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Incidental Findings on Lung Cancer Screening: Significance and Management

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Incidental findings are commonly detected by computed tomography, but distinguishing which findings have little or no clinical consequence and which are significant enough to require further evaluation is not always clear. This distinction is important for patient care and to ensure appropriate use of health care resources. This article aims to highlight some of the incidental findings detected by low-dose CT (LDCT) performed for lung cancer screening and to present an overview of currently accepted management recommendations.
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Introduction

The National Lung Cancer Screening Trial (NLST) not only showed a 20% reduction in lung cancer–specific mortality but also showed a 6.7% reduction in all-cause mortality with annual low-dose computed tomography (LDCT) lung cancer screening compared to chest radiography.[1] Although the LDCT technique is limited by lower radiation dose and lack of intravenous contrast, imaging from the lower neck to the upper abdomen leads to detection of actionable or potentially significant incidental findings (IFs). This may contribute to the reduction in all-cause mortality, since the population of screening patients aged 55-80 are at risk for age-related and smoking-related comorbidities.[2,3]

Owing to the various approaches to the reporting and management of screen-detected IFs, the reported prevalence and associated costs of these IFs is quite variable. In the NLST and other worldwide clinical trials for lung cancer screening, the rates of significant IFs varied from 1% in the Dutch-Belgian lung cancer screening trial (NELSON) up to 19% at a Canadian center participating in the International Early Lung Cancer Action Program (I-ELCAP).[1,4-9] Two recent studies of lung cancer screening programs implemented in the United States reported higher rate of IFs of 40.7%[10] and 94%[11] though only 2%-13% of patients required further evaluation.[10,11] Even in one multisite trial, the prevalence of reported IFs, using the same reporting guidelines, ranged from 20% at one site to 63% at another.[10]

There is no consensus among radiologists, either in the US, or throughout the world, as to the definition, reporting, or management of incidental findings detected at CT screening for lung cancer. It can be argued that emphysema and coronary artery calcification, the most commonly reported incidental findings, are not incidental but opportunistic findings, and representative of smoking-related disease.[12]

Included in the American College of Radiology (ACR) Lung CT Screening Reporting and Data System (Lung-RADS) is a category "S" modifier for clinically significant or potentially clinically significant non-lung cancer findings that can be added to any of the Lung-RADS category 0-4 coding for nodules. The ACR estimates the prevalence of "S" modifier use to be 10%.[13] The definition of what constitutes a significant finding and the management for such findings is left to the discretion of the radiologists, with some groups including only IFs that require further follow-up. Given the frequency of these IFs, a more thorough understanding of their significance and a standardized approach to the reporting and management of these findings are vital.

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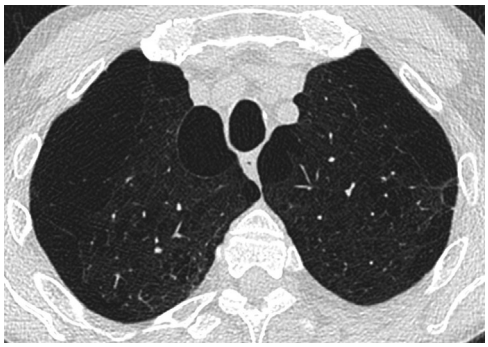

Figure 1 Emphysema. A 63-year-old male, former smoker, who quit 1 year ago with 40-pack-year smoking history. Axial LDCT image on lung window shows multilobular lucencies in the upper lobes consistent with severe confluent centrilobular and paraseptal emphysema.

Incidental pulmonary findings

Chronic Obstructive Pulmonary Disease

In the United States, smoking causes 79% of all cases of chronic obstructive pulmonary disease (COPD).[2] Imaging findings and grading of severity can serve as useful adjuncts to traditional assessment of COPD by pulmonary function testing. As outlined by the Fleischner Society, CT scans can be used to characterize COPD findings of emphysema, airway disease, and associated findings of large airway disease, interstitial lung abnormality, and pulmonary arterial enlargement. Emphysema should be characterized by pattern as centrilobular, panlobular, or paraseptal, and the severity may be graded as trace (<0.5% of a lung zone), mild (0.5%-5%), moderate (>5%), confluent (spanning several secondary pulmonary lobules), or advanced (with hyperexpansion of secondary pulmonary lobules and architectural distortion (Fig. 1).[14] Although quantification of emphysema has been shown to be challenging at extreme low doses below 30 mAs,[15] use of image processing techniques and reconstruction algorithms result in no significant difference in detection of emphysema between low dose and standard dose technique.[16,17] Several groups have shown that LDCT can accurately detect and quantify both emphysema and airway disease with comparable accuracy to pulmonary function testing.[18,19]

