Is lung cancer resection indicated in patients with idiopathic pulmonary fibrosis?

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Objective: The purpose of this study was to determine the implication of idiopathic pulmonary fibrosis on the surgical treatment for primary lung cancer.

Methods: Between January 1994 and June 2006, 870 patients with primary lung cancer were surgically treated. Fifty-six (6.4%) of 870 patients had complications with idiopathic pulmonary fibrosis, and their data were retrospectively reviewed. There were 50 men and 6 women with an average age of 68 years. The incidence of squamous cell carcinoma was 28 (50.0%). Surgical procedures consisted of 7 wedge resections of the lung, 5 segmentectomies, 43 lobectomies, and 1 bilobectomy.

Results: Surgery-related hospital mortality was higher in patients with idiopathic pulmonary fibrosis than in patients without (7.1% vs 1.9%; $P = .030$). Four (7.1%) of these 56 patients had acute postoperative exacerbation of pulmonary fibrosis and died because of this complication. No factors such as pulmonary function, serologic data, operative data, and histopathologic data were considered predictive risk factors for the acute exacerbation. The postoperative 5-year survival for pathologic stage I lung cancer was 61.6% for patients with idiopathic pulmonary fibrosis and 83.0% for patients without ($P = .019$). The causes of late death were the recurrence of cancer or respiratory failure owing to idiopathic pulmonary fibrosis.

Conclusions: Although idiopathic pulmonary fibrosis causes high mortality after pulmonary resection for lung cancer and poor long-term survival, long-term survival is possible in patients with these two fatal diseases. Therefore, in selected patients, idiopathic pulmonary fibrosis may not be a contraindication to pulmonary resection for stage I lung cancer.

Supplemental material is available online.

Idiopathic pulmonary fibrosis (IPF) is known to be concomitant with primary lung cancer (PLC) and sometimes causes catastrophic results after pulmonary resection. Acute postoperative exacerbation of IPF is one of the fatal complications after lung resection. Mortality after the occurrence of this complication is very high (80%–100%).[1,2] Although some efforts have been made to establish the cause of acute postoperative exacerbation in order to prevent it,[3,4] the influence of the existence of IPF as a comorbidity on postoperative mortality, morbidity, and long-term survival after pulmonary resection for PLC has not been well studied. Hence, this study examines the implication of IPF on surgical results of pulmonary resection for PLC.

PATIENTS AND METHODS

Patients

Between January 1994 and June 2006, 870 patients with PLC were surgically treated in our institute. Sixty-eight of 870 patients had complications with diffuse parenchymal lung disease. Ten patients with diffuse parenchymal lung disease and concomitant collagen diseases (rheumatoid arthritis in 3, Sjögren syndrome in 3, mixed collagen tissue diseases in 2, and progressive systemic sclerosis in 2) and 2 patients with nonspecific interstitial pneumonia were excluded from this study because these types of diffuse parenchymal lung diseases have different outcomes from IPF. Therefore, the inclusion criteria of this study were surgically treated patients with PLC concomitant with IPF (n = 56) and patients with PLC without diffuse parenchymal lung disease (n = 802). The medical records of 858 consecutive patients with PLC were retrospectively reviewed. Data acquisition and analysis were approved by our institutional review board. The records contained preoperative patient characteristics, disease status, operative procedures, pathologic diagnosis, and follow-up data. Idiopathic interstitial pneumonia was preoperatively diagnosed in all patients with IPF. This included 45 confident chest computed tomography diagnoses of IPF with consistent clinical features: fine crackles (resembling the sound of hook-and-loop fasteners) on chest auscultation and abnormalities, such as peripheral reticular opacity or honeycombing, on preoperative chest computed tomography. Furthermore, after surgery, idiopathic pulmonary fibrosis/usual interstitial pneumonia (IPF/UIP) was definitively diagnosed in all patients with IPF by histopathologic assessment of the resected lung (architectural destruction, fibrosis often with honeycombing,

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Abbreviations and Acronyms

ARDS = acute respiratory distress syndrome
$FEV_{1.0}$ = forced expiratory volume in one second
IPF = idiopathic pulmonary fibrosis
OLV = one-lung ventilation
PF = pulmonary fibrosis
PLC = primary lung cancer
UIP = usual interstitial pneumonia
VC = vital capacity

scattered fibroblastic foci, patchy distribution, and involvement of the periphery of the acinus or lobule). The incidence of male sex, squamous cell carcinoma, wedge resection, and lower lobe tumor was higher in patients with IPF than in patients without. Furthermore, the percentage of diffusion capacity of the lung for carbon monoxide was higher in patients with IPF than in patients without. Patients with IPF underwent 7 wedge resections of the lung, 5 segmentectomies, 43 lobectomies, and 1 bilobectomy as surgical treatment for lung cancer. Pathologic stages were I in 28, II in 5, III in 14, and IV in 3 patients (Table 1).

