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Chest wall resection for non-small cell lung cancer: A case-matched study of postoperative pulmonary function and quality of life

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ABSTRACT

Background: To assess the pulmonary function and quality of life (QOL) after chest wall resection for non-small cell lung cancer.
Material and methods: One hundred and thirty-five patients (cases) who underwent pulmonary resection with chest wall removal were identified from January 1997 to December 2015. Propensity score matching (1:3) was applied to balance known confounders for pulmonary function and QOL between the cases and the control group who underwent pulmonary resection without chest wall invasion. Matched analyses were performed to compare perioperative mortality and morbidity, postoperative pulmonary function, overall QOL, and specific symptoms.
Results: Perioperative mortality and morbidity did not differ significantly between cases and controls, but the hospital stay was longer in cases than in controls (mean, 12.8 vs 8.9 days; $p < 0.001$), The decline of postoperative pulmonary forced vital capacity (FVC) and the percentage of predicted FVC (FVC%) was more obvious in cases than in controls at 6 months and 2 years after surgery, but there was no obvious decline in the forced expiratory volume in one second (FEV1), the percentage of predicted FEV1 (FEV1%), the diffusion capacity of the lung for carbon monoxide (DLCO) and the percentage of predicted DLCO (DLCO%) in cases compared with controls. No significant difference was observed between the two groups in scores for overall QOL, pain, fatigue, cough, dyspnea, appetite, hemoptysis, lung cancer symptoms, and normal activities.
Conclusions: When chest wall resection is inevitable, it does not worse the QOL and pulmonary function of patients who underwent pulmonary resection with chest wall removal obviously compared with patients underwent pulmonary resection without chest wall invasion.

1. Introduction

The proportion of lung cancers involved the chest wall by direct extension from lung cancers is about 5% [1,2]. In TNM staging system, patients with such type of lung cancer is classified as T3, and can be further divided into stage IIB to IV according to the presence of lymph node and distant metastasis. The surgical treatment of lung cancer with chest wall invasion started with the report by Coleman in 1947 [3]. Long-term survival after chest wall resection has been well studied, the incompleteness of resection and the presence of lymph node metastases are major prognostic factors for this disease.

When chest wall resection is inevitable, in addition to lung cancer itself patients also want to know more about the effect of chest wall resection on their life. Therefore, the information about the changes of quality of life (QOL) after surgery is also needed for thoracic surgeons and patients [4–6]. The Lung Cancer Symptom Scale (LCSS) is a reliable and validated disease-specific instrument for QOL assessment [7,8]. It measures major symptoms associated with lung cancer and their effect on overall QOL, symptomatic distress and functional activity. Patients' self-reported QOL has become an important end point for treatment comparisons, therefore clinical investigators are increasingly interested in assessing QOL in lung cancer clinical trials. In addition, a pulmonary function test

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(PFT) is an objective predictor of patients' perceptions of physical limitations in daily activities. It aids in diagnosis, helps monitor responses to treatment, and can guide decisions regarding further treatment and intervention. However, the effect of chest wall resection on QOL and postoperative pulmonary function has been assessed rarely. We focus on the change of QOL and pulmonary function and hypothesize that QOL and results of PFT would be poorer in non-small cell lung cancer patients who underwent pulmonary resection with chest wall resection than those without chest wall resection. Because small cases of this type of lung cancer and randomized trials designed for chest wall resections are difficult to perform, propensity matching was used for comparison in this study.

2. Material and methods

2.1. Study cohort and data collection

The study protocol was reviewed and approved by the Mayo Clinic Institutional Review Board. The detail of study protocol has been previously reported [9]. In brief, from January 1997 to December 2015 at Mayo Clinic (Rochester, MN), all patients pathologically diagnosed and treated with primary non-small cell lung cancer, have been prospectively enrolled and followed for outcome research through written informed consent. A cohort of 2235 consecutive patients with stage IIB and IIIA disease underwent pulmonary resection were identified, of whom 135 had combined chest wall resection. The medical record data included age, sex, smoking status, surgical type, mortality, complications, hospital stay, histopathological features, preoperative and postoperative pulmonary function. The patients underwent disease staging postoperatively according to the seventh edition of the TNM staging system of the American Joint Committee on Cancer.

