Comparisons of Prognosis between Surgically and Clinically Diagnosed Idiopathic Pulmonary Fibrosis Using Gap Model

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Editorial

Although a multidisciplinary approach has become an important criterion for an idiopathic pulmonary fibrosis (IPF) diagnosis, lung biopsies remain crucial. However, the prognosis of patients with surgically diagnosed IPF (sIPF) is uncertain. We aimed to investigate the prognosis of patients with clinically diagnosed IPF (cIPF) and sIPF. In this retrospective observational study, the Korean Interstitial Lung Disease Study Group conducted a national survey to evaluate the clinical, physiological, radiological, and survival characteristics of patients with IPF from January 1, 2003 to December 31, 2007. Patients were recruited from 54 universities and teaching hospitals across the Republic of Korea. IPF diagnoses were established according to the 2002 American Thoracic Society (ATS)/European Respiratory Society criteria (ERS) guideline. A total of 1685 patients with IPF (1027 cIPF and 658 sIPF) were enrolled. Patients with sIPF were significantly younger, predominantly female, and nonsmokers (all $P<0.001$). sIPF group had significantly better initial pulmonary function. The proportion of computed tomography-based honeycomb findings of patients with cIPF was higher than in those with sIPF ($P<0.001$). A Kaplan-Meier analysis showed that the sIPF group had a better prognosis ($P=0.001$). A survival analysis showed that age, pulmonary function parameters, pulmonary oxygen tension, honeycombing change, and combined lung cancer had a significant influence on patient prognosis. However, there was no significant difference in prognosis between the cIPF and sIPF groups after adjusting for GAP (gender, age, physiology) stage. The patients with sIPF had better clinical features than those with cIPF. However, after adjusting for GAP stage, the sIPF group showed similar prognoses as the cIPF group. This study showed that after adjusting for GAP stage, the prognosis of patients with IPF is the same regardless of the diagnostic method used. Idiopathic pulmonary fibrosis (IPF) is the most common form of idiopathic interstitial pneumonias. IPF is defined as a specific form of progressive and chronic fibrosing interstitial pneumonia without a definite cause. It occurs primarily in older patients, especially in the sixth and seventh decades, and is limited to the lungs. It is also associated with increasing respiratory symptoms and irreversible respiratory failure. Although IPF could be diagnosed clinically in the absence of a surgical lung biopsy, it was recognised as a distinct clinical entity that was associated with the histologic pattern of usual interstitial pneumonia (UIP). In the last few years, the paradigm of diagnosis of IPF has gradually changed from a situation in which biopsy was the criterion standard to a complex situation in which the multidisciplinary approach was necessary. Such approach encompasses clinical, radiological, and pathologic data. However, surgical biopsy is still needed for IPF diagnoses because there are cases that cannot be diagnosed without the histologic pattern. It is well known that the median survival of patients with IPF is <3 years. To provide precise prognostic information and timely treatment to these patients, many predictive models have been investigated. Previous studies have shown that older age at diagnosis, male sex, decreased pulmonary function, and impaired exercise capacity predict a worse outcome in patients with IPF.

However, the prognosis of patients with IPF with a nontypical computed tomography pattern, who were eventually diagnosed by surgical lung biopsy examination, was largely unknown. In 2012, Ley et al reported a simple-to-use GAP (gender, age, physiology) model for predicting IPF mortality, which is a scoring and staging system like the one for lung cancer. This novel model consists of 4 clinical variables: gender (G), age (A), and 2 pulmonary physiology parameters (P, FVC, and DLCO). Each variable was assigned 1 to 3 points and then added for staging; stage I (0–3 points), stage II (4–5 points), and stage III (6–8 points). The purpose of this study is to evaluate whether clinically diagnosed IPF (cIPF) and surgically diagnosed IPF (sIPF) have different characteristics. Furthermore, we aimed to evaluate the role and effect of surgical biopsy in predicting prognosis in conjunction with the GAP staging system. According to the international consensus classification, a surgical lung biopsy is required for the definitive diagnosis of IPF. However, a diagnosis of IPF can be considered in the absence of a surgical lung biopsy specimen if certain major and minor criteria are met. In such cases, all 4 major criteria and at least 3 of the 4 minor criteria must be satisfied. When a biopsy specimen was not available, all the major criteria except the last (transbronchial lung biopsy specimen or bronchoalveolar [BAL] fluid sample showing no features to support an alternative diagnosis) applied optionally, and at least 3 of the 4 minor criteria had to be fulfilled. For patients with a surgical biopsy specimen showing UIP, only the major criteria were considered relevant. Although a surgical lung biopsy is required for accurate diagnosis, a patient who was too old and had a low lung function was diagnosed clinically at the physician's discretion without undergoing a biopsy. Additionally, a patient who refused to undergo the surgical lung biopsy was diagnosed clinically. The Student t test was used to compare continuous variables, whereas Pearson $\chi 2$ test was used to compare categorical variables. Patients were censored if they were still alive when last contacted (censored at the last status date), or had received a lung transplant (censored at the time of the transplant). Survival time was calculated as the time since diagnosis. The survival was estimated using the Kaplan–Meier method models. The log-rank statistic was used to compare survival among groups. The effect of each variable on the risk of death after controlling for age, sex, and pulmonary function (GAP predictive variables) was modelled using the Cox proportional hazards regression