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Influence of chronic obstructive pulmonary disease on postoperative lung function of lung cancer patients and predictive value of lung perfusion scan

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[Abstract] **Background and Objective:** Postoperative lung function is closely related to the prognosis of lung cancer patients after lobectomy. This study was to explore the influence of chronic obstructive pulmonary disease (COPD) on postoperative lung function in patients undergoing lobectomy for non-small cell lung cancer (NSCLC), and to assess the predictive value of lung perfusion scan for lung cancer patients with COPD before operation. **Methods:** Clinical data of 65 NSCLC patients who underwent lobectomy were analyzed. Of the 65 patients, 25 had COPD (COPD group) and 40 had normal lung function (control group). The change of forced expiratory volume in 1st second (FEV1) after lobectomy and deference between postoperative FEV1 and preoperative predictive postoperative (ppo) FEV1 were compared between the two groups. For ten patients with COPD who had undergone lung perfusion scan before operation, ppo'FEV1 by lung perfusion scan and ppoFEV1 by equation were compared. **Results:** The mean percent loss of FEV1 was less in COPD group than in control group (8.98% vs. 22.47%, $P<0.05$). The value of postoperative FEV1 minus ppoFEV1 and the ratio of postoperative FEV1 to ppoFEV1 were significantly higher in COPD group than in control group (6.90 vs. 0.83, $P<0.05$; 1.14 vs. 1.01, $P<0.05$). For the ten patients undergone lung perfusion scan, the mean value of ppo'FEV1 minus ppoFEV1 was 4.04%, with a 95% confidence interval of 3.01%–5.07%. **Conclusions:** The mean loss of lung function after lobectomy is less in lung cancer patients with COPD than in patients with normal lung function. Lung perfusion scan before operation may help to predict postoperative lung function of lung cancer patients with COPD.

Key words: chronic obstructive pulmonary disease, lung neoplasm, lung function, lobectomy, lung perfusion scan

Postoperative complications are quite common in lung cancer patients undergoing lobectomy, the incidence rates of which depend substantially on the dimension of surgical resection, preoperative concomitant medical conditions and cardiopulmonary function reserve.[1] Preoperative predictive postoperative FEV_1 ($ppoFEV_1$) has been one of the measures indicated for operation since it was accepted as an independent risk factor for postoperative complications in 1990s.[2] However, recent study reported[3] that

$ppoFEV_1$ was an effective predictive factor for postoperative complications in lung cancer patients with $FEV_1 > 70\%$ expected only while it was not in patients with $ppoFEV_1 \leq 70\%$ expected. And some study [4] also indicated that, compared to the lung cancer patients with normal pulmonary function, those complicated with chronic obstructive pulmonary disease (COPD) varied in postoperative pulmonary function after the lobectomy. Pulmonary perfusion scan was rarely reported in the preoperative assessment for lung cancer patients complicated with COPD for selective lobectomy. And lung cancer patients complicated with COPD were hereby compared with their counterparts with normal pulmonary function in terms of postoperative change in pulmonary function and $ppoFEV_1$, aiming to investigate the effects of COPD on postoperative change in pulmonary function for lung cancer patients undergoing lobectomy and the practical value of pulmonary perfusion scan in preoperative assessment of lung cancer patients complicated with COPD.

