Feasibility of Pulmonary Resection for Lung Cancer in Patients With Coronary Artery Disease or Atrial Fibrillation

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Background. **The aim of this study was to clarify the outcomes of lung resection for lung cancer in patients with cardiac disease, especially coronary artery disease, in a large-scale multi-institutional cohort.**

Methods. **We retrospectively analyzed the data on 1,254 patients who underwent major lung resection for lung cancer and had been diagnosed with coronary stenosis, atrial fibrillation, or both, in 58 institutions in Japan between January 2009 and December 2011. The primary outcome was 90-day postoperative mortality or in-hospital death.**

Results. **Among the 1,254 patients, 902 (71.9%) and 452 patients (36.0%) were preoperatively diagnosed with coronary stenosis and atrial fibrillation, respectively, and 951 patients (75.8%) received antiplatelet therapy. Among the patients with coronary stents (n = 532; 42.4%), 204 (16.3%) received drug-eluting stents. The 90-mortality or in-hospital death rate was 2.6% (n = 32), including stent thrombosis (n = 1), thromboembolic events without stent thrombosis (n = 2), and bleeding events (n = 2). In the multivariate analyses, blood transfusion, history of cerebrovascular disease, amount of bleeding, and history of congestive heart failure were associated with a higher independent risk of 90-day mortality or in-hospital death (odds ratio, 9.400, 3.574, 2.827, and 2.945, respectively). Preoperative discontinuation of antiplatelet therapy was not associated with an independent risk of 90-day mortality or in-hospital death on univariate analysis.**

Conclusions. **Major lung resection for lung cancer in patients with coronary artery disease is feasible. Our study suggests that discontinuation of antiplatelet therapy may not increase postoperative complications in patients with coronary artery disease.**

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Concomitant with the global increase in life expectancy, the population of older patients diagnosed with lung cancer has increased. Aging is associated with a significant prevalence of comorbidities, including coronary artery disease (CAD) [1]. In fact, a report derived from The Society of Thoracic Surgeons national database showed that the incidence of CAD as a comorbidity in patients who underwent major lung resection was greater than 20% [2]. A single-institution study, conducted in Japan, reported that the incidence of CAD in patients who underwent lung resection for lung cancer was 6.9%, and the corresponding value was 10.0% in patients older than 70 years of age [3]. Data from the annual report of The Japanese Association for Thoracic Surgery in 2008 showed that cardiovascular disease is the fifth leading cause of 30-day death [4].

Patients with CAD are frequently treated with coronary artery stents with a bare metal stent (BMS), a drug-eluting stent (DES), or both, as well as continuous antiplatelet therapy (APT) to minimize the risk of stent thrombosis (ST) [5–7]. Patients with atrial fibrillation (AF) often require anticoagulant therapy to minimize the risk of a thromboembolic event [8]. One of the most important factors for patients who undergo major thoracic operations with antithrombotic therapy is perioperative management of antithrombotic agents. Many reports have shown that premature interruption of APT, especially in the period of noncardiac surgical intervention, significantly increases ST [6, 9–14]. However, continuation of

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*A list of study investigators and participating institutions of The Japanese Association for Chest Surgery appears at the end of this article.

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Abbreviations and Acronyms

AF = atrial fibrillation
APT = antiplatelet therapy
BMS = bare metal stent
CABG = coronary artery bypass grafting
CAD = coronary artery disease
CI = confidence interval
CVD = cerebrovascular disease
DES = drug-eluting stent
OR = odds ratio
PCI = percutaneous coronary intervention
ST = stent thrombosis

APT at the time of operation may increase the risk of bleeding complications [15]. Recommendations from the Science Advisory and Coordinating Committee of the American Heart Association [16], and several other reports [17, 18], suggested APT management during noncardiac operations in patients with coronary stents. However, in general thoracic surgery, an appropriate management strategy has not been established, and postoperative mortality and morbidity rates for patients with coronary stents are unclear because there are no large-scale clinical data.

