Incidence of and Risk Factors for Cardiovascular Complications After Thoracic Surgery for Noncancerous Lesions

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<u>Objective</u>: The purpose of this study was to determine the incidence of and risk factors for cardiovascular complications after thoracic surgery for noncancerous lesions.

Design: Retrospective cohort study.

Setting: A tertiary medical center.

<u>Participants</u>: All consecutive patients undergoing either thoracotomy or thoracoscopy for noncancerous lesions between 2005 and 2011 were included.

<u>Measurements and Main results</u>: The primary outcomes were the incidence and types of cardiovascular complications such as cardiac arrhythmias, cardiac arrest, heart failure, and myocardial ischemia during hospitalization. A total of 719 patients were recruited, 60% of whom had infections. The incidence of cardiovascular complications after thoracic surgery was 6.7% (48 of 719), of which cardiac arrhythmia was the most common (25 of 48, 52%). The multivariate risk regression analysis showed that age >55 years (risk ratio [RR] = 4.0; 95% confidence interval [CI] =

▲ARDIOVASCULAR COMPLICATIONS after thoracic surgery for cancerous and noncancerous lesions have been reported to occur in 7% to 31% of thoracic surgical patients.¹⁻⁶ Consequently, these complications can cause mortality and morbidity that lead to increased medical costs and prolonged hospital stays.^{7,8} Shapiro et al⁹ demonstrated that thoracic surgery for patients with noncancerous lesions caused about 2.8 times higher morbidity and higher mortality (7.1% versus 5.3%) than those with cancerous lesions. Thoracic surgery for noncancerous lesions is common in developing countries in which the most likely etiology is infection. A wide range of procedures is involved from non-parenchymal to extensive lung parenchymal resection. Previous studies reported the incidence and risk factors of overall complications, but the risk factors for cardiovascular complications in patients with noncancerous lesions have not been explored extensively. The purpose of this study was to determine the incidence of and risk 2.1-7.5; p<0.01), diabetes mellitus (RR = 3.0; 95% Cl = 1.7-5.3; p<0.01), coronary artery disease (RR = 4.8; 95% Cl = 2.3-10.2; p<0.01), duration of surgery >180 minutes (RR = 2.6; 95% Cl = 1.3-5.1; p<0.01), intraoperative hypotension (RR = 2.6; 95% Cl = 1.6-4.3; p<0.01), and positive fluid balance >2,000 mL (RR = 2.5; 95% Cl = 1.4-4.5; p<0.01) were independent risk factors for cardiovascular complications.

<u>Conclusions</u>: Knowledge of risk factors could help surgical teams to identify high risk patients and adjust modifiable risk factors including optimization of medical conditions, correction of intraoperative hypotension, and appropriate blood and fluid administration in order to reduce perioperative morbidity and mortality.

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factors for cardiovascular complications after thoracic surgery for only noncancerous lesions.

METHODS

Data of consecutive patients undergoing thoracic surgery were collected prospectively between 2005 and 2011 for a retrospective review in a single university hospital. Approval was given by the institutional review board. The inclusion criteria included patients aged ≥ 18 years, American Society of Anesthesiologists (ASA) classification 1-4, who were undergoing either thoracotomy or thoracoscopy for noncancerous lesions. Patients with thoracic injury or thoracic spine surgery were excluded from this study. If thoracic patients underwent more than 1 operation, only the cardiovascular events of the first operation would be included. Anesthesia was induced with intravenous thiopental or propofol and intubation was facilitated by vecuronium or atracurium. For anesthesia maintenance, patients received general anesthesia with sevoflurane or isoflurane in oxygen or air mixture supplemented with fentanyl or morphine. Intravenous opioid infusion or thoracic epidural analgesia was used for postoperative pain control. Noncancerous lesions covered all benign intrathoracic and mediastinal diseases, including empyema, aspergilloma, granulomatous disease, bullous disease, benign lung nodule, and mediastinal or esophageal mass.

Cardiovascular complications included cardiac arrhythmias, cardiac arrest, pulmonary embolism, myocardial ischemia, and heart failure that occurred during hospitalization or within 30 days after surgery. Cardiac arrhythmia was diagnosed as a new onset of arrhythmias, confirmed by a 12-lead electrocardiogram (ECG). Cardiac arrest was an event requiring cardiopulmonary resuscitation. Pulmonary embolism was diagnosed by clinical symptoms and contrast-enhanced chest computed tomography.³ Myocardial ischemia was diagnosed by relevant ECG changes, including a new onset of Q-wave or persistent changes in the ST-segment on a 12-lead electrocardiogram and increased serum creatine kinase MB or tropinin I level. The diagnosis was confirmed by cardiologists.¹⁰ Heart failure was diagnosed by signs or symptoms of pulmonary congestion (shortness of breath), signs of right or left heart failure (cardiomegaly, jugular venous distention, peripheral edema), and abnormal changes of chest radiography.¹⁰ If thoracic

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patients underwent more than one operation, only cardiovascular events of the first operation were counted.

