Lung Cancer Screening

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KEYWORDS

• Lung cancer • Screening • Low radiation dose chest CT scans
• Smoking cessation interventions

KEY POINTS

- Lung cancer screening with low radiation dose chest computed tomography scans decreases lung cancer mortality.
- It is important to balance the benefits of screening with the potential harms, including evaluation of false-positive results, complications from diagnostic testing, overdiagnosis, and the impact of radiation exposure.
- Integration of smoking cessation interventions may augment the benefits of lung cancer screening.
- Widespread implementation and access to high-quality lung cancer screening programs remains a challenge.

INTRODUCTION

Lung cancer is the second most common cancer diagnosed in men and women, and is the leading cause of cancer-related deaths in the United States.[1] Early detection is an important strategy to try to modify these statistics, complementing public health strategies aimed at decreasing smoking rates. Screening with a low radiation dose chest computed tomography scan (LDCT) is performed to identify lung cancer in a preclinical or asymptomatic phase. The ultimate goal is to diagnose lung cancer at an earlier stage, where curative intent treatment is more successful, resulting in a decrease in lung cancer–specific mortality.

Several professional societies have endorsed lung cancer screening based on the results of the National Lung Screening Trial (NLST).[2] It remains the strongest evidence of reduced mortality from screening with LDCT. In 2013 the US Preventive Services Task Force (USPSTF) recommended annual screening for lung cancer with LDCT for adults between 55 and 80 years old who have a 30 pack-year smoking history and who currently smoke or have quit within the last 15 years.[3] In 2015, the Centers for Medicare and Medicaid Services (CMS) issued a decision requiring Medicare coverage of lung cancer screening for its beneficiaries.[4] Several lung cancer screening programs have been implemented nationwide and many lessons have been learned since then.

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Lung cancer screening is a complex task. A multidisciplinary team is necessary to run a screening program. Screening involves appropriate patient selection, shared decision making, balancing benefits and potential harms, and the management of screen-detected lung nodules and other findings. In this article, we discuss the evidence that supports screening and the different considerations in developing a high-quality lung cancer screening program.

EVIDENCE THAT SUPPORTS LUNG CANCER SCREENING

Early lung cancer screening trials evaluated chest radiographs (CXR) and sputum cytology as screening tests. Despite finding improved survival for those with screen detected lung cancer, the trials failed to demonstrate a reduction in lung cancer specific mortality.[5–7] Improvements in computed tomography (CT) scanning techniques, leading to increased sensitivity to detect small lung cancers, raised the interest to evaluate LDCT scans as a lung cancer screening tool.

The Early Lung Cancer Action Project and other prospective cohort studies showed that LDCT was able to identify more lung nodules and more early stage lung cancers than CXR, but this study design did not allow for a comparison of lung cancer mortality.[8]

The NLST was the first randomized controlled trial to report a significant reduction in lung cancer mortality owing to screening.[2] Between 2002 and 2009, the NLST enrolled 53,456 individuals between the ages of 55 and 74. All had a history of smoking of at least 30 pack-years and were either current smokers or former smokers who had quit within the past 15 years. The trial compared LDCT (26,723) with CXR screening (26,733) with a baseline scan followed by 2 annual LDCT or CXR rounds with 6 to 7 years of follow-up. Data from 33 medical centers in the United States showed that 3 rounds of LDCT resulted in a 16% to 20% relative reduction in the rate of death owing to lung cancer. In the LDCT arm, there were 354 deaths from lung cancer, compared with 442 in the CXR arm. Based on these results, using the NLST protocol, 320 patients would need to undergo screening to prevent 1 death owing to lung cancer. The trial also showed a 6.7% decrease in all-cause mortality with LDCT screening (1877 deaths in the LDCT arm compared with 2000 deaths in the CXR arm).

