

# Comparison of perioperative characteristics and prognostic performance in patients with pulmonary lobectomy in early or later period after percutaneous coronary intervention

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**Background:** In order to analyze the feasibility of pulmonary lobectomy for non-small cell lung cancer (NSCLC) in early period after percutaneous coronary intervention (PCI), the current study was designed to compare perioperative characteristics and prognostic performance of patients with pulmonary lobectomy within 3 months or 3 months later after PCI.

**Methods:** This study enrolled 349 patients simultaneously with NSCLC and coronary stenosis. There were 198 and 151 patients with pulmonary lobectomy within 3 months or 3 months later after PCI, respectively.

**Results:** Age of all patients was 62 [53–75] years. There was no difference in demographic characteristics, medical histories, cancer locations and stent numbers between two groups (P>0.05 for all). Operation time, blood loss and hospital stay after pulmonary lobectomy had no difference between two groups (P>0.05 for all). Compared with those with pulmonary lobectomy 3 months later after PCI, survival rate during 5 years after pulmonary lobectomy was significantly higher in patients with pulmonary lobectomy within 3 months after PCI (P<0.05 for all).

**Conclusions:** Patients with pulmonary lobectomy within 3 months after PCI had similar perioperative characteristics and better prognostic performance, as compared to those with pulmonary lobectomy 3 months later after PCI. The current study could provide valuable information in patients simultaneously with NSCLC and coronary stenosis to decide the timing of pulmonary lobectomy, and it might be feasible to perform pulmonary lobectomy in early period after PCI.

**Keywords:** Percutaneous coronary intervention (PCI); coronary stenosis; non-small cell lung cancer (NSCLC); pulmonary lobectomy

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# Introduction

Both non-small cell lung cancer (NSCLC) and coronary artery disease (CAD) have high incidence and mortality, and cause social and economic burden all over the world (1). Previous study has suggested that 26.5% of patients diagnosed with lung cancer also had different degrees of CAD (2). Moreover, as the most effective treatment of NSCLC, pulmonary lobectomy leads to a deadly cardiovascular risk (3). During perioperative period of pulmonary lobectomy, cardiovascular risk has been estimated to be as high as 4.2% (4). In patients with lung cancer combined with CAD, percutaneous coronary intervention (PCI) has been considered as the optimal treatment to lower cardiovascular risk (5). Lacking antithrombotic therapy after PCI should be responsible for increased stent thrombosis and cardiovascular risk (6,7). Based on the recommendation by general guidelines, non-cardiac surgery is not very appropriate for patients who received PCI within 3–6 months (8).

However, it is not a good choice for patients with NSCLC to wait for delaying pulmonary lobectomy due to antithrombotic therapy after PCI. NSCLC cells with distinct differentiation degrees and histological types have a doubling time varying from 33 to 183 days, and its area could increase up to 373% after a median time of 54 days (9). Previous literature has shown that 26% of patients with lung cancer lost the opportunity to receive radical resection due to antithrombotic therapy (10). Simultaneous coronary artery bypass grafting and pulmonary lobectomy in patients with NSCLC have been tried previously, with a result of prolonged time of operation and hospitalization, as well as increased incidence of postoperative complications (11-13). The issue on how to perform pulmonary lobectomy as soon as possible without increasing cardiovascular risk is of great importance and needs to be clarified. In order to analyze the feasibility of pulmonary lobectomy for NSCLC in early period after PCI, the current study was designed to compare perioperative characteristics and prognostic performance of patients with pulmonary lobectomy within 3 months or 3 months later after PCI.

# Methods

# Study population

From January 2006 to December 2012, this retrospective study analyzed 562 patients who simultaneously had lung cancer and coronary stenosis in Chinese People's Liberation Army Hospital. Chest-enhanced computed tomography revealed that all of them had a diagnosis of lung cancer, and then 65 patients were excluded due to multiple pulmonary lobes or severe cancer metastasis found in examinations and no need of pulmonary lobectomy. A diagnosis of lung cancer was excluded in 12 patients due to pathological examination during operation. All patients with symptoms of myocardial ischemia received computed tomography angiography, which revealed that they had coronary stenosis and required coronary angiography. There were 123 patients excluded due to no severe coronary stenosis found in coronary angiography and no need of PCI, and 13 patients excluded due to small cell lung cancer and no need of pulmonary lobectomy. In all, 349 patients simultaneously received the treatment of pulmonary lobectomy and PCI. There were 198 and 151 patients who received pulmonary lobectomy within 3 months or 3 months later after PCI, respectively.

