

## Pulmonary complications in patients with chronic obstructive pulmonary disease following transthoracic esophagectomy

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**CONCLUSION:** The criteria of COPD are the critical predictor for pulmonary complications in esophageal cancer patients undergoing esophagectomy. Severity of COPD affects the incidence rate of the pulmonary complication, and percent-predicted FEV1 is a good predictive variable for pulmonary complication in patients with COPD. Arterial blood gases are helpful in directing perioperative management.

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**Key words:** Chronic obstructive pulmonary disease; Arterial blood gas; Esophageal cancer; Complication

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### Abstract

**AIM:** To investigate the incidence of various types of postoperative pulmonary complications (POPCs) and to evaluate the significance of perioperative arterial blood gases in patients with esophageal cancer accompanied with chronic obstructive pulmonary disease (COPD) after esophagectomy.

**MEHTODS:** Three hundred and fifty-eight patients were divided into POPC group and COPD group. We performed a retrospective review of the 358 consecutive patients after esophagectomy for esophageal cancer with or without COPD to assess the possible influence of COPD on postoperative pulmonary complications. We classified COPD into four grades according to percent-predicted forced expiratory volume in 1 s (FEV1) and analyzed the incidence rate of complications among the four grades. Perioperative arterial blood gases were tested in patients with or without pulmonary complications in COPD group and compared with POPC group.

**RESULTS:** Patients with COPD (29/86, 33.7%) had more pulmonary complications than those without COPD (36/272, 13.2%) ( $P < 0.001$ ). Pneumonia (15/29, 51.7%), atelectasis (13/29, 44.8%), prolonged O<sub>2</sub> supplement (10/29, 34.5%), and prolonged mechanical ventilation (8/29, 27.6%) were the major complications in COPD group. Moreover, patients with severe COPD (grade II B, FEV1 < 50% of predicted) had more POPCs than those with moderate (grade II A, 50%-80% of predicted) and mild (grade I  $\geq$  80% of predicted) COPD ( $P < 0.05$ ). PaO<sub>2</sub> was decreased and PaCO<sub>2</sub> was increased in patients with pulmonary complications in COPD group in the first postoperative week.

### INTRODUCTION

Radical esophagectomy remains the most effective method in patients with esophageal cancer, and the five-year survival rate of 40% or higher can be achieved<sup>[1-3]</sup>. However, esophagectomy may be one of the greatest surgical operations. Postoperative pulmonary complications (POPCs) are common after esophagectomy<sup>[4,5]</sup>.

Chronic obstructive pulmonary disease (COPD) is a common fatal disease in China. Postoperative pulmonary complication after thoracotomy is the major complication in patients with COPD<sup>[6-8]</sup>.

COPD is considered as an important risk factor for pulmonary complications due to low cardiopulmonary reserve<sup>[9-12]</sup>. However, the incidence of each type of complications and its relationship with percent-predicted FEV1 after esophagectomy in patients with COPD are unclear.

Our study was to document the effect of COPD on complication rates and the incidence of various types of pulmonary complications in esophageal cancer patients with or without COPD following esophagectomy, to elucidate the relationship between percent-predicted FEV1 and pulmonary complications and to evaluate the change and significance of arterial blood gases after operation in patients with COPD.

## MATERIALS AND METHODS

A total of 358 patients who underwent esophagectomy at Beijing Friendship Hospital and Peking University First Hospital between July of 2001 and March of 2005 were included in this study. Eighty-six of the 358 patients were diagnosed having COPD.

We divided COPD into 4 grades: grade I: percent predicted FEV1%<sub>p</sub>  $\geq$  80 and FEV1/FVC < 70% (45 cases); grade II A: 50%  $\leq$  FEV1%<sub>p</sub> < 80%, FEV1/FVC < 70% (32 cases); grade II B: 30%  $\leq$  FEV1%<sub>p</sub> < 50%, FEV1/FVC < 70% (9 cases); grade III: FEV1%<sub>p</sub> < 30%, FEV1/FVC < 70% (0 case).

Table 1 summarizes the patient characteristics. The two groups were similar in terms of age, sex, presence of other medical conditions, type and duration of operation, cancer stage, anastomosis site, blood loss and serum albumin. All patients underwent radical resection of tumors in the middle or lower third thoracic esophagus which were confirmed to be squamous cell cancers of esophagus after surgery. In our study, patients with tumor of the cervical and upper third thoracic esophagus were excluded because of different oncological characteristics and treatment protocols.

