ORIGINAL ARTICLE

Trends in Subpopulations at High Risk for Lung Cancer

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ABSTRACT

Introduction: Two-thirds of patients in the United States with newly diagnosed lung cancer would not meet the current U.S. Preventive Services Task Force (USPSTF) screening criteria, which suggests a need for amendment of the definition of *high risk*. To provide evidence of additional high-risk subpopulations and estimated gains and losses from using different criteria for screening eligibility, we conducted a two-step study using three cohorts.

Methods: The two prospective cohorts comprised 5988 patients in whom primary lung cancer was diagnosed between 1997 and 2011 (the hospital cohort) and 850 defined-community residents (the community cohort); the retrospective cohort consisted of the population of Olmsted County, Minnesota, which was observed for 28 years (1984–2011). Subgroups of patients with lung cancer who might have been identified using additional determinates were estimated and compared between the community and hospital cohorts. The findings were supported by indirect comparative projections of two ratios: benefit to harm and cost to effectiveness.

Results: Former cigarette smokers who had a smoking history of 30 or more pack-years and 15 to 30 quit-years and were 55 to 80 years old formed the largest subgroup not meeting the current screening criteria; they constituted 12% of the hospital cohort and 17% of community cohort. Using the expanded criteria suggested by our study may add 19% more CT examinations for detecting 16% more cases when compared with the USPSTF criteria. Meanwhile, the increases in false-positive results, overdiagnosis, and radiation-related lung cancer deaths are 0.6%, 0.1%, and 4.0%, respectively.

Conclusions: Current USPSTF screening criteria exclude many patients who are at high risk for development of lung cancer. Including individuals who are younger than 81 years, have a smoking history of 30 or more pack-years, and have quit for 15 to 30 years may significantly increase the number of cases of non-overdiagnosed screen-detected lung cancer, does not significantly add to the number of false-positive cases, and saves more lives with an acceptable amount of elevated exposure to radiation and cost.

Keywords: Lung cancer; Low-dose CT; Screening; Smoking cessation; Former smokers

Introduction

With the declining percentage of the U.S. population that smokes, the incidence of lung cancer and mortality due to lung cancer have been decreasing among men for

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the past three decades and, only recently, have begun showing a decrease among women.[1] Meanwhile, former cigarette smokers remain at high risk for lung cancer, albeit at lower risk than had they continued smoking.[2] As a consequence, more cases of lung cancer are now being diagnosed in former smokers rather than in current smokers.[3] Specifically, less than 18% of U.S. adults are current smokers and more than 30% are former smokers.[3,4] As of 2014, use of low-dose computed tomography (LDCT) screening for lung cancer was recommended by the U.S. Preventive Services Task Force (USPSTF) for annual screening of people aged 55 to 80 years who have a history of smoking cigarettes at a rate of 30 or more pack-years and either are current smokers or have quit within the past 15 years.[5,6] This recommendation was based on the entry criteria of the National Lung Screening Trial (NLST) but with an extension of the upper age limit of 74.[7] However, our recent report showed that approximately two-thirds of patients with newly diagnosed lung cancer would not have met the current USPSTF criteria for being at high risk for development of lung cancer and thus eligible for LDCT screening.[8] In particular, we found a 24% falloff in meeting the eligibility criteria for screening (from 57% in 1984–1990 to 43% in 2005–2011), which exceeded the 17% decline in incidence of lung cancer (from 53 to 44 cases per 100,000 population) within the same time intervals. Herein we report our further investigations to delineate the high-risk subpopulations on the basis of evidence from two prospective cohorts of patients with lung cancer and a retrospective community cohort. Our goal was to improve the identification of individuals at high risk for development of lung cancer by (1) demonstrating the chronological patterns of patients who would have been the beneficiaries or "missed-outs" under the USPSTF criteria for lung cancer screening in two contrasting cohorts and (2) providing indirect evidence of a new subpopulation that should be included in the definition of *high risk* and the potential benefit versus harm and projected cost versus effectiveness of including them.

Methods

Study Population

This study included two steps: description and validation. Step 1 used two prospectively observed cohorts of individuals with lung cancer, one based on patients referred to Mayo Clinic (i.e., the hospital cohort, n = 5988) and the other consisting of residents of Olmsted County, Minnesota (i.e., the community cohort, n = 850). The hospital cohort included patients who had pathologically confirmed primary lung cancer diagnosed at Mayo Clinic in Minnesota during a 15-year period (between January 1, 1997 and December 31, 2011)[9] and were not Olmsted County residents. The community cohort was matched to the same 15-year period of diagnosis as the hospital cohort.[8] All cases were identified using the Rochester Epidemiology Project database, which has for more than 60 years maintained a comprehensive system linking the medical records of almost all persons residing in Olmsted County.[10,11] This population comprises approximately 140,000 persons, 83% of whom are non-Hispanic whites; it is socioeconomically similar to the white population of the United States and is representative of the population of the midwestern United States. More details were published previously.[8,12] This study was approved by the institutional review boards of Mayo Clinic and Olmsted County Medical Center.

The objective of step 2 was to provide indirect evidence supporting the findings in step 1. We have derived comparative benefit-to-harm and cost-to-effectiveness ratios for three sets of criteria—NLST, USPSTF, and the expanded criteria suggested by our study on the basis of the information provided in the models by de Koning et al.[6] Although hypothetical and indirect, the comprehensive models built by de Koning et al. are very helpful in initial evaluation of the impact (positive and negative) of a potential high-risk subpopulation given the lack of individual-level smoking history data or up-to-date and accurate smoking history information for entire populations of interest. Briefly, the modeling groups standardized input data on smoking histories and non–lung cancer mortality to simulate life histories of the U.S. cohort born in 1950, which uses an updated version of the National Cancer Institute's smoking history generator. Their models assumed 100% adherence to screening criteria; the data derived from trials of short duration (e.g., 4 to 9 years) were extrapolated to lifetime follow-up, and smoking history data from one to two decades ago were assumed to be current.[6,13–16]

Specifically, we have adapted and integrated the following 11 items selected from Tables 1 and 2 in the article by de Konig et al.[6]: (1) total number of CT examinations, including screening examinations; (2) number of screening-detected cases; (3) reduction in lung cancer mortality; (4) total cases detected at an early stage; (5) average number of screening examinations per person screened; (6) screening examinations per averted death from lung cancer; (7) screening examinations per life year gained; (8) average number of false-positive results per person screened; (9) number of instances of overdiagnosis; (10) overdiagnosis as a percentage of screening-detected cases; and (11) radiation-related lung cancer deaths.

Their comprehensive models standardized input data on smoking histories and non-lung cancer mortality to simulate life histories of the U.S. 1950 birth cohort.[15–18]