Association of impaired heart rate recovery with cardiopulmonary complications after lung cancer resection surgery

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Objectives: Patients who undergo lung resection surgery are at risk for postoperative morbidity and mortality. Appropriate selection of the surgical candidate is crucial in the treatment of lung cancer. Heart rate recovery is a measure of physical fitness. We aimed to investigate the association of impaired heart rate recovery with cardiopulmonary complications after lung resection surgery for treatment of lung cancer.

Methods: Data from consecutive patients who, between 2009 and 2013, underwent heart rate recovery evaluation after 6-minute walk tests before lung resection surgery were retrospectively reviewed. Impaired heart rate recovery was defined as a 12-beat or less decrease in peak heart rate at 1 minute after the 6-minute walk test. Postoperative cardiopulmonary complications were as defined by the Society of Thoracic Surgeons General Thoracic Surgery Database. Logistic regression was performed, including previously known risk factors for postoperative complications after lung resection surgery.

Results: A total of 96 patients had heart rate recovery evaluated within 6 months of lung resection surgery for treatment of lung cancer. Thirty-one patients had impaired heart rate recovery, 17 of whom (55%) had cardiopulmonary complications. A total of 65 patients had normal heart rate recovery, 17 of whom (26%) had cardiopulmonary complications. In multivariable logistic regression analysis, impaired heart rate recovery was significantly associated with postoperative cardiopulmonary complications (odds ratio, 4.97; confidence interval, 1.79-13.8; $P = .002$). No patient died within 30 days after surgery.

Conclusions: Impaired heart rate recovery after the 6-minute walk test is associated with postoperative cardiopulmonary complications in patients who underwent lung resection surgery for treatment of lung cancer. (J Thorac Cardiovasc Surg 2015;149:1168-73)

See related commentary on page 1174.

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Surgery is the standard of care for managing patients with early-stage lung cancer.[1] Unfortunately, only 20% to 25% of patients with lung cancer are able to undergo surgical resection, either because of the stage of the cancer at the time of diagnosis or because of comorbidities.[1,2] The surgical mortality rate for patients undergoing lung resection can be as high as 6.7%.[3] Therefore, appropriate selection of surgical candidates for lung resection is crucial in the management of lung cancer to minimize postoperative morbidity and mortality while maximizing the number of patients who can undergo surgical resection.

Guideline-based preoperative assessment algorithms use pulmonary function testing and measures of cardiopulmonary fitness to risk stratify patients.[1,2,4] Other predictors of mortality and major morbidity for lung cancer resection include body mass index (BMI), male gender, Zubrod performance status, renal dysfunction, induction chemotherapy, corticosteroid therapy, pneumonectomy, bilobectomy, and urgent procedures.[5] Despite the numerous predictors of morbidity and mortality, controversy exists as to the optimal cutoff values for the variables tested and the identification of patients whose risk profile favors surgical versus nonsurgical management of early-stage lung cancer.

Heart rate recovery (HRR) is commonly used to evaluate autonomic activity and is thought to reflect one's physical fitness. It is typically evaluated after the 6-minute walk test (6MWT) and is measured as a reduction in heart rate in the first minute after cessation of exercise. An abnormal postexercise HRR is defined as a decline of 18 beats/min or less when exercise stops abruptly or 12 beats/min or

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Abbreviations and Acronyms

BMI = body mass index
CI = confidence interval
CPC = cardiopulmonary complication
DL_{CO} = diffusion capacity of carbon monoxide
FEV_1 = forced expiratory volume within 1 second
HRR = heart rate recovery
OR = odds ratio
$ppoDL_{CO}$ = predicted postoperative DL_{CO}
$ppoFEV_1$ = predicted postoperative FEV_1
SBP = systolic blood pressure
SBRT = stereotactic body radiation therapy
6MWT = 6-minute walk test

less when a cool-down period is used.[6] In patients being considered for surgery, impaired HRR can suggest poor performance status/physical fitness and therefore increased surgical risk. We aim to investigate the association of impaired HRR with postoperative cardiopulmonary complications (CPCs) in patients who underwent lung resection for treatment of lung cancer. We hypothesize that impaired HRR is associated with an increased risk for postoperative CPCs.

