening Advisory Committee to engage stakeholder professional societies in lung cancer computed tomography (CT) screening implementation across the globe. The charge was to deliver guidelines for radiologic screening, clinical workup for indeterminate nodules, pathology reporting of nodules, and recommendations for surgical and therapeutic interventions for suspicious nodules. In addition, societies were charged to create guidelines and recommendations for identification of high-risk individuals for lung cancer CT screening and integration of smoking cessation. The IASLC framed these goals for the integration of lung cancer screening guidelines into the existing healthcare structure of each nation. The

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Abbreviations and Acronyms

AATS = American Association for Thoracic Surgery
CT = computed tomography
CXR = chest x-ray
FEV_1 = forced expiratory volume in 1 second
IASLC = International Association for the Study of Lung Cancer
LDCT = low-dose computed tomography
NLST = National Lung Screening Trial

American Association for Thoracic Surgery (AATS) has begun this process for the United States and Canada.[2]

MATERIALS AND METHODS

The AATS convened a lung cancer screening and surveillance task force to examine the evidence in favor of lung cancer screening. The specific goal of this panel was to provide guidelines to health care practitioners who care for high-risk populations, including smokers and nonsmokers, with additional risk factors. An additional specific mandate was to develop guidelines for screening lung cancer survivors. This multidisciplinary panel included representatives from thoracic surgery, medical oncology, pulmonology, pathology, and radiology, with members selected on the basis of demonstrated expertise in identifying risks and benefits of screening lung cancer using LDCT. Although the following recommendations of this task force may be applicable to many parts of the world, they are specifically intended to guide screening within the United States and Canada. This recommendation is based on the high incidence of lung cancer within these 2 highly developed nations, a rate that exceeds other regions of North America. Specifically, the age-standardized incidence rate is 42.13 per 100,000 people of all ages and both sexes in the United States (third largest in the world) and 35.88 per 100,000 in Canada (ninth largest in the world).[3] Other areas of Latin America and the Caribbean have age-standardized incidence rates less than 10 per 100,000 people.

In broad overview, our task force guidelines build on the work of the NLST,[1] as recommended by the IASLC Computed Tomography Screening Workshop of 2011 report.[2] Our recommendations further expand the recently published National Comprehensive Cancer Network Guidelines Version 1.2012 for Lung Cancer Screening.[4] We do not limit screening to the highest risk group of smokers recruited to the NLST trial, but recommend screening for a larger population by both age and by broadening the risk categories. We support the development of databases for refinement of evidence-based guidelines. We believe LDCT provides an opportunity for a "teachable moment" for tobacco cessation. Furthermore, we identify future areas of research that are likely to influence the screening of lung cancer in the near future, such as the incorporation of biomarker data into screening decisions.

RESULTS

The American Association for Thoracic Surgery Guidelines for Lung Cancer Screening in North America

Our present culmination of knowledge leads this panel to offer tiered recommendations in regard to 3 screening populations (Figures 1-5). Tier 1 includes those subjects at highest risk for whom there is level 1 evidence[5] to recommend screening (ie, randomized prospective clinical trial data). Tier 2 includes those subjects with level 2 evidence (ie, data from case-control or nonrandomized trials) or level 3 evidence (ie, our consensus opinion) and sufficient evidence to recommend screening for individuals within this group.

Tier 1 Guideline for Highest Risk Population

Annual lung cancer screening should begin at age 55 years for smokers and former smokers with a 30 pack-year history of smoking. Annual screening may continue to age 79 years (Figure 1). LDCT is the screening technology to be used. CXR alone should not be used as a screening tool. Individuals for whom adequate treatment cannot be offered because of comorbidity or functional status, regardless of age, should not undergo screening.

