#### **News Release**

#### **Title**

Identification of a smoking-related risk factor on perioperative complications and survival among patients with resected lung cancer

~The clinical study to promote improvement of therapeutic outcomes for lung cancer by clarifying clinical impact of combined pulmonary fibrosis and emphysema~

### **Key Points**

- Patients with combined pulmonary fibrosis and emphysema (CPFE) comprised 8.3% of patients with resected lung cancer.
- Overall, the 30-day mortality in patients with CPFE group was 5.3%, as compared with 0.7% in the study population.
- Although the overall survival is likely affected by advanced stage cancer, CPFE remained a critical risk factor for overall survival independent of age and advanced stage lung cancer.

# **Summary**

Dr. Naozumi Hashimoto in Nagoya University Hospital (Director: Naoki Ishiguro, M.D., Ph.D.) and Prof. Yoshinori Hasegawa (Department of Respiratory Medicine) and Prof. Kohei Yokoi (Department of Thoracic Surgery) in Nagoya University Graduate School of Medicine (Dean: Masahide Takahashi, M.D., Ph.D.) demonstrated that coexistence of combined pulmonary fibrosis and emphysema (CPFE) was an independent factor associated with worse overall survival for patients with resected lung cancer: the adjusted hazard ratio of overall survival for the CPFE group versus the normal group was 2.990 (95% confidential interval, 1.801-4.962).

As older patients with a history of smoking have increased, there have been more increasing opportunities to treat lung cancer patients involving coexistence of chronic lung diseases such as chronic obstructive pulmonary disease (COPD)/emphysema and pulmonary fibrosis. In Japan, the total number of surgery for lung cancer in 2012 has reached 35,667. Nevertheless, clinical impact of CPFE on perioperative and survival outcomes among patients with resected lung cancer remains elusive. In the study, data were reviewed from 685 patients with resected lung cancer between 2006 and 2011. The CPFE group comprised 8.3% of the study population. The incidence of prolonged postoperative stays, 30-day mortality, and postoperative complications including acute

lung injury, was significantly higher in the CPFE group. Although the overall survival is likely affected by advanced stage cancer, CPFE remained a critical risk factor for overall survival independent of age and advanced stage lung cancer. Recent studies show that multidisciplinary team management of lung cancer might improve survival outcomes. Now, new therapeutic options for stable chronic lung diseases such as COPD/emphysema and pulmonary fibrosis are available in the world. The study provides a basis for further investigation in improving postoperative outcomes in the population through multidisciplinary team involving pulmonary specialists.

# **Research Background**

Lung cancer remains a leading cause of cancer-related death worldwide. Smoking is closely associated not only with lung cancers but also with chronic lung diseases including chronic obstructive pulmonary disease (COPD) and pulmonary fibrosis. Recent studies suggest that the presence of emphysema or fibrosis might clinically affect postoperative and survival outcomes for lung cancer patients undergoing thoracic surgery. Combined pulmonary fibrosis and emphysema (CPFE) might be considered as an entity that is distinct from either emphysema or fibrosis. Nevertheless, there is only limited information on the clinical impact of both emphysema and fibrosis-as determined by thin-section computed tomography (TSCT) on postoperative and survival outcomes for patients with resected lung cancer.

### **Research Results**

The study population comprised 685 patients. Patients with CPFE comprised 8.3% of patients with resected lung cancer (Figure 1). Overall, the 30-day mortality in patients with CPFE group was 5.3%, as compared with 0.7% in the study population. The incidence numbers of perioperative complications including acute lung injury were significantly higher in the CPFE group. Overall, the 30-day mortality in patients with CPFE group was 5.3%, as compared with 0.7% in the study population. The CPFE group also showed a significantly higher incidence of cancer recurrence for pathological stage I disease as compared with the other groups. Death due to lung cancer or other causes was also significantly higher in the CPFE group than the other groups. When the relative hazard ratio (HR) of overall survival (OS) for the emphysema and fibrosis groups versus the normal group was adjusted by age, gender, smoking history, pathological stage, and histology, the emphysema and fibrosis groups were not independent risk factors for OS. By contrast, CPFE was shown to have a significantly high HR of OS (2.990; 95% confidential intervals [CI], 1.801-4.962) (Figure 2).

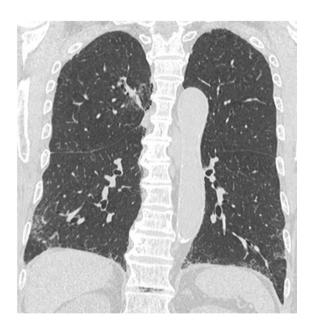


Figure 1. TSCT-determined CPFE (coronal plane)

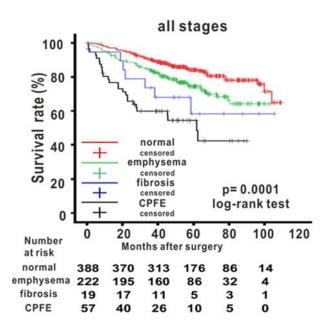


Figure 2. Kaplan-Meier estimates of overall survival in 686 cases including one case with pStage IV categorized by TSCT findings.

red lines: normal, green lines: emphysema, blue lines: fibrosis, black lines: CPFE

# **Research Summary and Future Perspective**

Although the overall survival is likely affected by advanced stage cancer, CPFE remained an independent factor for OS with a high hazard ratio of 2.990. Recent studies show that multidisciplinary team management of lung cancer might improve survival outcomes. Furthermore, new therapeutic options for stable chronic lung diseases such as COPD/emphysema and pulmonary fibrosis have been utilized in the world. The study provides a basis for further investigation in improving postoperative outcomes in the population through multidisciplinary team involving pulmonary specialists.

#### **Publication**

Hashimoto N, Iwano S, Kawaguchi K, Fukui T, Fukumoto K, Nakamura S, Mori S, Sakamoto K, Wakai K, Yokoi K, Hasegawa Y. Impact of thin-section computed tomography-determined combined pulmonary fibrosis and emphysema on outcomes among patients with resected lung cancer. *Ann Thorac Surg*, May.5,2016.

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