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The Frequency of Gene Mutations and Related Factors in Lung Adenocarcinomas: A Multicentric Prospective Study in Turkey

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Objectives: Mutation analyzes are becoming more important in lung cancer to determine the targeted therapies. The frequency of Epidermal growth factor receptor (EGFR), Anaplastic lymphoma kinase (ALK) and c-ros oncogen 1 receptor tyrosine kinase (ROS1) mutation analyzes were associated with age, sex and smoking history. Enough information about EGFR, ALK and ROS1 gene mutations and related factors has not been formed yet in Turkey. The aim of this study was to investigate the frequency of mutations in lung adenocarcinoma (LA) and the relationship between asbestos exposure (AE) and the frequency of mutations in rural areas.

Methods: The analysis results of the demographic characteristics, smoking and AE history, radiological findings associated with AE and gene mutations of 1,904 patients diagnosed as LA in 12 hospitals from different centers in Turkey were recorded in a shared database, prospectively. Multiple logistic regression analysis was performed to determine the effect of AE on mutations by the presence of mutation as a dependent variable, as an independent variable age, gender, smoking and AE history.

Results: The mean age (SD) of the patients included in the study was 61.5 (\pm 10.0) years and the ratio of male to female was 3.6/1. The frequencies of EGFR, ALK and ROS1 mutations were 14.5%, 3.7% and 0.9% respectively. The frequencies of EGFR exons (exon 18, exon 19, exon 20, exon 21) were 1.2%, 8.7%, 1.0% and 4.3%, respectively. While EGFR mutation positivity was higher in women, at extreme ages (\geq 70 years and $<$ 50 years), in non-smokers, having history of AE and radiological findings associated with AE ($p<0.001$), ALK rearrangement was detected higher in female patients, with younger age ($<$ 50 years), non-smokers and having history of AE ($p<0.001$). EGFR and ROS1 mutations did not correlate with AE regardless of age, sex and smoking history in logistic regression model used to analyze the risk of mutation positivity (OR (95% GA) 1.26 (0.92-1.73) 0.153, OR (95% GA) 0.80 (0.16-3.95) 0.785). However, AE was associated with ALK translocation regardless of age, gender and smoking history (OR (95% GA) 1.95 (1.11-3.43) 0.020).

Conclusion: While EGFR mutation was found to be associated with sex, age and smoking history as shown previously, ALK translocation was associated with age, smoking and AE history.

Keywords: Lung adenocarcinoma, genetic mutation, asbestos exposure