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Title: Increased levels of circulating interleukin 6, interleukin 8, C-reactive protein, and risk of lung cancer

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Body: Introduction: Previous studies that were based primarily on small numbers of patients suggested that certain circulating proinflammatory cytokines may be associated with lung cancer; however, large independent studies are lacking. Methods: Associations between serum interleukin 6 (IL-6) and interleukin 8 (IL-8) levels and lung cancer were analyzed among 123 case patients. Associations between biomarkers and lung cancer were estimated using logistic regression models adjusted for smoking, stage, histology, age, and sex. The 10-year standardized absolute risks of lung cancer were estimated using a weighted Cox regression model. Results: Serum IL-6 and IL-8 levels in the highest quartile were associated with lung cancer (IL-6, odds ratio [OR] = 2.89, 95% confidence interval [CI] = 1.28 to 6.23; IL-8, OR = 2.46, 95% CI = 1.02 to 4.12) and with lung cancer risk (IL-6, OR = 1.93, 95% CI = 0.87 to 2.36; IL-8, OR = 1.62, 95% CI = 1.56 to 2.48), compared with the lowest quartile. Increased IL-6 levels were only associated with lung cancer diagnosed within 2 years of blood collection, whereas increased IL-8 levels were associated with lung cancer diagnosed more than 2 years after blood collection (OR = 2.03, 95% CI = 1.05 to 2.73). The 10-year standardized absolute risks of lung cancer were highest among current smokers with high IL-8 and CRP levels (absolute risk = 7.46%, 95% CI = 4.52% to 10.25%). Conclusions: Although increased levels of both serum IL-6 and IL-8 are associated with lung cancer, only IL-8 levels are associated with lung cancer risk several years before diagnosis.