MATERIALS AND METHODS

This study was approved by the Cleveland Clinic Institutional Review Board (Study #13-317). We retrospectively reviewed consecutive patients who, between September 2009 and February 2013, underwent HRR evaluation after 6MWTs as part of their preoperative assessment for lung resection surgery at the Cleveland Clinic. 6MWTs and HRR evaluation were obtained at the discretion of the practicing pulmonologists. Data collected included age, gender, BMI, beta-blocker therapy, forced expiratory volume within 1 second (FEV_1) % predicted,[7] diffusion capacity of carbon monoxide (DL_{CO}) % predicted,[8,9] type of surgery, predicted postoperative FEV_1 ($ppoFEV_1$), predicted postoperative DL_{CO} ($ppoDL_{CO}$), and predicted postoperative product. Postsurgical complications were recorded at our institution as part of the Society of Thoracic Surgeons General Thoracic Surgery Database (Appendix E1). Our primary end point was CPCs within 30 days after surgery; 30-day mortality was a secondary end point.

6MWTs were performed as suggested by the American Thoracic Society Pulmonary Function Standards Committee,[10] modified to include HRR evaluation. Testing began after patients have been seated for 10 minutes. Pulse oximeters (Ohmeda Biox 3740 or Ohmeda 3900, Datex-Ohmeda Inc, Laurel, Md) with finger probes were used to obtain heart rates at different time intervals. HRR was defined as the difference in heart rate at the 6th minute of the 6MWT and 1 minute after completion of the test, with the patient in a seated position. Impaired HRR was defined as a 12-beat or less decrease in heart rate 1 minute into the cool-down period after the 6MWT, as suggested by previous literature.[11] The segment method and quantitative lung perfusion scintigraphy (when available) were used to calculate $ppoFEV_1$ and $ppoDL_{CO}$.[12] Predicted postoperative product was calculated as the product of $ppoFEV_1$ and $ppoDL_{CO}$.[13]

Postoperative CPCs were as defined by the Society of Thoracic Surgeons General Thoracic Surgery Database, and included atelectasis, pleural effusion requiring drainage, acute respiratory distress syndrome, respiratory failure, mechanical ventilation at 48 hours postoperatively, deep vein thrombosis/pulmonary embolism, pneumothorax, pneumonia, empyema, atrial or ventricular arrhythmias, and myocardial infarction.

To assess the generalizability of this predictor, we analyzed the HRR of patients who underwent stereotactic body radiation therapy (SBRT) for treatment of lung cancer. Patients were selected for SBRT after it was determined that they had too high a risk for surgical resection based on traditional measures of cardiopulmonary fitness and discussion at our institutional tumor board.

Statistical Analysis

Descriptive statistics were summarized as means and standard deviations for all continuous variables and as counts and percentages for all categoric variables. The Student *t* test and Pearson's chi-square tests were used to compare baseline characteristics of our patient cohort with other patients with lung cancer who underwent surgical resection in the same time period. Univariable logistic regression analyses were performed on all independent variables that could contribute to the composite outcome of interest (CPCs). Multivariable logistic regression analyses, using a stepwise approach, were performed on independent variables whose *P* values were less than .1 in univariable logistic regression analyses. A maximum number of 3 covariates were used in each multivariable logistic regression analysis, keeping with an approximately 11:1 patient-to-event ratio. Independent variables were retained in the models if they were statistically significant and nonlinear to other covariables, with the exception of beta-blocker therapy, which was included in the model regardless of statistical significance due to possible interaction with HRR. Odds ratios (ORs) and 95% confidence intervals (CIs) were used whenever appropriate. All analyses were 2-tailed. Statistical significance in the multivariable models was defined as the difference in Akaike information criterion having a $P < .05$. Receiver operating characteristic curves were generated to assess the HRR's ability to predict postoperative CPCs. Because the optimal cutoff for impaired HRR in the patient population with lung cancer is unknown, the Youden method was used to confirm the optimal cutoff for HRR in predicting CPCs.[14] SAS 9.3 and JMP Pro software (SAS Institute Inc, Cary, NC) were used for all analyses.

RESULTS

A total of 571 patients underwent surgical resection for lung cancer during the study period, 96 (16.5%) of whom had HRR data available. Compared with other patients who underwent lung resection within the same time period, patients who had HRR evaluation after 6MWTs did not have statistically significant differences in age, gender, BMI, corticosteroid therapy, preoperative chemotherapy, history of cardiothoracic surgery, creatinine and hemoglobin levels, FEV_1, DL_{CO}, performance status, and clinical stage (Table E1).

Of those who had HRR evaluation, 34 (35%) had a total of 42 postoperative CPCs (Table E2). There were no significant differences in patient characteristics and standard pulmonary function measures between those with and without CPCs, including FEV_1 % predicted, DL_{CO} % predicted, $ppoFEV_1$, $ppoDL_{CO}$, and predicted postoperative product. The majority (86%) of patients had clinical stage I or II lung cancer. A higher number of patients in the CPC group had clinical stage III disease (7 vs 2). One patient had oligometastatic disease. There was no difference in tumor location or type of surgery

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