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Title: Accelerated lung function decline increases the risk of lung cancer

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Body: Impaired lung function (LF) has been described as an important risk factor for lung cancer (LC). However, most studies assess LC risk based on LF status at baseline rather than on its change over time. Data on the relationship between LF progression and LC risk is limited. The cohort is from an ongoing LC screening program using low-dose chest CT scans held at our institution. Between 2000 and 2012, active and former smokers ≥40 years of age, with at least 10 pack-years of smoking, and with a baseline and at least 2 additional annual pulmonary function tests were selected. Individual mean annual changes in FEV1 (in ml and % predicted) and in FEV1/FVC were calculated using linear regression. Cox proportional hazards method was used to assess the association between LC and different rates of LF decline. A total of 362 subjects met the inclusion criteria (Table 1). Mean annual declines were 37±66 ml, 0.2±2 units and 0.5±1, for FEV1 (ml), FEV1% predicted and FEV1/FVC, respectively. Thirteen cancer diagnoses were made. The Cox analysis showed significant hazard ratios (HR) at higher rates of decline (Table 2). Significant HR were observed for declines >80 ml/year, >2 units of FEV1% predicted and >1 unit of FEV1/FVC ($p<0.001$, 0.002 and <0.001, respectively). Accelerated LF decline appears to be an important risk factor for LC and could be useful when selecting high risk subjects suitable for LC screening.