### Study procedure

Demographic characteristics and medical histories were obtained in all patients. Chest-enhanced computed tomography and computed tomography angiography were performed to assess lesion condition and severity. Cardiac and pulmonary function was assessed by echocardiogram and respiratory function instrument. Patients with suspected central-type lung cancer also received electronic fibre bronchoscope. Brain computed tomography, radionuclide bone scanning and ultrasounds in abdomen and lymph nodes were performed to identify patients with severe cancer metastasis who did not require pulmonary lobectomy. Perioperative characteristics and prognostic performance were compared between patients with pulmonary lobectomy within 3 months or 3 months later after PCI. Survival rate was the primary end-point, and no one was lost, during 5 years after pulmonary lobectomy.

# **Operative** procedure

Patients received coronary angiography under local anesthesia by one surgical team. Patients received stent implantation due to severe coronary stenosis. PCI had a success rate of 100%. Patients received open and videoassisted thoracoscopic pulmonary lobectomy under double lumen endotracheal intubation and general anesthesia by one surgical team. Single lung ventilation was performed in health lung. The upper lobe was resected from the fourth intercostal space, and the middle and lower lobes were resected from the fifth intercostal space. Hilar and mediastinal lymph nodes were dissected as follows: group 2-4 and 7-10 (right chest) and group 4-10 (left chest). Specimen was submitted to Pathology Department in Chinese People's Liberation Army Hospital for pathological examination. Success rate of pulmonary lobectomy was 100%, and there was no occurrence of pulmonary infection, wound infection, secondary operation and perioperative death. Postoperative chemotherapy was applied based on the TNM stages of patients as shown in Table 1. It was applied in patients with TNM stage II and TNM stage IIIa

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Characteristics	All (n=349)	Within three months (n=198)	Three months later (n=151)	P value
Age, year	62 [58–67]	61 [58–67]	63 [58–68]	0.452
Women, n (%)	85 (24.4)	51 (25.8)	34 (22.5)	0.485
CAD type, n (%)				0.451
Unstable angina	76 (21.8)	46 (23.2)	30 (19.9)	
Myocardial infarction	273 (78.2)	152 (76.8)	121 (80.1)	
Hypertension, n (%)	107 (30.7)	63 (31.8)	44 (29.1)	0.591
LVEF, %	49 [45–56]	49 [45–56]	50 [45–56]	0.804
Cancer locations, n (%)				0.778
Left upper	113 (32.4)	68 (34.3)	45 (29.8)	
Left lower	62 (17.8)	34 (17.2)	28 (18.5)	
Right upper	55 (15.8)	29 (14.6)	26 (17.2)	
Right middle	25 (7.2)	16 (8.1)	9 (6.0)	
Right lower	94 (26.9)	51 (25.8)	43 (28.5)	
TNM stages				0.861
I	81 (23.2)	48 (24.2)	33 (21.9)	
II	128 (36.7)	71 (35.9)	57 (37.7)	
Illa	140 (40.1)	79 (39.9)	61 (40.4)	
Pulmonary lobectomy				0.715
Open	168 (48.1)	97 (49.0)	71 (47.0)	
VAT	181 (51.9)	101 (51.0)	80 (53.0)	
Stent numbers, n (%)	777	456	321	0.739
LAD	303 (39.0)	176 (38.6)	127 (39.6)	
LCA	274 (35.3)	158 (34.6)	116 (36.1)	
RCA	200 (25.7)	122 (26.8)	78 (24.3)	

Table 1 Comparison of perio	operative characteristics bet	ween patients with puln	nonary lobectomy within	3 months or 3 months later after PCI

PCI, percutaneous coronary intervention; CAD, coronary artery disease; LVEF, left ventricular ejection fraction; LAD, left anterior descending artery; LCA, left circumflex artery; RCA, right coronary artery; VAT, video-assisted thoracoscopic.

rather than TNM stage I.

#### Antithrombotic treatment

Patients were administered loading doses (300 mg) of aspirin and clopidogrel before PCI (14,15). During PCI, patients were firstly administered unfractionated heparin (3,000 U). An additional dose (50–100 U/kg) of unfractionated heparin was administered after determining the protocol of PCI (16). Tirofiban was administered (5–8 mL/h) for 3 days after PCI, and patients took a daily dose of aspirin (100 mg) and clopidogrel (75 mg). Aspirin and clopidogrel were discontinued 7 days before pulmonary lobectomy, and low molecular heparin was administered until 12 hours before pulmonary lobectomy. Tirofiban (5–8 mL/h) was administered 3 days after pulmonary lobectomy, lasting for 7–14 days or until hospital discharge. Patients took a daily dose of aspirin (100 mg) and

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Within three months (n=198) Characteristics All (n=349) Three months later (n=151) P value 155 [142-171] 0.423 Operation time, min 156 [142-172] 155 [142-171] Blood loss, mL 191 [175-206] 192 [176-208] 189 [175-205] 0.346 751 [737-766] Chest drainage, mL 718 [488-757] 485 [468-501] < 0.001 Drainage time, d < 0.001 4 [2-7] 6 [2-8] 2 [1-5] Hospital stay, d<sup>a</sup> 11 [9-13] 11 [9-13] 11 [8-13] 0.305 Survival rate, n (%)<sup>a</sup> 81 (23.2) 54 (27.3) 27 (17.9) 0.039

Table 2 Comparison of prognostic performance between patients with pulmonary lobectomy within 3 months or 3 months later after PCI

PCI, percutaneous coronary intervention. <sup>a</sup>, After pulmonary lobectomy.

clopidogrel (75 mg) after hospital discharge.