Several other randomized, controlled trials evaluating LDCT screening for lung cancer have provided valuable insight about the effectiveness of the test as a screening method, and about the natural course of the disease (**Table 1**).[9–15] The largest trial among these, the Nederlands-Leuvens Longkanker Screening Onderzoek (NELSON) trial,[9] had a smaller sample size than the NLST, but a longer follow-up (10 years), no scheduled screening in the control arm, and it included screening rounds with different intervals. Another major difference in the management of pulmonary nodules between NELSON and NLST was the use of nodule volume and volume doubling time to identify potential cases of early lung cancer. The final mortality results were recently published and they confirmed the mortality decrease with CT screening seen in the NLST.[16] The incidence of lung cancer in the screening group and no screening group was 5.58 and 4.91 cases per 1000 person-years, respectively. Lung cancer mortality was lower in the screening group by 24%. The protective effect was more pronounced in women than in men. CT screening decreased mortality by 26% in high-risk men and 33% in high-risk women over a 10-year period.[16]

POTENTIAL HARMS

An estimated 8.4 million individuals met the eligibility criteria for lung cancer screening as proposed by the USPSTF in 2013.[17] The potential eligible population was older, had a higher proportion of current smokers, and had more comorbidities than the NLST

Table 1
Trials that evaluated CT scanning for lung cancer screening

	Country	Recruitment Period	Sample Size	Screening Method	Interval	Age, Years	Smoking History	Smoking Cessation
NLST	USA	2002–2004	53,454	LDCT vs CXR	3 annual screenings	55–74	≥30 pack-years	<15 y
NELSON	Netherlands/ Belgium	2003–2006	15,822	LDCT vs usual care	4 screenings with different intervals: 1 y, 2 y, and 2.5 y	50–75	≥15 cigarettes per day for ≥25 y or ≥10 cigarettes per day for ≥30 y	≤10 y
DLCST	Denmark	2004–2006	4104	LDCT vs usual care	5 annual screenings	50–70	≥20 pack-years	≤10 y
MILD	Italy	2005–2011	4099	LDCT vs usual care	Annual and biennial for 5 y	≥49	≥20 pack-years	≤10 y
UKLS	UK	2011–2014	4055	LDCT vs usual care	Single screening LDCT	50–75	Predicted risk of lung cancer ≥5%	≤10 y
LUSI	Germany	2007–2011	4052	LDCT vs usual care	Annual screening for 5 y	50–69	≥15 cigarettes per day for ≥25 y or ≥10 cigarettes per day for ≥30 y	≤10 y
ITALUNG	Italy	2004–2006	3206	LDCT vs usual care	Annual screening for 4 y	55–69	≥20 pack-years	≤10 y
DANTE	Italy	2001–2006	2450	LDCT vs clinical review	Annual screening for 4 y	60–74	>20 pack-years	≤10 y

Data from Refs.[2,9–15]

population. This finding highlights the importance of balancing the benefits and potential harms of LDCT screening in clinical practice.[18] A clear understanding of the potential harms related to LDCT screening should be considered. Some of the major concerns are the identification of many benign lung nodules, the potential for overdiagnosis of lung cancer, complications related to diagnostic evaluation, and the potential impact of radiation exposure.

In the NLST, 96% of all positive results (defined as a lung nodule $\geq$4 mm in diameter) in the LDCT group were not cancer.[2] Approximately 20% of all surgical resections were performed in patients with screen-detected benign nodules. The frequency of death occurring within 2 months of a diagnostic evaluation of a detected finding was 8 per 10,000 individuals screened by LDCT and 5 per 10,000 individuals screened by CXR. Overall, the frequency of major complications occurring during a diagnostic evaluation of a detected finding was 33 per 10,000 individuals screened by LDCT and 10 per 10,000 individuals screened by CXR.[2,19]

This finding illustrates the importance of every screening program having strategies for lung nodule management that minimize potential complications from their evaluation.

