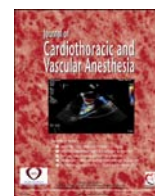




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Original Article

## Chronic Lung Disease and Mortality after Cardiac Surgery: A Prospective Cohort Study

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**Objective:** To investigate the 1-year survival in cardiac surgical patients with lung disease, including previously undiagnosed cases.

**Design:** Prospective cohort study.

**Setting:** Tertiary hospital.

**Participants:** Patients scheduled for elective coronary artery bypass graft (CABG) surgery.

**Interventions:** None.

**Measurements and Main Results:** Pulmonary function tests (PFTs) were performed in 454 patients before surgery. Abnormal respiratory patterns were defined as follows: obstructive (forced expiratory volume in 1 second/forced vital capacity < 0.70), restrictive (forced expiratory volume in 1 second/forced vital capacity ≥ 0.70 and forced vital capacity < 80% of predicted), and mixed. Overall 1-year mortality was 3.3%. Among 31 patients with documented chronic obstructive pulmonary disease (COPD), mortality was 9.6%, hazard ratio (HR) 1.28, 95% confidence interval (CI) 1.02-12.80,  $p = 0.04$ . Of 423 patients without history of COPD, 57 obstructive, 46 restrictive, and 4 mixed abnormal patterns were identified. Of a total of 72 with obstructive lung disease confirmed by PFT (ie, 15 of COPD patients and 57 newly identified cases), 6.9% died, HR 2.75, 95% CI 0.98-8.07,  $p = 0.06$ . When combined with cases of COPD where a respiratory abnormality was confirmed (26 patients), newly diagnosed obstructive lung disease (57 patients) was significantly associated with 1-year mortality, HR 4.13, 95% CI 1.50-11.42,  $p = 0.006$ . The adjustment for EuroSCORE II did not change the results.

**Conclusions:** Combination of confirmed preexisting lung disease and newly diagnosed cases provides a clear link to mid-term mortality.

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**Key Words:** pulmonary function tests; obstructive respiratory pattern; obstructive lung disease; chronic obstructive pulmonary disease; cardiac surgery; mortality

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IN THE CARDIAC SURGERY setting, coexisting pulmonary pathology is associated with increased risk of both short- and long-term morbidity and mortality.<sup>1,2</sup> Moreover, evidence suggests that more patients with airflow limitation die from cardiovascular causes than from underlying pulmonary disease.<sup>3</sup> With pulmonary function tests (PFTs), such as spirometry or body plethysmography, pulmonary disease may be

expressed in terms of obstructive, restrictive or mixed respiratory patterns, improving risk stratification in cardiac surgery.<sup>4</sup> Chronic obstructive pulmonary disease (COPD), characterized by airflow limitation that is not fully reversible,<sup>5</sup> is present in up to 21% of cardiac surgical patients, with serious implications for postoperative outcome.<sup>2</sup> Pulmonary function tests were demonstrated to help reclassify COPD in 31% to 39% of patients,<sup>4,6</sup> with considerable underestimation of the severity of the disease in those misclassified.<sup>4</sup> In spite of the seemingly abundant evidence on the impact of chronic lung disease on postoperative outcome in cardiac surgery, serious methodological limitations, such as retrospective design<sup>1,2,7</sup> or high risk of selection bias,<sup>6</sup> make drawing conclusions difficult. These considerations, along with the fact that routine preoperative assessment of pulmonary function is rarely, if ever, adopted, warrant improvement in this area.

The authors recently confirmed that PFT allowed reclassification of 24.7% of preoperative lung diseases in patients scheduled for coronary artery bypass graft (CABG) surgery in their institute.<sup>8</sup> The aim of the present study was to assess the 1-year survival in this cohort of patients with reclassified lung disease.

