Screening Criteria Evaluation for Expansion in Pulmonary Neoplasias Using Molecular and Immunologic Markers (SCREEN II).

Objective: The primary objective of SCREEN II was to assess the molecular and immunologic profile of light-or-never-smokers (LONS) and heavy smokers, defined by National Lung Screening Trial (NLST) and by Nederlands–Leuven Longkanker Screenings Onderzoek (NELSON) criteria, separately. The hypothesis was that molecular and immunologic profiles differ between LONS and heavy smokers.

Methods: A retrospective review of 1,156 lung cancer cases from 2005-2018 at a tertiary Canadian institution was conducted. Multivariable logistic regression was used to compare the rate of KRAS, EGFR, BRAF, PIK3CA, ALK, and PD-L1 (<1%, 1-49%, >50%) between LONS and heavy smokers while adjusting for sex, previous cancer history, family history of cancer, symptoms, histological diagnosis, grade, stage, urban or rural environment, and geographic radon levels. Survival differences were assessed between LONS and heavy smokers using multivariate regression while adjusting for clinical, molecular, and immunologic variables.

Results: The cohort was comprised of 45.7% (NLST, n=536) and 63.5% (NELSON, n=745) heavy smokers. LONS had a higher rate of stage I cancer using NELSON criteria [56.3%, (n=240) vs 49.0% (n=365); p = 0.041]. LONS were more likely EGFR-positive in both NLST [OR 0.79, 95% CI 0.21-1.37; p = 0.008] and NELSON [OR 0.79, 95% CI 0.28-1.31; p = 0.002] models. Female LONS were more likely than male LONS to be EGFR-positive in NELSON [OR 0.59, 95% CI 0.06-1.12; p = 0.031] but not NLST [OR 0.51, 95% CI 0.02-1.05; p = 0.058] models. LONS were more often PIK3CA-positive using NLST [OR 1.33, 95% CI 0.54-2.13; p = 0.001] and NELSON [OR 1.19, 95% CI 0.49-1.90; p = 0.001] models. Heavy smokers were more often KRAS-positive in both NLST [OR 0.35, 95% CI 0.04-0.67; p = 0.029] and NELSON [OR 0.43, 995% CI 0.09-0.76; p = 0.012] models. No differences in ALK, BRAF, and PD-L1 were observed between LONS and heavy smokers using NELSON or NLST models. LONS in the NELSON model were at higher risk for mortality (Figure 1).

Conclusions: When defined by NLST or NELSON criteria, LONS have a higher rate of EGFR and PIK3CA mutations. There was no difference in the rate of ALK, BRAF, or PD-L1 mutations. LONS with non-small-cell lung cancer may be at increased risk for mortality compared to heavy smokers. Molecular profiling, particularly where targeted therapy is available, should be considered in establishing criteria for lung cancer screening.

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