This recommendation is based on the prospective randomized NLST.[1] According to the US Preventive Services Task Force, this achieves level 1 evidence (ie, data from a well-designed randomized control trial).[5] The entry criteria for the NLST trial included ages 55 to 74 years, 30 pack-years of tobacco exposure, and, if the subject had quit smoking, smoking within the previous 15 years. We have dropped the third entry criteria, believing the primary risk generators are age and tobacco exposure, thus simplifying the recommendation.

The NLST included 3 annual screens and identified a 20% reduction in lung cancer–specific mortality within the first 3 years of screening. The cancer risk does not end after 3 years, however, and there is no scientific evidence to suggest that screening should be stopped after the initial 3 annual low-dose scans.

We recognize the constraint of the trial design of the NLST protocol whereby asymptomatic individuals without a previous cancer diagnosis (excluding skin cancer) at high risk because of smoking exposure (at least 30 pack-years) and age were selected for screening over 3 years. These constraints in the study population that were necessary to complete the trial that established the efficacy of LDCT to reduce lung cancer mortality would exclude many Americans who would benefit from a lung cancer screening program. These constraints need to be examined as we move from a successful clinical trial to screening guidelines.

We recommend that annual LDCT screening be performed each year from age 55 to 79 years, and not just 3 screening scans in the lifetime of the patient. The risk of lung cancer does not decrease in subsequent years according to the NLST data. In the NLST, participants were screened yearly with LDCT or chest x-ray (CXR) for 3 years. After the period of active screening, they were followed but not screened for another 4 years. At the end of 3 years, there were 649 cancers detected in the LDCT arm compared with 279 cancers in the CXR arm. The number of lung cancers increased each year to a total of 1060 in the LDCT arm and 941 in the CXR arm at the end of the study. The original NLST report (Figure 6) shows an

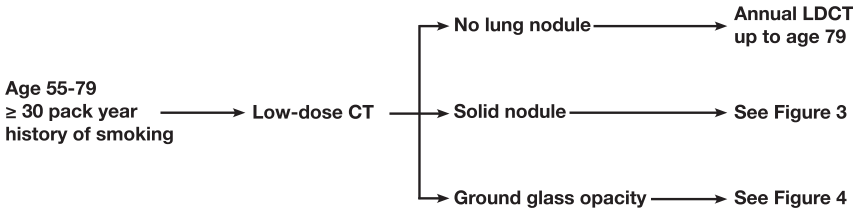

FIGURE 1. AATS lung cancer screening guidelines category 1 for highest risk. *CT*, Computed tomography; *LDCT*, low-dose computed tomography.

increase in the detected cancers in the LDCT arm compared with the CXR arm for the first 3 years (active screening period), but does not demonstrate any obvious change in the yearly rates of lung cancer on either arm for the last 4 years of the study (observation period during which time there was no screening LDCT). Furthermore, 63% of the lung cancers (400/635) were diagnosed as stage I on the LDCT arm during the first 3 years of active screening, and 21% (130/635) were diagnosed in stage III B/IV. At the end of the study in the LDCT arm (3 years active screening plus 4 years of follow-up only), the percentage diagnosed in stage I had decreased to 50% (520/1040), and the stage III B/IV cases had increased to 33% (348/1040). It is likely that if active LDCT screening had been maintained for the 7 years of the study that the percentage of diagnoses in stage I would have been higher and the percentage diagnosed in stage III B/IV would have been lower than those reported in the final NLST results. CT screening for 7 years is likely to have translated into a substantially greater mortality reduction than the 20% reported in the final NLST results.

We recommend continued screening to age 79 years for the following reasons:

1. The peak incidence of lung cancer is age 70 years in the United States.[6]
2. The average life expectancy is currently 78.6 years; thus, approximately half of all Americans are expected to live until approximately 80 to 89 years of age.[7]
3. Age alone is a risk factor for lung cancer. Age-specific incidence of lung cancer in American men increases in a linear fashion with age, with rates of 336 per 100,000 aged 66 to 70 years, 490 per 100,000 aged 71 to 75 years, and 517 per 100,000 aged more than 75 years. For women, the peak incidence is 350 per 100,000 from ages 71 to 75 years, and then decreases to 307 per 100,000 for women aged more than 75 years, still higher than the incidence of 248 per 100,000 for women aged 66 to 70 years.[8]
4. The average life expectancy remains greater than 9 additional years for all Americans up to age 79 years.