Overdiagnosis is an intrinsic feature of screening, because screening will detect not just aggressive tumors, but also indolent tumors that otherwise may not be clinically significant. In addition, screening individuals with comorbidities (possibly related to age and smoking history) means that a portion of those screened will die of other causes before even a typical lung cancer would have impacted their lives. These overdiagnosed cases may result in additional cost, anxiety, and morbidity associated with treatment of a screen-detected cancer that otherwise would never have needed to be detected. Patz and colleagues[20] estimated that the probability that a lung cancer detected by LDCT screening was an overdiagnosed cancer was 18.5% overall, 22.5% if the cancer detected was a non-small cell lung carcinoma, and 79% if the histology was a noninvasive adenocarcinoma in the NLST. The number of cases of overdiagnosis found among 320 participants who would need to be screened in the NLST to prevent 1 death from lung cancer was 1.38.[20]

Although there is variation in clinical practice, the effective dose of radiation of an LDCT is estimated to be 1.5 mSv per scan, which is 3 to 4 times lower than a diagnostic CT scan.[21] Estimates of the impact of cumulative radiation exposure have varied greatly. At one extreme, it was estimated that 1 in 2500 patients screened may die of radiation-related malignancy from the cumulative radiation received during screening.[19] The radiation risk may only manifest many years later and, thus, it may be less relevant for older individuals than it is for younger individuals or those with a lower risk of developing lung cancer.

IMPLEMENTATION OF SCREENING PROGRAMS

In December 2013, the USPSTF released a grade B recommendation to screen high-risk individuals, defined as those age 55 to 80 who have a minimum smoking history of 30 pack-years and who currently smoke or have quit within the past 15 years.[3] The Affordable Care Act (ACA) required that commercial insurance plans participating in the health care exchange cover screening services that receive a grade B recommendation from the USPSTF, guaranteeing coverage to insured patients younger than 65 years of age. The CMS released a decision to cover CT screening for Medicare beneficiaries who are age 55 to 77 and have the same minimum smoking history required by the USPSTF.[4] These policies minimized concern about insurance coverage becoming a barrier for screening implementation.

The adoption of lung cancer screening in the United States is growing, but remains low.[22,23] It is estimated that approximately 3.9% of 6.8 million eligible smokers were screened in 2015 according to the National Health Interview Survey.[22] It should be noted that this survey was conducted the same year as CMS approval, and current evidence suggests a substantial growth in screening program numbers and capacity. Despite this, the majority of those eligible are still not being screened. The reasons for the low adoption rate are not clear. Possible explanations include a lack of awareness, challenges related to how to best incorporate mandatory shared decision making into patient visits, uncertainty about the best approach to integrate effective treatment for tobacco dependence, and barriers related to the stigma of smoking and lung cancer itself.

Another possible reason is a lack of resources. The distribution of screening programs varies significantly across states. Kale and colleagues[23] analyzed the geographic variation of lung cancer screening facilities that are in the national registry, which is a requirement for reimbursement by CMS. They reported a cluster of states (Alabama, Arkansas, Georgia, Kentucky, Louisiana, Missouri, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, and West Virginia) that had the highest lung cancer burden but the lowest number of screening programs. There is insufficient evidence to conclude that cost sharing or a lack of insurance coverage are causes of this disparity. However, 8 of those 12 states have not expanded Medicaid. It is not known whether the uptake of lung cancer screening in states with Medicaid expansion, as a part of the ACA implementation, is different than in nonexpansion states, but a lack of insurance coverage might contribute to the lower number of screening programs.