Materials and methods

Clinical data. Lung cancer patients (n=65) hospitalized in Department of Cardiothoracic Surgery, Sun Yat-sen Cancer Center between January 2004 and January 2008 were retrospectively reviewed. All patients underwent lobectomy with concomitant portal or mediastinal lymph node dissection for primary non-small cell lung cancer (NSCLC), of which 25 of which patients complicated with COPD included 23 males and two females. Patients ranged from 51 to 75 years of age whereby 16 patients were above 60 years and nine patients were below 60 years. In addition, 21 patients had known history of cigarette smoking and six patients reported the medical history of COPD. The counterparts with normal pulmonary function were enrolled into the control group (n = 40), including 31 males and nine females, age ranging from 35 to 79 years whereby 21 patients above 60 years. And 22 patients had known history of cigarette smoking but without reported the medical history of COPD. The COPD group consisted of nine patients with adenocarcinoma and 16 with squamous cell carcinoma (SCC), including 17 cases at stage I, six cases at stage II, and two cases at stage III. Right upper lobectomy was performed in seven patients, right lower lobectomy in five patients, right middle lobectomy in one patient, left upper lobectomy in seven patients, and left lower lobectomy in five patients, respectively. Moreover, the control group consisted of 22 patients with adenocarcinoma, 13 patients with SCC, two patients with adenosquamous cell carcinoma (ASCC) and three patients with alveolar cell carcinoma, including 22 patients at stage I, seven patients at stage II and 11 patients at stage III. Right upper lobectomy was performed in ten patients, right lower lobectomy in ten patients, right middle lobectomy in two patients, left upper lobectomy in 11 patients and left lower lobectomy in seven patients, respectively. One patient out of control group underwent lobectomy with additional partial resection of chest wall. Tumor staging was based on UICC 2002 Tumor Staging Guideline.

Methods and observation index. All patients were routinely examinedscreened with preoperative pulmonary function test in addition to fibrobronchoscopy and chest CT scan. Out of COPD group, ten patients underwent preoperative pulmonary perfusion scan; all patients undergoing lobectomy were followed up at postoperative one month using routine pulmonary function test. Patients presenting expected value of $FEV_1 < 80\%$ expected and $FEV_1/FVC < 70\%$ preoperatively were enrolled into the COPD group, whose pulmonary function was graded in accordance with GOLD 2006 Guideline [5] while those with preoperative expected value of $FEV_1 \geq 80\%$ expected and $FEV_1/FVC \geq 70\%$ were enrolled into the control group.

Preoperative FEV_1, chest CT and fibrobronchoscopy were routinely performed to determine the number of obstructed pulmonary segments, $ppoFEV_1$ and postoperative FEV_1. $ppoFEV_1$ was calculated with the following formula based on the anatomical pulmonary

segment: $ppoFEV_1$ = preoperative FEV_1 × [1 (number of resected segments number of obstructed segment)] while $ppoFEV_1$ was calculated directly from the results of preoperative pulmonary perfusion scan. Pulmonary function results were expressed as the percentage of expected value.

Changes in the ratio of postoperative FEV_1 to preoperative FEV_1, $\triangle FEV_1$ [$\triangle FEV_1$= (preoperative FEV_1 postoperative FEV_1)/preoperative FEV_1] were compared between the COPD group and the control group in addition to postoperative FEV_1 ($ppoFEV_1$) and postoperative FEV_1/$ppoFEV_1$. For ten patients with pulmonary perfusion scan, $ppoFEV_1$ was independently calculated with the same formula to compare the changes between the two methods.

Statistical analysis. All quantitative data were compare with t-test and 95% confidence interval (CI) was calculated in addition to analysis of normality. All tests were two sides and performed with SPSS 13.0, there was significant difference when $P<0.05$.

Results

Chest CT scan and fibrobronchoscopy. Obstructed pulmonary segments were detected in six (6/25) patients out of the COPD group in contrast to five (5/40) patients inin the control group.

Preoperative pulmonary function, ppoFEV1 and changes in pulmonary function of post-lobectomy. Preoperative FEV_1 ranged from 24.00% to 72.60% (mean = 59.57%) in COPD group, including 21 moderate, three severe and one extremely severe COPD patients; $ppoFEV_1$ averaged 46.91% and postoperative FEV_1 averaged 53.81%. Moreover, preoperative FEV_1 ranged from 81.00% to 117.10% (mean = 96.78%) in control group; $ppoFEV_1$ averaged 74.27% and postoperative FEV_1 averaged 75.10% . Less percentage changes in FEV_1 occurred in the COPD group than in the control group (8.98% vs 22.47% , $P<0.05$) while postoperative FEV_1 $ppoFEV_1$ averaged more in the COPD group than in the control group (6.90 vs 0.83, $P<0.05$). Moreover, postoperative FEV_1/$ppoFEV_1$ also averaged more in the COPD group than in the control group (1.14 vs 1.01, $P<0.05$) (Table 1).

