Editorial

Improving CT screening for lung cancer with a highly predictive risk model

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In 2011, the National Lung Screening Trial (NLST) found that low-dose CT screening in high-risk individuals reduced lung cancer mortality by 20% if compared to chest X-ray (1).

Since the publication of the NLST results, many medical organizations have recommended low-dose CT lung screening, based on NLST eligibility criteria or similar: age 55–74 years, a 30+ pack-year smoking history and current smoking status or having quit in the last 15 years.

Patient selection is one of the key points for an effective screening program since it remarkably influences the harms and benefits of screening and its cost-effectiveness. Unfortunately, to date, there is no common strategy for patient selection in CT screening (2). The NLST entry criteria do not quantify individual risk and a non-negligible proportion of Americans diagnosed with lung cancer fail to meet them (3).

The introduction of risk models into screening programs could have great benefit. In particular, three studies recently demonstrated that selection of individuals for lung cancer screening using accurate risk prediction models is superior to using NLST/USPSTF criteria (4-6).

In 2007, the Pan-Canadian Early Detection of Lung Cancer (PanCan) trial was designed to recruit individuals for lung cancer screening using a prototype of the PLCOm2012 risk model (7). Risk factors integrated as predictor variables to provide an individual risk stratification were: education level, family history of lung cancer, body mass index, the results of any chest X-ray performed within 3 years and presence of respiratory diseases (Table 1). The relevance of respiratory diseases for selection of high-risk subjects was confirmed by the literature (8,9). In particular, Wille et al. (10) recently reported a two-to-six fold increase in lung cancer risk in association with COPD and more than 35 pack-year, suggesting a potential beneficial effect of screening for this particular subgroup.

The study recently published in The Lancet Oncology by Tammemagi et al. (11) will have a significant impact on selection of high-risk subjects for lung cancer screening. In 2008–2010, they enrolled 2,537 eligible current and former smokers between 50 and 75 years, without a self-reported history of lung cancer, from eight centers across Canada. Enrolled participants must have a 6-year risk of lung cancer of at least 2%, as determined by the PanCan risk model. Patients were screened with low-dose CT scans at baseline (T0), at 1 year (T1) and finally at 4 years (T4). Median follow-up was 5.5 years; a long follow-up was crucial to assess the sensitivity and calibration of a model in which the predicted lung cancer risk is estimated for 5 or 6 years.

The primary outcome of the study was lung cancer cumulative incidence, while the secondary outcome was stage distribution of lung cancers by comparison with NLST.

One-hundred-sixty-four participants were diagnosed with lung cancer (172 total number of lung cancers), for a cumulative incidence of 6.5% (164/2,537) and an incidence rate of 138 per 10,000 person-years. The incidence was significantly greater than that observed in NLST (4%,...
Out of the 172 lung cancers detected, 137 (80%) were identified at T0, 8 (5%) were identified at T1 and T2, 17 (10%) at T4; ten were interval cancers. The proportion of interval lung cancers (6%) was lower than NLST (6.6%) (12,13). The proportion of lung cancers that were early stage was significantly higher in the PanCan study (77%) than in NLST (57%, 593/1,040) (12).

This was the first trial that prospectively recruit individuals for lung cancer screening using a predictive risk model, based on the evaluation of risk factors beyond age a smoking history.

The only other prospective study that used a risk prediction model to select candidates was the UK Lung Screening (UKLS) trial, which enrolled individuals with a 5-year lung cancer risk of at least 5% (14). After the baseline and 12-month CT, 42 (2.1%) of the 1,994 screened participants were confirmed to have lung cancer.

Waiting for the introduction of molecular biomarkers as a potential tool for a more tailored selection of high-risk subjects, the PanCan risk model should be considered for adoption in lung cancer screening programs.

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Footnote
Conflicts of Interest: The authors have no conflicts of interest to declare.

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