It is well-known that individuals of lower socioeconomic groups are less likely to receive cancer preventive services. The elimination of out-of-pocket expenses has helped to decrease this disparity, as seen in other cancer screenings, such as mammography for breast cancer.[24,25] There was a significant increase in screening mammography uptake after implementation of the ACA. The same trend was not consistently seen with colonoscopy; the uptake has been overall stagnant after ACA.[24] This difference suggests that the elimination of cost sharing is not sufficient to facilitate access to cancer prevention services. Although not sufficient, affordability is important for lung cancer screening uptake. Among respondents to the National Health Interview Survey in 2010 and 2015, more than 50% of smokers meeting criteria based on USPSTF recommendations for screening were uninsured or Medicaid insured.[22]

The implementation of a high-quality lung cancer screening program is complex. It requires the development of a broad infrastructure to meet regulatory mandates and clinical demands. Some of the aspects involved in a lung cancer screening program include patient selection, shared decision making, management of screen detected nodules, integration of smoking cessation interventions, and management of incidental findings.

Patient Selection

Several professional societies have endorsed lung cancer screening with LDCT (**Table 2**). The American College of Chest Physicians recommends screening similar to the entry criteria for the NLST: age of 55 to 77 years with at least a 30 pack-year smoking history who are current smokers or who quit within 15 years.[26] Other societies including the National Comprehensive Cancer Network and the American Association for Thoracic Surgery expanded the recommendations to include other risk factors such as environmental exposures.[27,28] For example, the American Association for Thoracic Surgery endorses LDCT screening for those ages 55 to 79 years with a 30 pack-year history of smoking; those ages 55 to 79 years with 20 a pack-year history of smoking

Table 2
USPSTF, CMS, and different profession societies recommendation regarding lung cancer screening

	Age, Years	Smoking History	Smoking Cessation	Interval	Other Recommendations
USPSTF (2013)	55–80	≥30 pack-years	<15 y	Annual	No conditions that substantially limit life expectancy
CMS (2014)	55–77	≥30 pack-years	<15 y	Annual	Shared decision making visit required.
ACCP (2018)	55–77	≥30 pack-years	<15 y	Annual	–
NCCN (2019)	55–74	≥30 pack-years	<15 y	Annual	20 pack-years, age >50, and additional risk factors
ACS (2013)	55–74	≥30 pack-years	<15 y	Annual	
AATS (2012)		≥30 pack-years		Annual	20 pack-years, age >50 y, and risk ≥5% over 5 y

Abbreviations: AATS, American Association for Thoracic Surgery; ACCP, American College of Chest Physicians; ACS, American Cancer Society; ASCO, American Society of Clinical Oncology; CMS, Center for Medicaid & Medicare Services; NCCN, National Comprehensive Cancer Network; USPSTF, United States Preventative Services Task Force.

Data from Refs.[3,4,26–28,63]

and additional comorbidities that increase the risk for lung cancer by more than 5% over 5 years; or for long-term survivors of lung cancer.[28] At the time of this writing the USPSTF has released a draft statement for public comment that would lead to an expanded pool (ages 50 to 80 years who have a 20 pack-year smoking history).

Other investigators have proposed the use of risk prediction models to select patients for screening. Two of the models that have been studied for this purpose are the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO) 2012 model and the modified Liverpool Lung Project models (LLPv2).[15,29] Understandably, the intention of expanding the screening eligibility criteria beyond the NLST entry criteria is to find other high-risk individuals who may benefit from screening, increasing the portion of all lung cancers that could be screen detected. Patient selection using these tools have not been assessed in randomized trials. The concern with screening populations at a lower risk for lung cancer than reflected by current eligibility criteria is that we would need to screen a greater number of individuals to prevent 1 death from lung cancer, and the balance of benefits and harms may be disrupted. The concern with screening other high-risk individuals, identified through the use of a risk calculator, is that the other risk factors included in these models, such as age, the presence of emphysema or a prior cancer, modify not just the risk of developing lung cancer, but the risk of finding a lung nodule, having a complication from evaluation of a lung nodule, and the success of early lung cancer treatment. Furthermore, the implementation of risk calculator–guided screening enrollment is more complex than current eligibility criteria.