Thus, if nothing else is different, the risk of developing lung cancer is slightly higher each year than the year before because of aging. For this reason, we believe annual screens should continue yearly up to the age of 79 years. Beyond the age of 79 years, it is unclear if there would be the same screening advantage in detecting an early-stage lung cancer because of competing causes of mortality. Life-table analysis suggests the probability of living 7 additional years decreases to less than 50% in the early ninth decade of life.[9] However, patients aged more than 79 years with preserved functional status may be a population with screening benefit, although inadequate data are currently available.

Tier 2 Guidelines for Lung Cancer Survivors and Patients With Combined Risk

Annual lung cancer LDCT screening should be performed in patients who have been treated for a primary bronchogenic carcinoma and have completed 4 years of radiographic surveillance without evidence for recurrence (level 3 evidence) or patients aged 50 to 79 years with a 20 pack-year smoking history and other factors that produce a cumulative risk of developing lung cancer that is 5% or more over the

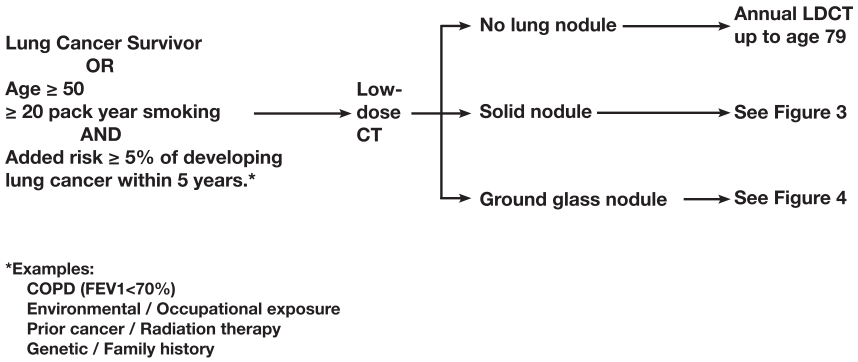

FIGURE 2. AATS lung cancer screening guidelines for combined risk or lung cancer survivor. *CT*, Computed tomography; *LDCT*, low-dose computed tomography; *COPD*, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second.

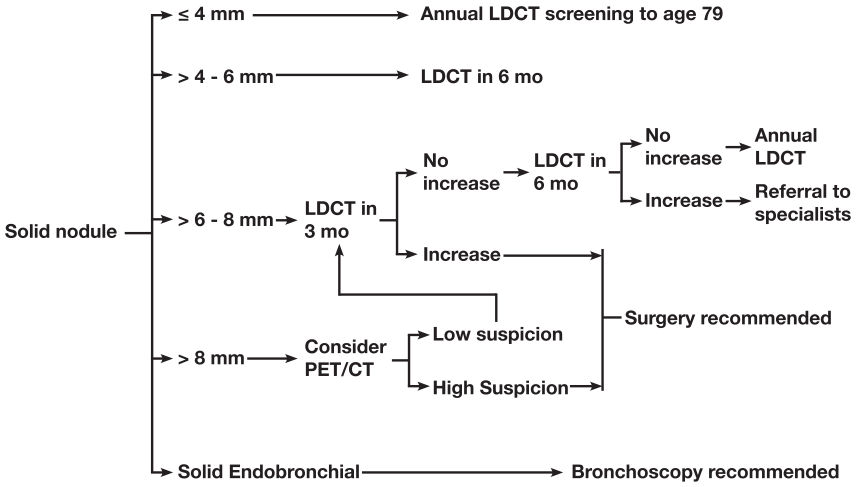

FIGURE 3. AATS lung cancer screening guidelines for solid nodules on low-dose computed tomography (*LDCT*). *PET/CT*, Positron emission tomography/computed tomography.