Comparison of pulmonary perfusion scan results with formula-derived $ppoFEV_1$. All the ten patients undergoing preoperative pulmonary perfusion scan presented non-uniform distribution in perfusion defects whereby the three patients improving in post- operative pulmonary function had their tumors located in the lobes with the most significant pulmonary perfusion defects, whose $ppoFEV_1$ deriving from pulmonary perfusion scan results (42.57%) averaged more than $ppoFEV_1$ deriving from the calculation based on anatomical pulmonary segments (38.53%); and $ppoFEV_1$ $ppoFEV_1$ averaged 4.04 (95% CI 3.01 5.07) (Table 2).

Discussions

Lung cancer and COPD share some risk factors such as cigarette smoking while lung cancer of

Table 1 Lung function changes after lobectomy in lung cancer patients with normal lung function or chronic obstructive pulmonary disease (COPD)

Item	Control group		COPD group	
	Mean+SD	95% CI	Mean+SD	95% CI
preFEV1 (%)	96.78±10.92	93.28,100.27	59.57±12.17[a]	54.55,64.59
postFEV1 (%)	75.10±10.71	71.67, 78.53	53.81± 9.83[a]	49.75,57.86
△FEV1 (%)	22.47± 5.73	20.64, 24.30	8.98± 7.59[a]	5.85,12.12
ppoFEV1 (%)	74.27± 9.92	71.09, 77.44	46.91± 8.83[a]	43.27,50.56
postFEV1-ppoFEV1(%)	0.83± 3.85	−0.40, 2.07	6.90± 4.59[a]	5.00, 8.79
postFEV1/ppoFEV1	1.01± 0.05	0.99, 1.03	1.14± 0.10[a]	1.11, 1.19

FEV1, forced expiratory volume in the 1st second; preFEV1, preoperative FEV1; postFEV1, postoperative FEV1; △FEV1, percent difference between FEV1 before lobectomy versus FEV1 after lobectomy; ppoFEV1, preoperative predictive postoperative FEV1. [a]$P<0.05$, vs. control group.

Table 2 Preoperative predictive postoperative FEV1 by lung perfusion scan and by equation in lung cancer patients with chronic obstructive pulmonary disease

Item	Mean±SD	95% CI
preFEV1 (%)	52.96±16.28	41.32,64.60
postFEV1 (%)	50.06±14.21	39.89,60.23
ppo′FEV1 (%)	42.57±12.41	33.70,51.44
ppoFEV1 (%)	38.53±12.14	29.84,47.22
ppo′FEV1-ppoFEV1(%)	4.04± 1.44	3.01, 5.07

ppo′ FEV1, preoperative predictive postoperative FEV1 by lung perfusion scan; ppoFEV1, preoperative predictive postoperative FEV1 by equation. Other abbreviations as in Table 1.

central type compresses bronchi and presented pulmonary function impairment of COPD feature.[6] Thus, some lung cancer patients also presented changes in pulmonary function similar to COPD. Zeiher et al.[2] reported in 1995 that ppoFEV_1 was an independent risk factor of post-lobectomy complications and mortality, since which ppoFEV1 was always taken as one of the key measures of preoperative pulmonary function assessment and patient screening. ppoFEV_1 mainly derived from the formulary calculation based on anatomical pulmonary segments or pulmonary perfusion scan. ACCP Evidenced-Based Clinical Practice Guidelines[7]suggested that ppoFEV_1 should be calculated based on anatomical pulmonary segments prior to lobectomy while ppoFEV_1 should be derived from pulmonary perfusion scan prior to total pneumonectomy, and operative risks would be substantially increased in case of ppoFEV1 < 40% expected value.

It was recently found that lung cancer patients complicated with COPD lostt significantly less pulmonary function than those with normal pulmonary function following lobectomy.[8-11] Brunelli et al.[3, 4] also found that ppoFEV_1 was only an independent predictive factor for post-lobectomy complications in lung cancer patients with FEV_1 > 70% expected while FEV_1 ≤ 70% expected couldnt predict the postoperative profiles, which could be attributed to the lung reduction effect following lobectomy pulmonary elastic retractility was recovered through surgical resection of impaired lung tissues, resulting in decreased airflow resistance and improved pulmonary ventilation/perfusion ratio.

