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CT screening for lung cancer: Importance of emphysema for never smokers and smokers

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ABSTRACT

Purpose: To address the prevalence of lung cancer in high and low-risk people according to their smoking history, age, and CT findings of emphysema.
Methods: We reviewed the baseline low-dose CT scans of 62,124 current, former and never smokers, aged 40–90 to determine the prevalence of lung cancer. We performed logistic regression analysis of the prevalence of lung cancer to determine the odds ratio (OR) for emphysema, conditionally on age, female gender, and ethnicity.
Results: The prevalence of lung cancer was 1.4% (95% CI: 1.3–1.6) for current smokers, 1.1% (95% CI: 1.0–1.2) for former smokers, and 0.4% (95% CI: 0.3–0.6) for never smokers. Emphysema was identified in 28.5% (6,684), 20.6% (5,422), and 1.6% (194) of current, former, and never smokers, respectively. The prevalence of lung cancer among current smokers was 1.1% for those without emphysema vs. 2.3% for those with emphysema (odds ratio [OR] 1.8; 95% confidence interval [CI]: 1.4–2.2) and the corresponding difference for former smokers was 0.9% vs. 1.8% (OR: 1.7; 95% CI: 1.3–2.2), and for never smokers, it was 0.4% vs. 2.6% (OR: 6.3; 95% CI: 2.4–16.9).
Conclusions: Identification of emphysema in low-dose CT scans increases the risk of lung cancer and is important in determining follow-up of current, former, and never smokers.

1. Introduction

The number of people who have a CT scan of the chest continues to increase in the United States and throughout the world for many indications, including CT screening for lung cancer. In 2009, it was estimated that in the US alone, almost 10 million CT scans of the chest were performed for lung and cardiac indications [1]. It is estimated that over 50% of these people had at least one non-calcified nodule (NCN) identified in the lung parenchyma, raising the possible diagnosis of lung cancer [2]. Beyond the identification of NCNs on CT scans, emphysema has been identified as an important risk factor for lung cancer which appears to be independent of the presence of airflow obstruction as measured by pulmonary function tests [3–6].

In light of the high lung cancer fatality rate, the management of findings on CT is of great concern. Different management strategies have been developed with a goal of diagnosing a possible cancer as early as possible while minimizing unnecessary diagnostic tests, invasive procedures, and surgery. These strategies have focused mainly on high-risk smokers in the context of CT screening studies [7–11]. The Fleischner Society Guidelines also addressed the recommended workup for NCNs in low-risk individuals, including never smokers [12]. These management strategies, however, do not use the information on findings provided by the CT scan other than the presence of NCNs.

In this report we address the prevalence of lung cancer according to the presence of emphysema as identified in the CT scan in both

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high and low-risk people as defined by their smoking history and age.

2. Methods

Participants (n = 62,124) enrolled in a program of CT screening for lung cancer in the International Early Lung Cancer Action Program (I-ELCAP) in 2000–2013 [13]. At the time of enrollment, all were 40–90 years of age (median age of 60) and asymptomatic for lung cancer. Consent for the research was obtained from all participants according to HIPAA-compliant protocols that were approved by the IRBs of the participating institutions.

2.1. Smoking status

All participants completed a baseline questionnaire that provided information on their smoking status, quantity smoked, and, if they had quit, when. Smokers were defined as participants who had smoked 100 or more cigarettes and were classified as being a current smoker if they had smoked more than 1 cigarette in the month prior to enrollment or quit within 1 year of enrollment (n = 23,415). The remaining smokers were classified as former smokers (n = 26,341). Never smokers (n = 12,368) were defined as having smoked less than 100 cigarettes in their lifetime; some 32% (3,982) may have had occupational exposure to lung carcinogens while the rest had some level of secondhand tobacco smoke exposure (SHTS). Current and former smokers were divided into three categories according to the total pack-years of smoking: light, if less than 30 pack-years, moderate if 30–59 pack-years, and heavy if 60 or more pack-years.

2.2. Baseline CT scan and diagnosis of lung cancer

Upon enrollment, the baseline low-dose CT scan was obtained according to a common protocol from the lung apices to the bases in a single breath hold at maximum inspiration at 120 kVp and 80 mAs or less [13]. No intravenous contrast material was used. The CT images were read by radiologists at the participating institutions who had undergone training at the center. The readings were performed using standard lung settings (width 1500 HU and level −650 HU) and standard mediastinal settings (width, 350 HU; level, 50 HU). Diagnoses of lung cancer resulting from the baseline CT scan were documented in the web-based management system and had pathologic confirmation.

2.3. Emphysema

The absence/presence of emphysema was ascertained from the baseline low-dose CT image and documented [6,13]. Emphysema was considered to be present if discrete areas of decreased attenuation could be identified anywhere in the lung parenchyma, or, if no discrete areas of decreased attenuation could be identified on the CT scan, when the blood vessels were splayed suggesting parenchymal expansion.

2.4. Secondhand tobacco smoke exposure score

All participants completed a background questionnaire about secondhand tobacco smoke (SHTS) exposure before age 18 as a child, and after age 18, as an adult at home and at work as previously described in detail [14]. The responses determined the *permission status*, *duration of SHTS exposure* (years), *daily intensity of the SHTS exposure* (packs per day) for each of these life-exposures as a child, and as an adult at home and at work. The permission status was 1.0 if smoking was allowed anywhere, 0.5 if smoking was restricted, or 0 if smoking was not permitted. The exposure duration was the sum of the years that the participant was exposed to SHTS divided by the maximum possible score. The total SHTS exposure score ranged from 0 to 0.70 and the entire range was divided into quartiles. The analysis focused on the two highest SHTS quartiles.

2.5. Statistical analysis

The prevalence of diagnosed lung cancers and emphysema was determined overall and for each decade of age. Percentages, median and interquartile range (IQR) were calculated as needed. The Chi-square test was used to compare percentages. The prevalence of lung cancer was addressed as a joint function of potential risk indicators using multivariate logistic regression analysis, adjusting for emphysema, age, sex and Asian ethnicity. All analyses were performed using the SAS (SAS, Cary, NC, Version 9.2) statistical package.

3. Results

The characteristics of the 62,124 participants at the time of the baseline CT scan are given in Table 1, separately for current, former and never smokers. On average, former smokers were older than current and never smokers (62 vs. 57 vs. 56 years of age, $P < 0.0001$). The median pack-years of smoking were 35 pack-years (IQR: 23–49) for current smokers and 30 (IQR: 19–47) for former smokers. For former smokers, the median years of quitting prior to

Table 1
Gender, ethnicity, age and smoking history for current, former, and never smokers.

	Current smokers N = 23,415	Former smokers N = 26,341	Never smokers N = 12,368	P-value
Gender				
Male	13,377 (57%)	16,263 (62%)	6,514 (53%)	<0.0001
Female	10,038 (43%)	10,078 (38%)	5,854 (47%)	
Ethnicity				
White	18,298 (78%)	23,532 (89%)	5,940 (48%)	<0.0001
Asian	2,385 (11%)	1,368 (5%)	5,800 (47%)	
Other	2,732 (12%)	1,441 (5%)	628 (5%)	
Age				
Median (IQR)	57 (52–63)	62 (57–68)	56 (50–65)	<0.0001
Smokers				
Median pack-years (IQR)	35 (23–49)	30 (19–47)		<0.0001
Median years quit (IQR)	–	15 (6–24)		