The aim of this study was to clarify the outcomes of pulmonary resection for lung cancer in patients with cardiac disease, especially CAD, in a large-scale multi-institutional cohort.

Patients and Methods

Study Design and Patients

This retrospective multicenter study was conducted by the advisory board of The Japanese Association for Chest Surgery in accordance with the ethical guidelines for epidemiologic research imposed by the Japanese Ministry of Health, Labor, and Welfare. The study protocol was approved by the institutional review boards of all participating hospitals, including that of the Ethics Committee, Juntendo University School of Medicine Tokyo, Japan (Approval Number: 12-135).

The clinical data of patients who underwent lung resection for non-small lung cancer who had a diagnosis of coronary stenosis, AF, or both, were collected from the medical records of 58 institutions in Japan between January 2009 and December 2011. Patients who underwent lung resection for diagnosis or biopsy were excluded.

The primary outcome was 90-day postoperative death or in-hospital death. The secondary outcomes were 30-day postoperative death or in-hospital death and postoperative morbidity. Postoperative death was evaluated according to the National Cancer Institute Common Terminology Criteria for Adverse Events (version 4.0).

Statistical Analysis

Univariate logistic regression analysis was performed between the outcomes and the following characteristics: use of APT, preoperative heparinization, history of coronary stents, comorbidities (coronary artery stenosis, congestive heart failure, cerebrovascular disease [CVD]), surgical procedure, operation time, amount of bleeding, blood transfusion, and intrathoracic pleural adhesion. Multivariate logistic regression analysis was used to identify independent risk factors for postoperative death and morbidity. All reported p values were two sided; p values less than 0.05 were considered to indicate statistical significance, and in multivariate logistic regression analysis with stepwise variable selection, p values less than 0.1 were used. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Inc, Cary, NC).

Results

Patients' Characteristics and Perioperative Management of Antiplatelet Therapy

Between January 2009 and December 2011, 1,254 patients were eligible for this cohort study. Patient-related characteristics are shown in Table 1. A total of 902 (71.9%) and 452 (36.0%) patients were preoperatively diagnosed with coronary artery stenosis and AF, respectively. In all, 532 patients (42.4%) had coronary stents, and 204 patients (16.3%) in this group were treated with DES (DES only, 159 [12.7%]; DES and BMS, 45 [3.6%]).

Perioperative management of antithrombotic agents is summarized in Table 2. Among 951 patients who used APT, 886 patients (93.2%) stopped taking antiplatelet agents preoperatively. Sixty-five patients (6.8%) received APT at the time of operation, and 58 patients (6.1%) took aspirin alone at the time of operation. In all, preoperative heparinization was performed on 564 patients (45.0%).

Postoperative Complications

Table 3 details the postoperative complications in all patients. All grade 4 or 5 complications occurred in 50 patients (4.0%), and in 7 of these patients, two grade 4 or 5 complications occurred. ST occurred in 1 patient (0.1%), who was a 78-year-old man with a history of coronary artery bypass grafting (CABG) and a coronary stent (BMS) for more than 1 year before undergoing lobectomy. He discontinued APT preoperatively and received heparinization as bridging therapy. Grade 4 or 5 bleeding events, thromboembolic events without ST, and other complications occurred in 7 (0.6%), 6 (0.5%), and 43 (3.4%) patients, respectively. Univariate analyses did not identify any characteristics, including the discontinuation of APT, preoperative heparinization, and a history of coronary stents ($p = 0.829$, 0.081, and 0.227, respectively), as risk factors for grade 4 or 5 complications and also did not identify any characteristics, including the discontinuation of APT, and preoperative heparinization ($p = 0.828$, and 0.180, respectively), as risk factors for grade 4 or 5 bleeding events (data not shown).

Study Outcomes in All Patients and the Subgroups

The primary outcomes (90-day death or in-hospital death) occurred in 32 patients (2.6%) (Table 4). Univariate