COPD is underdiagnosed in up to 80% of patients who show airway obstruction on spirometry. In the asymptomatic patient population undergoing lung cancer screening, LDCT may detect imaging manifestations of COPD at an earlier stage. A recent study showed that COPD was a known diagnosis in 31.6% of participants of an LDCT screening program but emphysema and bronchial wall thickening were reported in an even higher percentage of participants, 50.6% and 39.4% of scans, respectively.[11] Although management of COPD with inhaled bronchodilators with or without inhaled glucocorticoids has traditionally been initialized once patients are symptomatic, early intervention, particularly with smoking cessation, has been shown to reduce the societal burden of COPD, with a decrease in the number of exacerbations and hospital admissions secondary to COPD.[20,21]

In addition to early identification and treatment of COPD, the amount of emphysema on CT has been shown to be an independent risk factor of lung cancer and nonpulmonary cancer.[22] Hopkins et al[23] demonstrated a linear relationship between increasing severity of airflow limitation (as measured by GOLD scores) and risk of lung cancer. This supports the inclusion of COPD in models for selection of the optimal patient population for lung cancer screening.[24] A study of NLST participants with indeterminate 6-19 mm nodules by Chiles et al has shown that an emphysema-predominent COPD phenotype and increasing severity of centrilobular emphysema on LDCT were associated with an increased risk that the nodules are malignant.[25] Hence, evidence of emphysema on CT could also be incorporated into nodule risk prediction models.

Interstitial Lung Abnormalities

Cigarette smoking is associated with increased risk of interstitial lung diseases, including smoking-related interstitial fibrosis (SRIF), idiopathic pulmonary fibrosis (IPF), desquamative interstitial pneumonia (DIP), and respiratory bronchiolitis interstitial lung disease (RB-ILD) (Fig. 2). The distinction between nonfibrotic and fibrotic forms can be assessed based on the presence or absence of reticulations, honeycombing, architectural distortion, and groundglass opacities or nodules. In clinical trials for lung cancer screening, the prevalence of

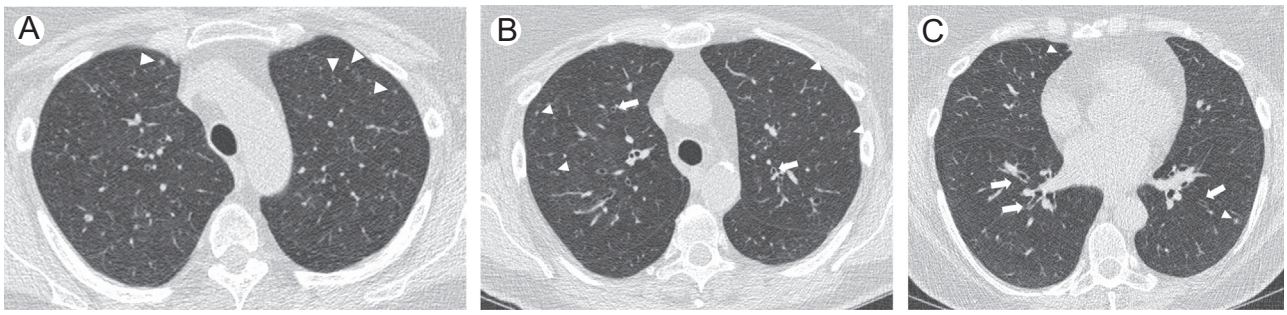

Figure 2 Respiratory bronchiolitis. A 70-year-old male, former smoker, who quit 2 years ago with 50 pack-year smoking history. (A-C) Axial LDCT images on lung window of a show diffuse ill-defined centrilobular groundglass micronodules (arrowheads) and airway thickening (arrows) consistent with RB.