It is important for those participating in lung cancer screening to be in good enough health to be able to tolerate the evaluation and treatment of screen-detected findings for screening to be effective. In the NLST, only 2% of patients diagnosed with stage I

lung cancer were treated with radiation only, which indicates that the majority of these patients were healthy enough to tolerate surgery.[2] An analysis of the screening-eligible population in the United States showed that they were older, more likely to be current smokers and to have comorbidities, and had a lower survival rate and life expectancy compared with the NLST cohort.[18] This finding suggests that the general population is more likely to have competing causes of death other than lung cancer, and comorbid conditions that could modify the benefit of screening. Unless an individual has an obvious severe, life-limiting condition, it is challenging to determine who is not well enough to participate in LDCT screening.

Shared Decision Making

The CMS has mandated a lung cancer screening counseling and shared decision-making visit before the screening examination to receive payment.[4] The purpose of the visit is to provide patients with the information and support they need to make value-based individualized decisions about whether to be screened. The shared decision-making visit is an opportunity for individuals to learn about their risk for developing lung cancer, and the benefits and potential harms of screening so that they can make informed choices that are consistent with their expectations and values.

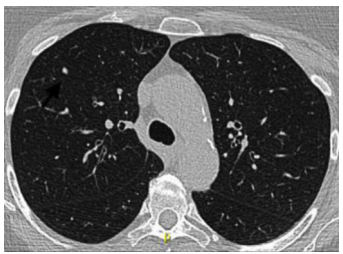
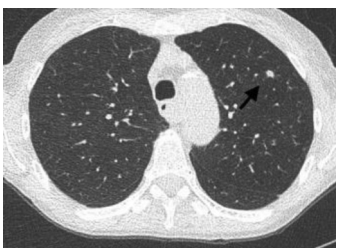
The most effective method to conduct a shared decision-making visit has not been determined. The CMS requires that it occurs during an in-person visit with a physician, advanced practice provider, or clinical nurse specialist.[4] Regardless of the health care professionals who are conducting it, they should be well-versed and comfortable discussing the risks, benefit, and the trade-offs as they are influenced by personal risk and comorbidities. This need puts primary care providers at a disadvantage because they may not be comfortable enough, or have time, to provide a comprehensive shared decision-making visit. Decision aids and risk prediction tools are effective ways to communicate complex topics to patients. They have been shown to increase understanding and improve the comfort with decision making.[30]

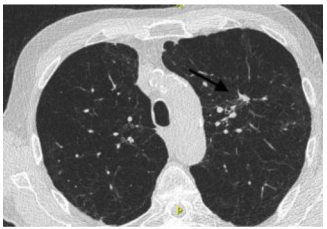
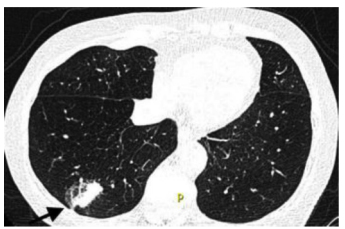
At the Cleveland Clinic, we developed a centralized counseling and shared decision-making visit for our lung cancer screening program. The visit begins with a review of patient eligibility for screening. Patients then watch a 6-minute narrated video that was developed by our program. It is followed by a discussion of the individual risk of developing lung cancer with the use of an on-line decision aid (www.shouldiscreen.com/), and an opportunity for questions to be answered and additional clinical data to be collected. During the visit, the expected results are discussed (ie, a high probability of finding a lung nodule), as is the importance of compliance with annual follow-up and recommendations for evaluating screen-detected findings. We studied the impact of this visit on patient knowledge and comfort with the screening decision, and there was a significant improvement in both as measured by a previsit and postvisit questionnaire.[31]

Management of Screen-Detected Lung Nodules

Based on consensus, the American College of Radiology developed a reporting system called the Lung CT Screening Reporting and Data System (Lung-RADS), which is similar to the Breast Imaging Reporting and Data System used for mammography reporting.[32,33] Lung-RADS is a tool designed to standardize lung cancer screening CT reporting and management recommendations to facilitate results interpretation and outcome monitoring. The classification couples a category of risk of lung cancer in a detected nodule with management recommendations, largely based on the nodule size, attenuation, and change over time. **Table 3** describes the criteria for