Basic hematological and biochemical tests, pulmonary function tests, electrocardiograph, chest CT scan, abdominal ultrasonography, barium contrast study and endoscopy were carried for all patients.

Patients were advised to stop smoking and to quit of alcohol two weeks prior to operation. Patients with hypercapnia and pulmonary hypertension were excluded. All patients in our study did not receive preoperative chemotherapy and chemoradiotherapy.

Esophagectomy via a left thoracotomy approach or cervical left thoracotomy approach was performed. Reconstruction of intestinal continuity was restored with a stomach placed in the left thoracic cavity or via orthotopic route when the anastomosis was carried out in the neck. The circular stapler was used when anastomosis was performed in the thoracic cavity and a hand-sewn anastomosis was done when it was in the neck. All patients received intravenous nutrition and continuous gastrointestinal decompression after esophagectomy.

All patients were followed up after surgery and complications occurring during the patient hospitalization were recorded. For this study, pulmonary complications were defined to include: pneumonia (manifesting fever, productive cough, increased white blood cell count, and marked infiltration on chest roentgenogram), atelectasis (manifesting segmental or lobar's atelectasis on chest roentgenogram without bronchial stenosis), pulmonary abscess (displaying intrapulmonary air containing space on chest roentgenogram and purulent exudation in the pleural cavity with fever and increased white blood cell count requiring drainage and antibiotic therapy), prolonged O<sub>2</sub> supplement (protracted supplemental oxygen  $\geq$  14 d), acute respiratory distress syndrome (ARDS; PaO<sub>2</sub>:FiO<sub>2</sub> ratio less than 250 for more than 24 h with pulmonary infiltrates, without clinical suspicion of volume overload, deterioration of respiratory status needing mechanical ventilatory support), and prolonged mechanical ventilation

Table 1 Baseline characteristics of study population with or without COPD undergoing transthoracic esophagectomy

Characteristics	COPD (n = 86, %)	Non-COPD (n = 272, %)	P value
Age, yr	61.3±5.5	63.2±7.1	0.522
Sex (male:female)	63/23	191/81	0.638
Smoking history	79 (91.9)	214 (78.7)	<0.01
Past medical history			
Hypertension	16 (18.6)	48 (17.6)	0.840
Cardiac disease	13 (15.1)	35 (12.9)	0.594
Diabetes	10 (11.6)	33 (12.1)	0.900
Cancer stage			
I	17 (19.8)	56 (20.6)	0.869
II	48 (55.8)	145 (53.3)	0.685
III	21 (24.4)	71 (26.1)	0.115
IV	0	0	-
Site of anastomosis			
Neck	32 (37.2)	108 (39.7)	0.679
Chest	54 (62.8)	164 (60.3)	0.679
Duration of operation (min)	162.75±51.05	185.15±66.24	0.239
Blood loss (mL)	365.50±219.36	434.00±232.48	0.344
Low serum albumin (<35g/L)	25 (29.1)	89 (32.7)	0.526
Spirometry			
FEV1 (L)	1.6±0.3	2.3±0.5	<0.01
FEV1,% predicted	51.5±10.5	80.4±13.1	<0.01
FEV1/FVC,%	57.6±8.9	73.3±6.8	<0.01
DLCO,% predicted	83.7±13.4	85.0±13.9	0.774

FEV1 = forced expiratory volume in 1 s; FVC = forced vital capacity; DLCO = diffusion capacity of the lung for carbon monoxide.

$\geq$  2 d<sup>[4,6,9,13]</sup>. Postoperative pulmonary complications studied included pulmonary parenchyma but not complications of pleural cavity such as hemothorax, pneumothorax, thoracic abscess, chylothorax, pleural effusion, mediastinal emphysema.

Arterial blood gases were tested daily from first preoperative day to the seventh postoperative day at 4-5pm. Patients with respiratory failure or mechanical ventilation 7 d prior to operation were excluded in order to avoid intervention. Statistical analysis was performed using *t-test*, *ANOVA* and *chi-square test*. *P* < 0.05 was considered statistically significant. All statistical analyses were performed using the SPSS statistical package (version 10.0, SPSS Inc., Chicago, IL).