# Discussion

# Statistical analysis

Continuous variables with normal distribution were described with mean (standard deviation), and compared between two groups with Student's *t*-test. Continuous variables with skewed distribution were described with median (interquartile range), and compared between two groups with Mann-Whitney U test. Categorical variables were described with number (percentage), and compared between two groups with Chi-square test. P value <0.05 was considered as statistically significant. Statistical analysis was performed by Statistic Package for Social Science (SPSS) version 17.0 software (SPSS Inc., Chicago, USA).

### Results

Age of all patients was 62 [53–75] years, and 75.6% were men (264 patients). As shown in *Table 1*, there was no difference in demographic characteristics, medical histories, cancer locations, TNM stages and stent numbers between two groups (P>0.05 for all). Operation time, blood loss and hospital stay after pulmonary lobectomy had no difference between two groups (P>0.05 for all; *Table 2*). Chest drainage was significantly less and drainage time was significantly shorter in patients with pulmonary lobectomy 3 months later after PCI than those with pulmonary lobectomy within 3 months after PCI (P<0.05 for all). Compared with those with pulmonary lobectomy 3 months later after PCI, survival rate during 5 years after pulmonary lobectomy was significantly higher in patients with pulmonary lobectomy was within 3 months after PCI (P<0.05 for all). In patients with NSCLC, pulmonary lobectomy is considered to be the most effective method with significant ability to improve their prognosis (3). Patients with pulmonary lobectomy often has different degrees of CAD and increased cardiovascular risk (2). Based on previous data, cardiovascular risk has been estimated to be as high as 4.2% in patients with pulmonary lobectomy (4). Antithrombotic therapy is crucial in patients with CAD to reduce stent thrombosis and cardiovascular risk (6,7). There is a controversy about the timing of pulmonary lobectomy and the safety of antithrombotic therapy after PCI. Previous study has suggested that pulmonary lobectomy in early period after PCI might worsen the prognosis of patients with NSCLC (17). However, rapid growth of NSCLC cells was irreversible if not be resected, and could cause patients to lose their opportunity for timely treatment (9,10). The current study compared perioperative characteristics and prognostic performance of patients with pulmonary lobectomy within 3 months or 3 months later after PCI to provide valuable information in clinical decision. Compared with those with pulmonary lobectomy 3 months later after PCI, the current study found similar perioperative characteristics and better prognostic performance in patients with pulmonary lobectomy within 3 months after PCI.

With regard to perioperative characteristics, patients with pulmonary lobectomy within 3 months after PCI had no obviously increased blood loss than those with pulmonary lobectomy 3 months later after PCI. The current study applied a clinically acceptable antithrombotic strategy, which might effectively balance perioperative hemorrhagic and thrombotic risk (14-16). As an antithrombotic drug

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with a short half-life period, tirofiban might be safe during perioperative period of pulmonary lobectomy after PCI. Chest drainage was significantly increased and drainage time was significantly lengthened by advanced pulmonary lobectomy. The dissociation of extensive adhesion aggravates pleural effusion, and antithrombotic therapy could further increase effusion (5).

Compared with those with pulmonary lobectomy 3 months later after PCI, these was no obviously prolonged operation time and hospital stay in patients with pulmonary lobectomy within 3 months after PCI. Operative complexity and patient recovery might not be affected by advanced pulmonary lobectomy. More importantly, survival rate during 5 years after pulmonary lobectomy was significantly improved due to advanced pulmonary lobectomy. Pulmonary lobectomy within 3 months after PCI combined with appropriate antithrombotic strategy might advance the timing of pulmonary lobectomy, improve the prognosis of patients with NSCLC and allow more patients to receive operative treatment.

#### Conclusions

The current study demonstrated similar perioperative characteristics and better prognostic performance in patients with pulmonary lobectomy within 3 months after PCI, as compared to those with pulmonary lobectomy 3 months later after PCI. The current study could provide valuable information in patients simultaneously with NSCLC and CAD to decide the timing of pulmonary lobectomy, and it might be feasible to perform pulmonary lobectomy in early period after PCI.

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#### Footnote

*Conflicts of Interest*: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi. org/10.21037/tcr.2019.09.23). The authors have no conflicts of interest to declare.

*Ethical Statement*: The authors are accountable for all aspects of the work in ensuring that questions related

to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study protocol has been approved by Ethics Committee of Chinese People's Liberation Army General Hospital (No: 2012-031) and it conforms to the Helsinki Declaration. Patient's consent was waived in this retrospective study.

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