Table 3
Examples of lung-RADS categories 2, 3 and 4 A/B

Lung-RADS	Lung Nodule Description (Average Size)	Lung-RADS Recommendation	Management Chosen	Comment
2	Right upper lobe 4.7 mm 	Continue annual screening with LDCT in 12 mo	Annual screening	Nodule remained stable. Patient continued with annual screening.
3	Left upper lobe 6.4 mm 	6 mo LDCT	6 mo LDCT	Nodule increased in size in 6 mo to average size of 8 mm. Upgraded to a Lung-RADS category 4B. Patient had left upper lobectomy for NSCLC.

4A	Left upper lobe 9.7 mm 	3 mo LDCT; PET/CT may be used when there is a ≥8 mm (≥268 mm^3) solid component	3 mo LDCT	Nodule remained stable in 3 mo received Lung-RADS category 2. Review of prior scans that were initially missed revealed that the nodule had remained stable for 2 y.
4 B	Right lower lobe part solid 23 mm 	Chest CT scan with or without contrast, PET/CT scan and/or tissue sampling depending on the probability of malignancy and comorbidities. PET/CT scan may be used when there is a ≥8 mm (≥268 mm^3) solid component.	Percutaneous biopsy	NSLC confirmed. Patient was treated with stereotactic ablative therapy owing to poor lung function.

Abbreviations: NSCLC, non-small cell lung cancer; PET, positron emission tomography.

defining Lung-RADS categories. It is the structured reporting system required for data entry into the only CMS-approved lung cancer screening registry.

In the NLST, the false-positive rate in the trial was 27.3%. Small nodules in the size range of 4 to 6 mm accounted for more than one-half of all positive screens across all 3 screening time points and were found to be malignant less than 1% of the time.[2] Lung-RADS increased the size threshold for a positive result from a 4-mm to a 6-mm transverse average. This effort aimed to decrease the false-positive rate at the expense of a small compromise of test sensitivity. Raising the threshold for a positive result to 6-mm would decrease the baseline NLST positive rate to approximately 13.4%.[2] In a study by Pinsky and colleagues,[34] when the authors applied Lung-RADS to the NLST group at baseline, the false-positive rate decreased from 26.6% to 12.8% and the baseline sensitivity decreased from 93.5% to 84.9%.

Small and low-risk nodules that are screen detected can be followed with an annual (category 2) or a 6-month (category 3) surveillance LDCT. The management of higher risk nodules, Lung-RADS category 4, is more challenging. Recommendations from Lung-RADS include short-term follow-up, PET scan, biopsy, or surgery.[32] Although Lung-RADS assigns a general lung cancer risk for a specific category, individual assessment of the malignancy risk is an important initial step for decision making for category 4 nodules. Malignancy risk estimation can be performed subjectively with intuition and clinical experience, or by using validated clinical prediction models. Several validated risk prediction models are available. It is important to recognize that they are most accurate when applied to individuals from populations similar to those in which they were developed. In the lung cancer screening setting, the Brock model is likely the best fit.

The Brock model was developed from the Pan-Canadian Early Detection of Lung Cancer Study (PanCan; a low-dose CT screening study), and validated on participants in cancer chemoprevention studies at the British Columbia Cancer Agency.[35] A parsimonious and a fuller model were developed from multivariable logistic regression, including known risk factors for malignant lung nodules. The variables included in the final model were age, sex, family history of lung cancer, presence of emphysema, nodule size, location of the nodule in the upper lobe, nodule attenuation on the CT scan, nodule count, and spiculated nodule border. The model showed excellent discrimination with an area under the curve of more than 0.90. Important strengths of this model are the analysis of single or multiple lung nodules and the inclusion of nodule attenuation as a variable. Although it was derived from a lung cancer screening population, it has been validated in populations with incidental nodules.[36]