The COPD group lost 8.98% of pulmonary function on average after lobectomy while the control group averaged 22.47% ($P<0.05$), consistent with the previous reports by Baldi et al.[8] and Subotic et al.[9] However, these studies only compared the changes of postoperative pulmonary function relative to preoperative one in lung cancer patients undergoing lobectomy other than the difference between postoperative FEV_1 and ppoFEV_1. However, lobectomy varied in the number of pulmonary segments resected; patients complicated with COPD were more likely to develop obstruction of pulmonary segments than the patients with normal pulmonary function due to the space-occupying effect of tumor whereby more nonfunctional pulmonary segments were resected in patients complicated with COPD than in patients with normal pulmonary function; pulmonary function changes varied among lobes for patients complicated with COPD. All the factors above mentioned were likely to result in the variations in pulmonary functional segments resected between two groups. Therefore, the comparison of pre/postoperative pulmonary function between two groups could not reflect the difference in pulmonary function after lobectomy between lung cancer patients complicated with COPD and those with normal pulmonary function. In our study, six patients out of the COPD group (6/25) presented obstruction of pulmonary segment or lobe while five patients out of the control group (5/40) presented obstruction of pulmonary segment. Control group averaged 0.83% in FEV_1 ppoFEV1 (95% CI [-0.40%, 2.07%]) and 1.01 in FEV_1/ppoFEV_1 (95% CI [0.99, 1.03]), suggesting that the calculation based on anatomical pulmonary segment could better predict postoperative pulmonary function for lung cancer patients with normal pulmonary function, consistent with the previous results.[12] And the COPD group averaged 6.90% in FEV_1 ppoFEV1 (95% CI [5.00%, 8.79%]) and 1.14 in FEV_1/ppoFEV_1 (95% CI [1.11, 1.19]), both higher than those in the control group, suggesting that patients complicated with COPD

varied from the counterparts with normal pulmonary function in postoperative pulmonary function changes, the difference between which was significantly less than the previous results though.

Both European and American preoperative pulmonary function assessment guidelines recommended pulmonary perfusion scan only for predicting postoperative pulmonary function prior to total pneumectomy but recommended the prediction of postoperative pulmonary function with the calculation based on anatomical pulmonary segment prior to lobectomy. Therefore, pulmonary perfusion scan was rarely reported in the study involving the effects of COPD on the postoperative pulmonary function changes for patients undergoing lobectomy. However, defected segments varied among lobes in patients complicated with COPD, which could not be detected on preoperative fibrobronchoscopy and chest CT scan. The calculation based pulmonary segment was likely to bias the prediction of postoperative pulmonary function in such patients. Our results showed that ten patients out of COPD group underwent preoperative pulmonary perfusion scan, all of whom presented non-uniform distribution of pulmonary function impairment whereby three patients had their tumors located at the regions with relatively marked dysfunction and obstruction of pulmonary segment was only detected in two patients on fibrobronchoscopy or chest CT scan. The $ppoFEV_1$ derived from pulmonary perfusion scan (42.57%) averaged more the $ppoFEV_1$ from the calculation based on anatomical pulmonary segment (38.53%); $ppoFEV_1$ $ppoFEV_1$ averaged 4.04% (95% CI [3.01%, 5.07%]). Obviously, The $ppoFEV_1$ derived from pulmonary perfusion scan was more close to the measured postoperative pulmonary function than that from the calculation based on anatomical pulmonary segment only, superior in preoperative assessment of lung cancer patients complicated with COPD. And our study was restricted by the small sample size, which should be validated in prospective control study.

In summary, lung cancer patients complicated with COPD varied from the counterparts with normal pulmonary function in changes in postoperative pulmonary function, who lost significantly less pulmonary function than the latter; ppoFEV1 calculated based on anatomical pulmonary segment could better predict postoperative pulmonary function for patients with normal pulmonary function; and pulmonary perfusion scan could better predict that for those complicated with COPD.

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