following 5 years (level 2 evidence, Figure 2). This is similar to the NCCN guidelines,[4] although we recommend continued annual screening beyond 3 years and up to age 79 years for the reasons stated. The data are consistent with US Preventive Services Task Force level 2 evidence (ie, data from nonrandomized trials). This recommendation achieved unanimous approval by the AATS Task Force.

High-resolution CT scans should be obtained for 4 years after surgical resection of stages 1A to IIIA NSCLC, followed by annual LDCT screening scan for a second primary lung cancer starting in the fifth year. Surveillance by LDCT should continue for the rest of the patient's life as long as the patient has functional status and pulmonary reserve needed for treatment of a new lung cancer. These patients are well served by the preservation of preoperative CT scans for comparison of small nodules over longer time periods. Baseline clinical CT scanning is recommended at 6 months after surgical resection. Because of the peak incidence of recurrence between 2 and 3 years, surveillance should be performed at least every 6 months during this period.

Those who have had lung cancer are at the highest risk for developing the disease because of recurrence and second primary. A history of lung cancer (and often other primary cancers) removes the individual from the group analyzed by screening studies. In fact, this group has been specifically excluded from the randomized trials to date because of trial design. Yet, such individuals need surveillance with continuing 3% risk of lung cancer diagnosis each year. There are currently more than 400,000 long-term lung cancer survivors in the United States.

The other risk factors accepted by the AATS Lung Cancer Screening Committee as contributing to the cumulative risk of developing lung cancer include (1) chronic obstructive pulmonary disease with forced expiratory volume in 1 second (FEV_1) of 70% or less than predicted, (2) environmental and occupational exposures, (3) any prior cancer or thoracic radiation, and (4) a genetic or family history.

The Liverpool Lung Project has combined case-control data with regional incidence rates to develop a model to project individual 5-year absolute risks of developing lung cancer.[10] Predictive variables of lung cancer risk within this model include age, gender, smoking duration, prior diagnosis of pneumonia, occupational exposure to asbestos, prior diagnosis of malignant tumor, and family history of lung

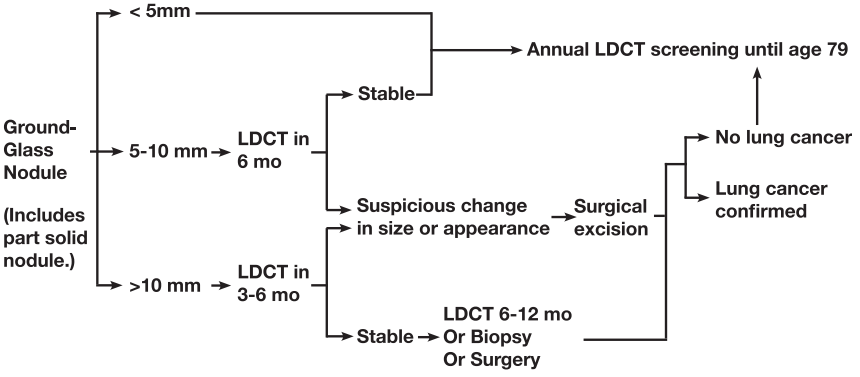

FIGURE 4. AATS lung cancer screening guidelines for ground-glass nodule. *LDCT*, Low-dose computed tomography.