All electronic medical records, anesthesia records, and daily medical progress notes were reviewed by at least 2 independent reviewers. Any disagreement was discussed in order to achieve a consensus. Details were recorded of preanesthesia conditions, anesthetic management, surgical data, intraoperative events, and postoperative outcomes, including perioperative complications. Demographic data included age, gender, ASA classifications, body mass index (BMI), and comorbidity. Surgical data were recorded, including type of surgery (parenchymal versus non-parenchymal resection), surgery approach (thoracotomy versus video-assisted thoracoscopic surgery [VATS]), side of operation, and duration of surgery. Parenchymal resection included wedge resection, segmentectomy, bullectomy, lobectomy and pneumonectomy; while non-parenchymal resection involved rib resection, decortications, excision, or other procedures. Anesthetic details included types of postoperative analgesia and intraoperative hypotension; use of vasopressor drugs, comprising ephedrine, dopamine, epinephrine or norepinephrine; amount of blood loss and fluid administration; and positive fluid balance ([amount of crystalloids + colloids + blood products]-[blood loss + urine output]) during the surgery and within 2 hours of postanesthesia care. Intraoperative hypotension was defined as systolic blood pressure (SBP) <80 mmHg or mean arterial pressure $(MAP) < 60 \text{ mmHg for more than 15 minutes.}^{11,12}$

All relevant data were extracted and transferred to an Excel spreadsheet. Statistical analysis was performed using Stata software (version 11.0, College Station, TX). Demographic data between patients with and without cardiovascular complications were analyzed using an appropriate statistical analysis. Continuous data were presented as mean and standard deviation or median with 25th to 75th percentiles according to data distribution. Categorical data were presented as frequency and percent. Continuous data were analyzed using the unpaired t-test or Wilcoxon rank sum test as appropriate. Categorical variables were calculated using the Chi-square or exact probability test, as appropriate. Risk factors for cardiovascular complications were analyzed using univariate and multivariate risk regression analysis, with a robust estimation, and presented as risk ratio (RR) and 95% confidenc interval (CI).¹³ Any risk factors with p values < 0.2 in the univariate risk regression analyses and other potential confounders associated with cardiovascular complications were selected for inclusion in the multivariate risk regression equation for analysis at a statistically significant level of 0.05. Cut-off points of independent variables, including age, duration of surgery, and positive fluid balance, were determined by the maximum-likelihood estimation method in order to achieve best discrimination between patients with and without cardiovascular complications.¹³ Sample sizes were calculated from the previous database of this study. The estimated sample size was calculated from the relative risks of exposure to all potential variables for cardiovascular complications. The calculated sample size was 680 patients with an accepted α of 5% and 90% power.¹⁴

RESULTS

Seven hundred nineteen patients were included over the study period, and 48 of those experienced 58 events of cardiovascular complications. The incidence of cardiovascular complications after thoracic surgery for patients with non-cancerous lesions was 6.7% (95% CI = 5.1-8.7). Patients developing cardiovascular complications had a significantly higher incidence of intensive care unit admissions (ICU) than those without cardiovascular complications (70% v 14%), and they required a longer hospital stay of 10 days (25th -75th percentiles = 8-20) versus 7 days (25th-75th percentiles = 5-11). Table 1 shows patient characteristics, including operative and

anesthetic details of thoracic surgical patients with or without cardiovascular complications. Patients with cardiovascular complications were older and had a higher ASA classification and more comorbid diseases than those without them. Infective lesions occurred in 60% of the patients. Patients experiencing cardiovascular complications had a higher percentage of thoracotomy and non-parenchymal resection and longer duration of surgery. The incidence of blood loss >1,000 mL and intraoperative hypotension occurred more commonly in patients with cardiovascular complications. There were a greater percentage of patients with cardiovascular complications receiving positive fluid balance >2,000 mL when compared with those without them.

Cardiac arrhythmias were the most common complication (52%) among patients with postoperative cardiovascular complications (Table 2). Atrial fibrillation (AF) was the most common type of cardiac arrhythmia (76%). Other cardiac arrhythmias included premature ventricular contraction (16%) and bradycardia (8%). Most AF occurred on postoperative day 2, with all patients requiring medical therapy, of whom 79% (15 of 19) could be converted to normal sinus rhythm, while arrhythmia in 21% (4 of 19) was still persistent but at an acceptably controlled rate. Cardiac arrests occurred in about 37% of the patients with cardiovascular complications, which were related mostly to cardiovascular complications (4 of 18, 22%) and other multiple etiologies (14 of 18, 78%). No patient experienced pulmonary embolism.

Univariate and multivariate risk regression are shown in Tables 3 and 4, respectively. The independent risk factors of cardiovascular complications from multivariable risk regression, were age >55 years (RR = 4.0; 95% CI = 2.1-7.5; p < 0.01), diabetes mellitus (RR = 3.0; 95% CI = 1.7-5.3; p < 0.01), coronary artery disease (RR = 4.8; 95% CI = 2.3-10.2; p value < 0.01), duration of surgery >180 minutes (RR = 2.6; 95% CI = 1.3-5.1; p < 0.01), intraoperative hypotension (RR = 2.6; 95% CI = 1.6-4.3; p value < 0.01), and positive fluid balance >2,000 mL (RR = 2.5; 95% CI = 1.4-4.5; p value < 0.01).

DISCUSSION

Thoracic surgery for noncancerous lesions can cause both pulmonary and cardiovascular complications. Previous studies reported that incidences of pulmonary complications varied from 15% to 46%.^{5,6,15} However, few studies focused on cardiovascular complications alone. This study showed an incidence rate of cardiovascular complications of 6.7%, which was lower when compared to pulmonary complications, and the clinical impact on ICU admission and hospital stay of patients with cardiovascular complications was significantly greater than that of patients without them. Therefore, the modification of risk factors or implementation of preventive strategies in reducing cardiovascular complications also should be considered as similar to pulmonary complications.

Cardiac arrhythmia was the most common cardiovascular complication in this study. Previous studies reported an incidence rate of 12% to 21% in cardiac arrhythmias after a pneumonectomy in patients with noncancerous lesions.^{5,6,15} The incidence of cardiac arrhythmias in this study was lower

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