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Title: Never-smoking history as a poor prognostic factor in surgically proven idiopathic pulmonary fibrosis

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Body: Objectives: Smoking is known as a risk factor of idiopathic pulmonary fibrosis (IPF), but the effect of smoking on survival has been reported variable. The objective of this study was to clarify the effect of smoking status on prognosis of IPF. Methods: We retrospectively analyzed 92 consecutive IPF patients (never smoker 28, ever smoker 64) who underwent surgical lung biopsy from 2001 to 2009, and evaluated pulmonary function and survival time from their first visit. Results: Twenty of 28 never smokers (71.4%) and five of 64 ever smokers (7.8%) were female ($p < 0.01$). Twelve of 28 never smokers (42.9%) had familial history of IPF, whereas only seven of 64 (10.9%) had that history. Age at disease onset, positivity of antinuclear antibody, serum level of KL-6 and SP-D, PaO2, %FVC, %DLco, composite physiologic index, and the incidence of acute exacerbation was not different in two groups. Five-year survival rate was lower in never-smoker group (19.4% vs. 57.7%, $p < 0.01$). In univariate analysis in all the 92 patients, never-smoking history, no emphysema in HRCT, familial history of IPF, lower pulmonary function, high level of KL-6, and neutrophilia in bronchoalveolar lavage fluid were poorer prognostic factors. In multivariate analysis, never-smoking history, no emphysema, lower %FVC, and lower DLco were independent poorer prognostic factors. Conclusions: Never smokers with IPF were female predominant with high prevalence of familial history of the disease, and showed poorer prognosis. IPF in never smokers may have different pathogenic factors form that in ever smokers.