## Methods

The methodologic details were reported previously.<sup>8</sup> Briefly, 454 consecutive patients scheduled for elective CABG surgery were recruited at a teaching hospital between March 2015 and August 2016. This prospective cohort study was approved by the local Ethics Committee and was conducted in compliance with the principles of the Declaration of Helsinki. The only inclusion criterion was planned CABG surgery. Exclusion criteria were: patient's refusal to participate, contraindications for PFTs,<sup>9</sup> emergency surgery, recent or ongoing myocardial infarction, and angina. After providing an informed written consent, all eligible patients underwent PFTs prior to surgery.

PFTs were performed the day before surgery, using full-body plethysmograph (Master Screen, Erich Jaeger, Germany), with compliance to the acceptability and reproducibility criteria.<sup>10</sup> Absolute and percent-of-predicted forced expiratory volume in 1 second (FEV<sub>1</sub>) and forced vital capacity (FVC), as well as FEV<sub>1</sub>/FVC ratio were estimated and used to define abnormal respiratory patterns. Obstructive pattern, also referred to as obstructive lung disease, was defined as FEV<sub>1</sub>/FVC < 0.70; restrictive respiratory pattern was defined as a combination of FEV<sub>1</sub>/FVC ≥ 0.70 and FVC < 80% of predicted; and mixed pattern was defined as a combination of FEV<sub>1</sub>/FVC < 0.70, FEV<sub>1</sub> < 80% of predicted, and FVC < 80% of predicted.

The primary outcome was 1-year mortality, defined as death from any cause within 1 year after surgery, including intraoperative mortality. Patient's status after hospital discharge (ie, 30-day and 1-year follow-up) was established via telephone call to either the patient or patient's next of kin, as indicated in the informed consent form.

## Statistical Analysis

Continuous variables are presented as mean ± standard deviation; ordinal data are presented as median (interquartile range). Categorical variables are expressed as frequencies (percentage). For survival analysis, periods at risk of death were defined in months for each participant. Each period between baseline (day of surgery) and fatal outcome, or between baseline and the end of the 12-month follow-up period, constituted a separate observation. An observation that did not result in an event could end in loss to follow-up or end of the study period. The cumulative probability of fatal outcome was estimated using the Kaplan–Meier estimator. The log-rank test was used to explore differences of survival probabilities between subgroups of patients. To examine the unadjusted and adjusted associations between baseline characteristics and fatal outcome, a multivariable Cox regression model was fitted. Baseline data and their transformations were considered for inclusion into the final model based on a set of univariable analyses. Any variable whose univariable test result attained a cut-off p value of less than 0.25, was considered a candidate for the multivariable model, as were all variables of known importance and possible confounders. A manual forward selection procedure was used for formulating the final model. The constant relative hazard assumption was investigated by correlating sets of scaled Schoenfeld residuals for each covariate with a suitable transformation of time, along with a global test for the model as a whole. The assumption of linearity between log-hazard ratio and covariates was assessed graphically by plotting Martingale residuals against each covariate. Based on the above methods, relevant assumptions of Cox proportional hazards model were considered as valid. A two-sided p value of less than 0.05 was considered statistically significant. All analyses were performed using R statistical software (R Core Team [2016]. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL <https://www.R-project.org/>).

## Results

All 454 patients included in the study completed the 1-year follow-up with 2 patients lost to 30-day follow-up who eventually re-contacted. The baseline characteristics were reported earlier<sup>8</sup> and are available in the [Supplemental Table 1](#). Of 31 (6.8%) patients with history of COPD, 15 cases of obstructive lung disease were confirmed, while 57 new cases were discovered among those without COPD. In 5 (16.1%) patients with history of COPD no respiratory abnormality was confirmed. Fifty (11.0%) and 11 (2.4%) patients had lung restriction and mixed disorders, respectively. Thus, PFT helped reclassify lung disease in 107 (24.7%) patients. Intraoperative and intensive care unit mortality was 5 (1.1%), with 4 fatal outcomes caused by perioperative myocardial infarction. One more patient required aortic hemiarch replacement for acute aortic dissection, and died from massive bleeding the same day.

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