## RESULTS

Postoperative pulmonary complications such as pneumonia and atelectasis occurred early after operation. Pulmonary complications in the 358 patients with or without COPD are shown in Tables 2 and 3. Patients with COPD (29/86, 33.7%) had more pulmonary complications than those without COPD (36/272, 13.2%) (*P* < 0.01). Pneumonia (15/29, 51.7%), atelectasis (13/29, 44.8%), prolonged O<sub>2</sub> supplement (10/29, 34.5%), prolonged mechanical ventilation (8/29, 27.6%) were the major complications in COPD group.

The rate of mortality was 3.5% (3/86) in the COPD group and 66.7% (2/3) of deaths were due to respiratory failure. In patients without COPD, the rate of mortality was 1.5% (4/272) and two patients (50%) had respiratory failure as their cause of death.

**Table 2 Pulmonary complications occurring in patients with or without COPD undergoing transthoracic esophagectomy**

Pulmonary complications	COPD (n = 86)	Non-COPD (n = 272)	P value
Pneumonia	15	19	<0.01
Atelectasis	13	15	<0.01
Pulmonary abscess	4	5	0.227
Prolonged O <sub>2</sub> supplement	10	11	<0.01
Prolonged mechanical ventilation	8	10	<0.05
Acute respiratory distress syndrome	5	4	<0.05

**Table 3 Degree of COPD and outcomes in patients with or without POPC in COPD group**

Severity of COPD	POPCs (n = 29)	Non-POPCs (n = 57)	P value
FEV1,%predicted			
Grade I (>80%)	10	35	<0.05
Grade II A (50%-80%)	13	19	
Grade II B (30%-50%)	6	3	
Grade III (<30%)	0	0	

POPCs = postoperative pulmonary complications.

**Table 4 Comparison of PaO<sub>2</sub> changes in the first postoperative week in patients with or without POPCs in COPD group (mean±SD)**

Time	POPCs	Non-POPCs	P
1 preoperative day	82.17±7.37	82.75±4.45	0.758
1 postoperative day	68.38±5.24	76.00±8.28	<0.01
2 postoperative day	61.83±7.03	69.05±7.78	<0.01
3 postoperative day	61.75±6.14	67.20±7.35	<0.05
4 postoperative day	62.71±4.93	70.15±9.34	<0.01
5 postoperative day	61.13±5.62	72.75±10.30	<0.001
6 postoperative day	61.83±6.49	76.55±9.62	<0.001
7 postoperative day	61.63±6.31	80.45±7.50	<0.001

PaO<sub>2</sub> = partial pressure of oxygen.

**Table 5 Comparison of PaCO<sub>2</sub> changes in the first postoperative week in patients with or without POPCs in COPD group (mean±SD)**

Time	POPCs	Non-POPCs	P
1 preoperative day	42.85±4.10	42.37±6.03	0.766
1 postoperative day	44.42±4.61	41.24±4.93	<0.05
2 postoperative day	45.35±4.97	41.38±5.19	<0.05
3 postoperative day	46.02±4.88	42.45±5.62	<0.05
4 postoperative day	46.01±5.56	39.10±3.59	<0.001
5 postoperative day	44.63±5.31	40.62±5.44	<0.05
6 postoperative day	45.95±6.56	42.03±5.60	<0.05
7 postoperative day	45.18±5.80	40.49±6.13	<0.05

PaCO<sub>2</sub> = partial pressure of carbon dioxide.

**Table 6 Comparison of SaO<sub>2</sub> changes in the first postoperative week in patients with or without POPCs in COPD group (mean±SD)**

Time	POPCs	Non-POPCs	P
1 preoperative day	94.48±1.93	94.44±1.51	0.940
1 postoperative day	94.56±1.18	93.78±1.80	0.095
2 postoperative day	94.01±1.94	94.30±1.39	0.572
3 postoperative day	95.39±1.15	94.56±1.75	0.077
4 postoperative day	94.65±1.27	95.31±1.15	0.079
5 postoperative day	94.94±1.39	94.26±1.81	0.176
6 postoperative day	94.88±1.60	94.96±1.74	0.868
7 postoperative day	95.02±1.16	94.61±1.90	0.399

SaO<sub>2</sub> = arterial oxygen saturation.

Moreover, patients with severe COPD (Grade II B, 30% ≤ FEV1%p < 50%) had more POPCs than patients with moderate (grade II A, 50% ≤ FEV1%p < 80%) and mild (grade I, FEV1%p ≥ 80%) COPD (P < 0.05).

