Letter to the Editor

Cancer Prevention Research

Lung Cancer Risk Prediction to Select Smokers for Screening CT — Letter

Robert P. Young and Raewyn J. Hopkins

In a recent article, Maisonneuve and colleagues described risk models identifying smokers at greatest risk of lung cancer for computed tomographic (CT) screening (1). We agree that such an approach will help increase lung cancer detection rates, improve cost-effectiveness, and reduce harm from unnecessary follow-up to screening. However, we propose below an alternative approach based on the current literature.

Among the risk models for lung cancer that they described (1), some were developed in populations including lifelong nonsmokers. As such, the relevance of these models in the context of CT screening, where exclusively current or former smokers are targeted, is not clear. Moreover, the model developed by Maisonneuve and colleagues (1) is based on age and smoking exposure (Bach model) and little comment is made of the sensitivity of such an approach. Using a representative sample of 446 lung cancer cases (2), we estimate that the eligibility criteria of the National Lung Screening Trial (NLST) and COSMOS trial would identify only 47% and 57% of cases, respectively. This means that approximately 40% to 50% of all lung cancer cases will occur outside these current screening programs.

We strongly agree with the study of Maisonneuve and colleagues (1) that additional clinical variables such as chronic obstructive pulmonary disease (COPD; airflow limitation and/or emphysema) will contribute significantly to the risk-based approach to optimizing CT screening. The epidemiologic data linking reduced FEV_1 (airflow limitation) to an elevated risk of lung cancer is strongly supported by both cross-sectional and prospective data (1–3). Using data from the Pittsburgh and NELSON CT trials (3, 4), simple spirometry identified COPD 89% and 84% of the time, respectively, compared with using CT-based emphysema which identified 49% and 67%, respectively (3, 4). More importantly, based on the Pittsburgh trial (3), 85% of lung cancer cases were identified among smokers with either airflow limitation and/or CT-based emphysema (see Fig. 1). In these trials, this constitutes 46% to 48% of all CT screening participants. Conversely, only 15% of lung cancers were detected in those who had normal lungs (normal spirometry and no emphysema). Consistent with the recently published National Comprehensive Cancer Network (NCCN) recommendations for lung cancer screening (www.NCCN.org), we have developed a risk model for lung cancer that includes age, COPD, and genetic risk variables (family history and genetic markers) that has use in all smokers, including those with normal lung function (5). This is currently undergoing further validation in the NLST. We conclude that the optimal target population for CT screening of lung cancer can be identified by risk models that include clinical variables indicative of COPD (1, 3, 5).

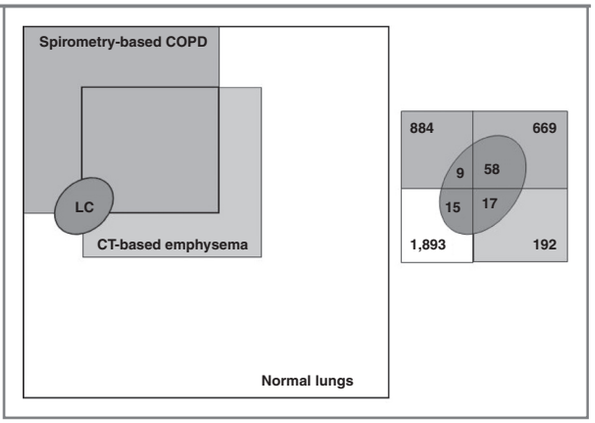

Figure 1. Relationship between spirometry-based COPD (GOLD I–IV; gray box) and CT evidence of emphysema (mild-severe: light gray box) in a CT screening study and overlap with CT-detected lung cancer (dark gray oval; ref. 3). LC, lung cancer.

Disclosure of Potential Conflicts of Interest

R.P. Young has commercial research grant (financial support) from Synergenz BioScience Ltd.; ownership interest (including patents) and patents related to genetic risk prediction and lung cancer held by Synergenz BioScience Ltd.; and is an unpaid consultant to Synergenz BioScience Ltd. R.J. Hopkins is employed with Synergenz BioScience Ltd.

Authors' Contributions

Conception and design of the study: R.P. Young, R.J. Hopkins.
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): R.P. Young.
Writing, review, and/or revision of the manuscript: R.P. Young, R.J. Hopkins.

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Authors' Affiliation: Schools of Biological Science and Health Sciences, University of Auckland, Auckland, New Zealand

Corresponding Author: Robert P. Young, Respiratory Genetics Group, University of Auckland, PO Box 26161, Epsom 1344, Auckland 1052, New Zealand. Phone: 649-6309968; Fax: 649-6236456; E-mail: roberty@adhb.govt.nz

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References

1. Maisonneuve P, Bagnardi V, Bellomi M, Spaggiari L, Pelosi G, Rampinelli G, et al. Lung cancer risk prediction to select smokers for screening CT—a model based on the Italian COSMOS trial. Cancer Prev Res 2011;4:1778–89.
2. Young RP, Hopkins RJ, Christmas T, Black PN, Metcalf P, Gamble GD. COPD prevalence is increased in lung cancer independent of age, gender and smoking history. Eur Respir J 2009;34:380–86.
3. Wilson DO, Weissfeld JL, Balkan A, Schragin JG, Fuhrman CR, Fisher SN, et al. Association of radiologic emphysema and airflow obstruction with lung cancer. Am J Respir Crit Care Med 2008; 178:738–44.
4. Mets OM, Buckens CFM, Zanen P, Isgum I, van Ginneken B, Prokop M, et al. Identification of chronic obstructive pulmonary disease in lung cancer screening computed tomographic scans. JAMA 2011;306: 1775–81.
5. Young RP, Hopkins RJ, Hay BA, Epton MJ, Mills GD, Black PN, et al. A gene-based risk score for lung cancer susceptibility in smokers and ex-smokers. Postgrad Med J 2009;85:515–24.