Perioperative mortality included the deaths occurring within 30 days of the operative procedure and deaths that occurred later during the initial perioperative hospitalization. The follow-up and recurrence data were collected through detailed medical record data abstraction and self-administered questionnaires This included present health and treatment updates starting within 6 months after diagnosis and annually thereafter. Vital status of each patient was verified annually through Mayo Clinic's electronic medical notes and registration database, next-of-kin reports, death certificates, and obituary documents filed in the patients' medical records as well as through the Mayo Clinic Tumor Registry and the Social Security Death Index website.

The studied PFT included forced expiratory volume in one second (FEV1), the percentage of predicted FEV1 (FEV1%), forced vital capacity (FVC), the percentage of predicted FVC (FVC%), diffusion capacity of the lung for carbon monoxide (DLCO) and the percentage of predicted DLCO (DLCO%). We focused on the pulmonary function performed within 30 days before surgery and within 24 months postoperatively. According to the testing time, patients were divided into two groups by cutoff point of 6 months [10], the change of pulmonary function was compared between cases and controls at 6 month and 2 year.

QOL was measured by the LCSS that focuses on the symptom and function of patients with lung cancer. This scale consists of 9 items (Supplementary Table S1), 6 measure major symptoms of lung cancer (appetite, fatigue, cough, dyspnea, hemoptysis and pain), and 3 assess total symptomatic distress, activity status and overall QOL. The intensity of patient response is measured by visual analog scales. Overall QOL and symptoms were assessed as scales varying from 0 to 10, higher scores are indicative of better quality of life [11,12].

2.2. Statistical analysis

The descriptive statistics for categorical variables are reported as frequencies and percentages and continuous variables as mean ± standard deviation or median. Nominal categorical variables were compared using $\chi 2$ tests and ordinal categorical variables were compared using Wilcoxon rank sum tests. Cumulative survival was estimated with a Kaplan-Meier model and calculated by using the time of diagnosis as the starting point. The patient whose follow-up time was less than 30 days or who died within 30 days after surgery was excluded from survival analysis. When conducting survival analysis, we used 10-year overall survival and 10-year disease-free survival data. A Cox proportional hazards model was estimated for both univariate and multivariate analyses. Univariate predictors significant at the 0.05 level of significance were considered for the multivariable models. All statistical analyses were carried out with SAS 9.3(SAS Institute, Cary, NC). All p values were two tailed and p value < 0.05 was considered significant.

We matched the cases between the imbalanced groups by propensity scores using the greedy algorithm. Before matching, we calculated the propensity score by incorporating the variables that could potentially affect the postoperative pulmonary function and QOL, including radiotherapy, chemotherapy, comorbidity, surgical type, complete resection, smoking status, age, gender, lobe and preoperative pulmonary function. Thereafter, we used 1:3 matching between two groups, resulting in a matched set of 540 patients. Matched analyses were performed to compare clinical outcomes between two groups, including perioperative mortality and morbidity, PFT and QOL.

3. Results

3.1. The clinical features

In unmatched cohort, age at diagnosis ($p = 0.0214$), sex ($p = 0.0068$), smoking status ($p = 0.0001$), cell type ($p < 0.0001$), lobe ($p = 0.0001$), tumor grade ($p < 0.0001$), stage ($p = 0.0001$), surgical type ($p = 0.0039$), complete resection ($p = 0.0005$) and radiotherapy ($p < 0.0001$) were observed with imbalance between two groups. After the 1:3 propensity score matching, 540 patients in the two groups were well balanced on all baseline characteristics. The demographic and pathological data of two groups in matched sets were shown in Table 1.

3.2. Perioperative mortality and morbidity

In the perioperative period, 6 deaths (4.4%) in cases and 8 (2.0%) in controls occurred, and no difference was found in perioperative mortality between two groups. The hospital stay was longer in cases than in controls (mean, 12.8 vs 8.9 days; $p < 0.001$). The complications were shown in Table 2 and there was no significant difference in perioperative morbidity rates between the two groups in 540 matched patients.

3.3. Pulmonary function

Table 3 showed the comparisons of preoperative and postoperative PFT of two groups in 540 matched patients. Among 540 matched patients, 124 patients in cases and 366 in controls had undergone preoperative PFT; 48 patients in cases and 152 in controls, had undergone both preoperative and postoperative PFT. The declined value of postoperative PFT was found in both cases and controls compared with preoperative PFT. The value of FVC and FVC% declined dramatically and there was a significant difference in FVC and FVC% between two groups in postoperative PFT at 6