The perioperative changes in arterial blood gases in patients with or without POPCs in COPD group are listed in Tables 4-6. In non-POPC group PaO<sub>2</sub> decreased in the first three days after operation and then gradually returned to its normal level. Values for PaCO<sub>2</sub>, SaO<sub>2</sub> and pH were in normal range. However, in POPC group, PaO<sub>2</sub> dropped significantly, recovered more slowly, and failed to return to normal at the end of the first week compared with non-POPC group. PaCO<sub>2</sub> in POPC group was significantly higher than that in non-POPC group in the first 7d, reaching more than 6Kpa in first postoperative week. In addition, there was no significant difference in SaO<sub>2</sub> and pH between the two groups.

## DISCUSSION

Transthoracic esophagectomy displays a remarkable effect on pulmonary function, including lung and chest wall compliance reduction, ventilation function reduction, increase of oxygen consumption<sup>[14]</sup>. Pulmonary complication is considered as one of the most serious and threatening complications after esophagectomy, and is associated with poor short- and long-term outcomes<sup>[9,15]</sup>. Postoperative pulmonary complications occur frequently after transthoracic esophagectomy for esophageal cancer, accounting for 7.3%-50%<sup>[9,13,16-18]</sup>. In addition to surgical techniques and perioperative management strategies, different definition criteria for pulmonary complications, patient selection and willingness of surgeons to undertake high-risk cases may influence the outcomes<sup>[4,19,20]</sup>.

COPD is considered as a postoperative pneumonia risk index and is significantly associated with the occurrence of pulmonary complications<sup>[21,22]</sup>. According to our definition, a higher rate of pulmonary complication is associated with esophageal resection for esophageal cancer with COPD, particularly in patients with percent-predicted FEV1 less than 50%. Pneumonia, atelectasis, prolonged O<sub>2</sub> supplement and prolonged mechanical ventilation are the major complications after esophagectomy. The incidence rate of pulmonary complication in COPD group was higher than that in non-COPD group. The incidence rates of acute respiratory distress syndrome and pulmonary abscess were lower. Moreover, pulmonary complications are associated with postoperative mortality and regarded as the most common cause of operation death.

To assess the independent effect of COPD, we matched

patients with severe COPD to comparison groups of patients with moderate and mild COPD. The rate of pulmonary complication increased along with percent-predicted FEV1 reduction, suggesting that percent-predicted FEV1 is a good risk factor for anticipating postoperative pulmonary complications after esophagectomy.

Previous studies indicate that various factors predispose to pulmonary complications<sup>[4,10,23-27]</sup>, including advanced age, history of smoking, cirrhosis and diabetes, abnormal chest radiograph or lung disease, blood loss and low serum albumin, preoperative chemoradiotherapy, general performance status, inadequate postoperative analgesia and stage of disease. Some cell factors have a relation with pulmonary complications after esophagectomy, such as secretory leukocyte protease inhibitor and angiotensin-converting enzyme<sup>[28,29]</sup>. Our analysis also demonstrated a correlation between percent-predicted FEV1 and pulmonary complication in patients with esophagectomy.

The changes of arterial blood gases coincided well with the timing of pulmonary complications in our patients which occurred in the first postoperative week. The pathophysiologic feature of this group was a further depression and patients had a poor prognosis. However, pH values and oxygen saturation had no remarkable change in the two groups.

Our study was not designed to determine if perioperative care could decrease the rate of pulmonary complications in patients with COPD after esophagectomy, but we believe that aggressive treatment is important in improving the outcome of pulmonary complication so that patients with COPD benefit from radical procedure. It was reported that effective treatment can reduce pulmonary complications<sup>[13]</sup>. Rehabilitation training, proper antibiotics and eliminating phlegm's drugs, atomization, stopping smoking, nutritional supplementation may have some benefits to patients with COPD before operation<sup>[30-32]</sup>. Regulation of intravenous transfusion volume can effectively prevent postoperative pulmonary edema and improve oxygenation<sup>[33]</sup>.

In conclusion, chronic obstructive pulmonary disease is the critical factor for the occurrence of postoperative pulmonary complications in esophageal cancer patients undergoing esophagectomy. Pulmonary complications go up along with the severity of COPD. Percent-predicted FEV1 is a good predictor for postoperative pulmonary complications. Arterial blood gases are helpful in directing perioperative management.

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