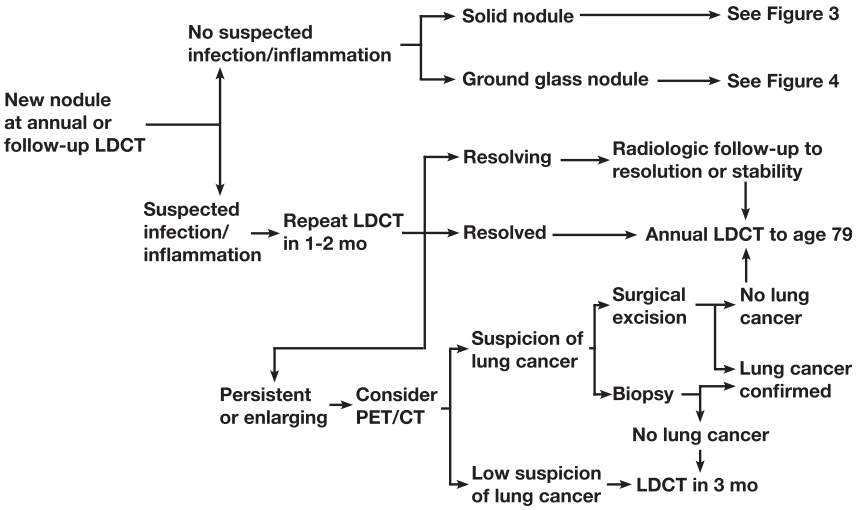

FIGURE 5. AATS lung cancer screening guidelines of new nodule on screening scan on low-dose computed tomography (*LDCT*). *PET/CT*, Positron emission tomography/computed tomography.

cancer. There is a nonlinear relationship between decrease in FEV_1 and cancer risk. However, randomized Italian trials identified an FEV_1 of less than 70% predicted to be a threshold to identify a high-risk lung cancer population among smokers with a 20 pack-year smoking history.[11]

Exposure to asbestos is known to be synergistic with tobacco smoking. Another environmental factor associated with a synergistic effect on lung cancer risk includes silicosis.[12] As environmental medicine expands, other exposures will likely be identified that increase the risk of bronchogenic malignancy. In the face of these types of environmental or occupational exposures, CT screening should be considered even with significantly less exposure to tobacco smoke. Other environmental exposures and radon exposure in the home increase risk but are difficult to quantify.

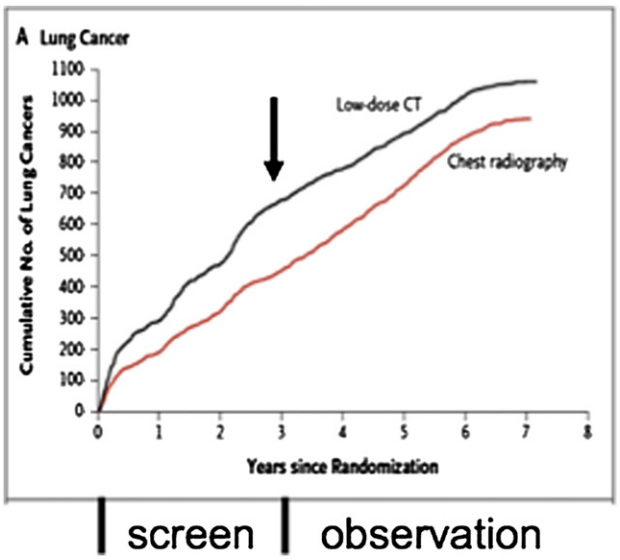

FIGURE 6. Annual screening should produce greater than 20% reduction in lung cancer–specific mortality. There is an increase in detected cancers in the LDCT arm during the active screening period, but not after the start of the observation period (*arrow*). Reprinted with permission.[1] Copyright the Massachusetts Medical Society.