Inclusion Criteria for Pulmonary Resection

Lobectomy was selected when the postoperative predictive forced expiratory volume in 1 second ($FEV_{1.0}$) was 1.2 L or greater. However, segmentectomy was selected when lobectomy could lead to a postoperative predictive $FEV_{1.0}$ of less than 1.2 L. Furthermore, segmentectomy was aggressively selected also when the greatest diameter for resection was 20 mm or less, even when the postoperative predictive $FEV_{1.0}$ was 1.2 L or more.

Definition of Each Disorder

In this study, we used the criteria of acute exacerbation of IPF as described previously by Yoshimura and associates,[5] namely, (1) intensified dyspnea, (2) increase in the interstitial shadow on chest radiograph, (3) increase in fine crackles on auscultation, (4) elevation of serum lactate dehydrogenase, and (5) decrease in arterial oxygen tension of more than 10 mm Hg under similar condition. Furthermore, we added the elevation of serum surfactant protein-D or sialylated carbohydrate antigen KL-6 to criterion 4. Diagnosis of acute exacerbation was confirmed if patients included all of 1, 2, and 3 plus at least either of 4 or 5 of the criteria.

Pneumonia was diagnosed by the presence of new and/or progressive pulmonary infiltrates on chest radiography plus two or more of the following criteria: fever (38°C), leukocytosis (12×10^9/L), purulent sputum, or isolation of pathogen in respiratory secretions.

Regarding acute respiratory distress syndrome (ARDS), we used the American–European Consensus Conference Definition for acute respiratory distress syndrome.[6]

Perioperative and Postoperative Management

Chest radiographs were routinely taken on the first and third postoperative days and on the day after chest tube removal. Additional chest radiographs were taken, depending on the patients' clinical state, as opposed to including all symptoms and signs. If infiltrates were revealed on chest radiograph suggestive of ARDS or acute pulmonary embolism, high-resolution computed tomographic scan was performed for the differential diagnosis of these lung diseases.

Oxygen inhalation was administered at minimal level to maintain oxygen saturation at 92% or greater if patients did not have dyspnea or if they underwent any change in cardiorespiratory conditions owing to mild hypoxia.

The steroid pulse therapy with methylpredonisolone (1 or 2 g per day for 3 or 4 days as one course) was used as the first line treatment for acute postoperative exacerbation of IPF. In this series, neither immunosuppressive agent nor nitric oxide inhalation therapy was used.

Statistical Analysis

Statistical evaluation was performed by standard computer software (SPSS 9.0; SPSS, Inc, Chicago, Ill). All data are presented as mean ± standard deviation. Differences in continuous and categorical values were tested by unpaired the Student t test and χ^2 square test (or Fisher's exact test), respectively. To account for the risk factor of morbidity or mortality after pulmonary resection for lung cancer, we used the logistic regression analysis. Furthermore, to account for the risk factor of late death after operation for patients with PLC in combination with IPF, we used the Cox proportional hazard model. Clinicopathologic related factors were quantified by univariate analysis and then all factors with $P < .10$ in the univariate analysis were included in the multivariate Cox hazard model together.

RESULTS

Acute postoperative exacerbation of IPF, ARDS, and the need for prolonged mechanical ventilatory assist (> 2 days) for respiratory failure were more common in the patients with IPF than in those without (Table 2). IPF was a risk factor for causing these postoperative respiratory complications.

Four (7.1%) of these 56 patients had acute postoperative exacerbation of IPF, which occurred on about postoperative day 5 (range day 3–7). Two patients recovered from the first exacerbation with respiratory failure necessitating mechanical ventilation, but the subsequent exacerbations developed on the 24th and 27th postoperative days, accompanied by more severe respiratory dysfunction. All patients died of the exacerbation within 42 days after the operation. Bacterial pneumonia developed in 3 of the 4 patients (Table E1).

The percentage of diffusion capacity of the lung for carbon monoxide showed no differences between patients with the exacerbation and patients without it. No patient who underwent wedge resection of the lung had an exacerbation after the operation. There were no differences in the other values of pulmonary function, serologic data, operative factors, and histopathologic factors between the two groups (Table 3).

Hospital death after pulmonary resection for lung cancer was more common in patients with IPF than patients without (7.1% vs 1.9%), and the odds ratio was 4.036 ($P = .016$) (Table 4).

Postoperative Pulmonary Function After Lower Lobectomy

Postoperative pulmonary function in 4 to 6 months after a lower lobectomy was compared between patients without IPF (n = 25) and patients with IPF (n = 36). Although no substantial differences were observed in postoperative vital capacity (VC) and $FEV_{1.0}$ between the two groups, percentages of postoperative VC to preoperative VC (78.3% in patients without IPF vs 67.0% in patients with IPF; $P = .038$) and postoperative $FEV_{1.0}$ to preoperative $FEV_{1.0}$ (81.3% vs 67.7%; $P = .006$) was significantly lower in patients with IPF than in patients without IPF (Table E2).