Surgical lung resection is the main curative intent treatment for early stage lung cancer. Therefore, thoracic surgeons are key components of the multidisciplinary team. Lobectomy with mediastinal lymph node evaluation remains the standard in the treatment of early stage NSCLC. The minimally invasive approach with video-assisted thoracoscopy has been associated with lower morbidity, including decreased perioperative pain, less blood loss, and a shorter hospital length of stay.[37–39] Sublobar resections can be considered in patients with limited lung function or small primary tumors. The advantage of sublobar resection in high-risk patients are a lower perioperative morbidity and mortality, as well as preservation of lung function.[40,41] Segmentectomy is preferred over a wedge resection when a nodule is known to be malignant. Segmentectomy includes dissection of the bronchial tree exposing lymph nodes that are not visualized during a wedge resection, and surgical margins or more than 1 cm are more likely to be achieved.[42–44] Multiple case series have demonstrated equivalent regional recurrence rates and survival, particular in patients with tumors less than 2 cm in diameter and in elderly patients (age >75 years).[45–47] Localization techniques such as fiducial placement, labeling, and marking techniques can be

used to facilitate resection of subcentimeter solid nodules deep in location, and nodules that are subsolid in attenuation that can be difficult to find by digital palpation.[48–50]

As discussed elsewhere in this article, one of the major concerns of lung cancer screening is overdiagnosis. Subsolid nodules should be managed differently than solid nodules because of their indolent behavior. A persistent subsolid nodule may be due to focal fibrosis or may represent a lesion in the spectrum of adenocarcinoma, from noninvasive atypical adenomatous hyperplasia to invasive adenocarcinoma. The prevalence of malignancy is relatively high and depends on the nodule size as well as the presence of a solid component on imaging.[51] The solid component represents the invasive foci of adenocarcinomas and it helps determine the management plan. For example, a persistent part solid nodule with solid components 8 mm or greater would be classified as Lung-RADS 4B (suspicious) and the recommendation would include consideration for a diagnostic CT scan, PET scan, or biopsy.[32] In contrast, a ground glass nodule that measures 20 mm with no solid component would be classified as Lung-RADS 2 and would be recommended to continue annual screening. Subsolid nodules typically do not require immediate resection because of their indolent behavior despite the relatively high risk of malignancy in these nodules. Supporting the conservative approach to subsolid nodules, Yankelevitz and colleagues[52] showed in a large-scale screening study that adenocarcinomas presenting as pure ground-glass nodules had an excellent prognosis with overall survival rate of 100% regardless of the time to treatment.

Integration of Smoking Cessation Interventions

Cigarette smoking is the major risk factor for lung cancer.[53] The importance of smoking cessation in the setting of lung cancer screening cannot be understated. Screening is not an alternative to smoking cessation. Rather, lung cancer screening is seen as a teachable moment for smoking cessation interventions. Every smoker should be encouraged to quit and be offered evidence-based treatment at every screening visit. It is an essential component of a screening program.[54] The integration of smoking cessation into screening programs maximizes the clinical benefit of lung cancer screening and its cost effectiveness. Tanner and colleagues[55] analyzed the effects of smoking abstinence among the individuals who participated in the NLST. The study showed that former smokers in the control arm of the NLST who were abstinent for 7 years had a 20% mortality reduction compared with active smokers, which is comparable with the benefit seen from LDCT screening. The maximum benefit was seen with the combination of smoking abstinence at 15 years and LDCT screening, which resulted in a 38% decrease in lung cancer-specific mortality.[55] Furthermore, Villanti and colleagues[56] developed a simulation model to estimate the cost-utility of annual LDCT over 15 years. The simulation showed that the addition of smoking cessation to annual screening with LDCT improved the cost effectiveness of screening between 20% and 45%. Smoking cessation resulted in increases in both the costs and quality-adjusted life years saved, reflected in cost utility rations ranging from $16,198 per quality-adjusted life years gained to $23,185 per quality-adjusted life years gained.[56]

