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Title: Correlation between EGFR mutations and emphysematous changes in heavy smokers with lung cancer

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Body: Background: Demographic and clinical analyses have shown that smoking is predictive of the frequency on epidermal growth factor receptor (EGFR) mutations. We examines whether there was a clinical difference between heavy smokers with adenocarcinomas with wild-type and mutated EGFR status. Methods: EGFR mutations status was determined. The records of 179 patients with lung adenocarcinoma were retrospectively reviewed. All patients were heavy smokeres, >10 pack years, the male/female ratio was 162/17, and the average age was 70 years, EGFR mutation status was wild-type in 133 individuals (74%) and mutated in 46 (36%). Two expert chest radiologists classified the patients into 2 groups on the basis of computed tomography morphological findings: the non-emphysema and emphysema groups. We compared EGFR status in these groups with each clinical factor. Results: The cumulative smoking dose was higher (p=0.0003), and the forced expiratory volume/forced vital capacity ratio (FEV1/FVC) was lower (p=0.021) in the wild-type EGFR group than in the mutated EGFR group. Interestingly, the rate of emphysema was lower in the mutated EGFR group (p=0.0008), and the presence of emphysematous changes was an independent risk factor for reduced frequency of EGFR mutations in multivariate analysis (odds ration 3.47, p=0.005). Conclusion: Tumores from patients with no or low emphysematous changes in the lungs had a higher rate of EGFR mutations than those with severe emphysematous changes, although the pathological diagnosis in both cases was of adenocarcinoma. These data suggest that oncogene or driver mutations causing lung cancer in smokers could be different between the emphysema and non-emphysema groups.