Risk calculators, available on the Internet, are recommended for assistance in evaluation. In an example provided by the Liverpool Lung Project, an English 77-year-old man, never smoker, but with an early-onset family history of lung cancer and occupational exposure to asbestos, has an estimated 5-year risk of developing lung cancer of 3.17%. The general population risk in England and Wales for men aged 75 to 79 years is approximately 2.5%.[10] Our threshold to screen for cumulative risk of 5% or greater over 5 years was in conformity with the UK Lung Screen trial, which uses the Liverpool Lung Project to calculate risk.[13]

A second model using prospective data from the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial offers an online nomogram to allow estimation of the 9-year probability of lung cancer given an individual's specific risk factors. This model includes age, socioeconomic status, body mass index, family history of lung cancer, chronic obstructive pulmonary disease, and smoking duration.[14] We believe these databases can be made available to all citizens through Internet sources, thus allowing self-assessment of lung cancer risk. Our guidelines were intended to be flexible enough to guide this potential demand for screening advice.

Antecedent cancer history increases the probability that a lung nodule is malignant.[15] Furthermore, antecedent cancers may reflect complex genetic or environmental factors that predict cancer development at an earlier age and lower tobacco exposure. Although this subgroup was ineligible for participation in previous screening trials, we believe antecedent cancer becomes an indication to start lung cancer screening at an earlier age and lesser tobacco exposure.

Radiation treatment for prior thoracic malignancy may also increase risk of lung cancer at an earlier age. Radiation risks are linear with dose, and the risk for radiation-related cancer typically begins approximately 2 decades after exposure.

Incompletely understood genetic susceptibilities likely contribute to the development of lung cancer and may well underlie the variability of development of lung disease in response to exposure to tobacco smoke. Family history is disconcerting to patients, particularly when family history includes multiple cancers and multiple first-degree relatives who have died from lung cancer (especially those aged < 60 years). This risk may be higher in women and African Americans. In addition, there may be a hereditary susceptibility toward lung cancer that is largely unexplored.

Management of Low-Dose Computed Tomography Findings

A baseline LDCT scan that shows a solid or part-solid nodule should follow the algorithm depicted in Figure 3. A baseline LDCT scan that shows a ground-glass opacity or nonsolid nodule should follow the algorithm depicted in Figure 4. A new nodule found on an annual LDCT scan should be managed on the basis of the probability of suspected inflammation as depicted in Figure 5. Further explanations of these flowcharts are available in a simultaneous publication.[16]

DISCUSSION

The AATS recommends lung cancer screening for 3 distinct groups. Level 1 evidence in favor of screening currently exists for North Americans aged 55 to 79 years with a 30 pack-year smoking history. Furthermore, lung cancer survivors are an extremely high-risk group for developing a second lung cancer and should be screened with LDCT starting 5 years after treatment. Finally, younger patients (aged 50 years) with a 20 pack-year smoking history should be screened if they have an additional risk factor that produces a 5% risk of developing a lung cancer over the next 5 years.

The AATS recommends continuing reevaluation of lung cancer screening presented in this document and will encourage the interdisciplinary and intersociety engagements that will further standardize the understanding and availability of LDCT screening for the early detection of lung cancer. We agree with the IASLC guidance on screening, which suggests those considering screening should do so in environments where multidisciplinary teams are available for the management of indeterminate and positive screening scans.[2] Furthermore, the provision of care by an interdisciplinary team of thoracic surgeons working with radiologists, pulmonologists, and oncologists is required to ensure decreased mortality from lung cancer outside of strict clinical trials in academic centers and appropriate minimally invasive capabilities. It is most desirable to create a program for lung cancer screening that also supports smoking cessation and collection of data that will allow study of outcomes that are important for the practice of evidence-based medicine in the era of personalized health care.

CONCLUSIONS

Within the 75-year lifespan of the American Association of Thoracic Surgery, lung cancer has become an epidemic, and initial clinical trials to use screening CXR or sputum cytology were unsuccessful in reducing lung cancer–specific mortality. Now a useful screening method in LDCT has been proven to increase the survival of those with this disease. The future will bring refinements in screening and one day may make a blood, urine, or breath test available. However, at this time and for the first time in medical history, we can say, ''lung cancer screening—the time has come.''

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