The most effective smoking cessation intervention in the screening setting has not been determined. However, the methods applied should not be passive. Undergoing screening alone has not been shown to be enough to modify smoking behavior, but it seems that patients with abnormal findings were more likely to quit than those with normal results.[57,58] Low-intensity interventions such as providing written educational materials or brief counseling have not made a significant impact on smoking behavior.[59] A combination of counseling, behavioral, and pharmacologic treatment is most effective, but research is needed to determine if specific interventions are

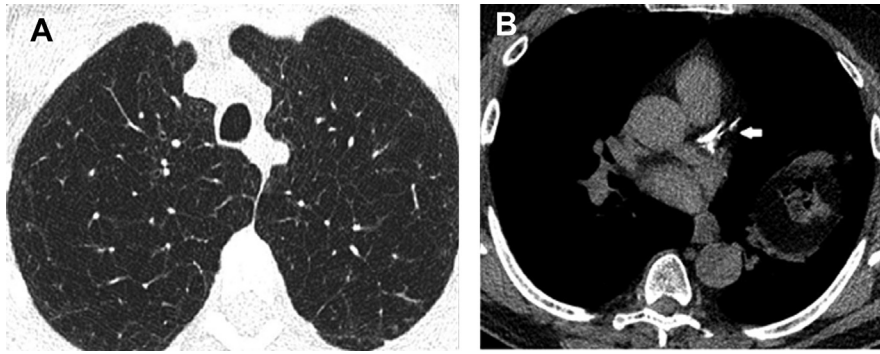


Fig. 1. Examples of pulmonary and cardiac incidental findings. (*A*) Moderate upper lobe emphysema, (*B*) Severe coronary calcification: left anterior descending (*white arrow*).

more effective for this specific group of smokers.[60] While we study the optimal timing and methods for smoking cessation interventions, it is important for screening programs to integrate their own smoking cessation resources or make referrals to established programs.

Management of Incidental Findings

Pulmonary and extrapulmonary incidental findings are common on screening LDCT.[61] In a systematic review, 14% of scans had findings that merited some form of additional evaluation.[62] The prevalence depends on how incidental findings are defined and each program's threshold to report them. We recently published our experience with incidental findings and reported every finding described by our radiologists.[61] Our study revealed that incidental findings were present in 94% of the patients screened. The most frequently reported findings were in the respiratory and cardiovascular systems (Fig. 1). Most findings were not felt to be actionable. Approximately 15% lead to referral to subspecialty consultants and 13% had further evaluation with testing. Serious diagnoses were found including severe coronary artery disease requiring intervention, and extrapulmonary malignancies. The evaluation of incidental findings had a significant impact on reimbursement generated by the screening program. Because incidental findings on LDCT sans are common and their impact may be significant, they should be discussed during the shared decision-making visit, and screening programs should be prepared to manage them according to their own resources.

FUTURE DIRECTIONS

Many lessons have been learned since the early stages of implementation of lung cancer screening programs. Likewise, many questions and challenges remain. The major concerns are related to how to improve patient selection for screening, how to minimize the potential harms, and how to facilitate implementation and access to screening programs. Eligibility based on age and smoking history has the advantage of its simplicity, but risk-based strategies using validated models may be able to expand screening eligibility to include other healthy high-risk individuals and assist with determining the interval between scans. Advances in molecular biomarker testing and computer-assisted image interpretation may improve the accuracy of patient selection and lung nodule management with the potential to minimize harms related to

the evaluation of benign nodules. We also need to further our understanding of the reasons for the overall low uptake of lung cancer screening in the United States. Additional research and health policy evolution with a focus on access to preventive services and smoking cessation in disadvantaged populations will be necessary to optimize the impact of this life-saving tool.

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