Thoracic Cancer
Open Access
Thoracic Cancer ISSN 1759-7706

ORIGINAL ARTICLE

Video-assisted thoracoscopic lobectomy after percutaneous coronary intervention in lung cancer patients with concomitant coronary heart disease

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Keywords
Coronary heart disease; lung cancer; percutaneous coronary intervention; VATS.

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Received: 11 May 2017;
Accepted: 7 June 2017.

doi: 10.1111/1759-7714.12471

Thoracic Cancer **8** (2017) 477–481

Abstract

Background: In recent years, based on clinical observations, the number of lung cancer patients with concomitant coronary heart disease (CHD) has gradually increased. However, because of the requirement of long-term anticoagulant therapy after percutaneous coronary intervention (PCI), some of these patients lose the opportunity for surgical treatment, resulting in tumor progression. The objective of this study was to determine the appropriate timing of video-assisted thoracic surgery (VATS) lobectomy after PCI without increasing perioperative cardiovascular risk.

Methods: This study retrospectively analyzed clinical data of patients with a combination of NSCLC and CHD who underwent selective pulmonary lobectomy by VATS in the early postoperative PCI period between 2010 and 2015 at Beijing Chaoyang Hospital, China.

Results: Fourteen patients received VATS lobectomy after PCI. The disease had progressed to T stage in two patients after PCI. No perioperative death occurred. Two patients suffered postoperative atrial fibrillation: one had a pulmonary infection, and the other had acute coronary syndrome. All patients recovered and were discharged.

Conclusion: For NSCLC patients with severe CHD, the use of VATS lobectomy in the early postoperative PCI period could not only advance the timing of surgery, but may also control perioperative hemorrhage and CHD event risks within acceptable ranges, which could provide more patients with an opportunity to undergo surgical treatment.

Introduction

In 2015, epidemiological data indicated that mortality and incidence rates of pulmonary carcinoma continue to increase.[1] A study employing a Japanese cohort estimated that 26.5% of patients diagnosed with pulmonary carcinoma also had different degrees of coronary heart disease (CHD).[2] The perioperative risk of cardiovascular events in such patients is estimated to be as high as 4.2%.[3,4]

In patients with pulmonary carcinoma combined with CHD, percutaneous coronary intervention (PCI) is considered the most effective method to reduce the occurrence of postoperative acute coronary syndrome (ACS).[5] According to American Heart Association/American College of Cardiology (AHA/ACC) guidelines, patients could undergo selective non-cardiac surgery at some point between four and six weeks after bare-metal stent (BMS) implantation; however, because dual antiplatelet therapy takes longer than six weeks, ~26% of patients with lung cancer lose the opportunity to undergo radical resection treatment.[6] In addition, affected by degrees of differentiation and various other factors, the doubling time of different non-small cell lung cancer (NCSLC) cells of various histological types ranged from 33 to 183 days.[7,8] After a median duration of ~54 days, the sectional area of the tumor could increase up to 373%;[9] therefore, delaying surgery because of lengthy anticoagulant therapy after PCI is not recommended for patients diagnosed with pulmonary carcinomas. On the

other hand, previous studies have also indicated that insufficient anticoagulant therapy after PCI (within four weeks) could obviously increase the occurrence rate of myocardial infarction and massive hemorrhage.[10,11] Therefore, concern remains over how to perform surgery as soon as possible without increasing perioperative cardiovascular risks.

This study primarily aimed to summarize and discuss the clinical data of patients with a combination of NSCLC and CHD who underwent selective pulmonary lobectomy by video-assisted thoracic surgery (VATS) in the early postoperative PCI period to provide information on the perioperative treatment of these patients.

Methods

This retrospective study initially involved 890 patients with NSCLC who underwent selective VATS lobectomy between 2010 and 2015 at the Department of Thoracic Surgery at Beijing Chaoyang Hospital, China. After admission, the patients' tumors were assessed and their cardiac and pulmonary functions were evaluated. Before surgery, all patients received chest-enhanced computed tomography (CT) examinations to reevaluate the tumors. The 286 patients aged >60 years or who had symptoms of myocardial ischemia underwent a CT coronary angiography (CTCA), which revealed that 93 patients suffered from coronary artery stenosis and required a coronary angiography (CAG); 14 of these patients received PCI treatment during CAG because of severe coronary artery stenosis. The coronary stenosis index of these 14 patients was >75%, and they had symptoms of coronary artery disease in the last month before hospitalization.

Thus, we recorded and analyzed the general baseline, previous medical history, risk factors of heart and lung disease, and medication compliance of these 14 patients. Surgical data on PCI and VATS surgeries, postoperative data, and safety-related indicators (e.g. surgical complications) were also analyzed.

Patient data

The clinical data of the 14 patients (13 men) diagnosed with a combination of NSCLC and CHD who underwent selective pulmonary lobectomy by VATS in the early postoperative PCI period between 2010 and 2015 were collected. The mean age of the patients was 67.50 ± 8.94 years. Medical examinations revealed that eight of these patients had a combination of NSCLC and CHD, four had positive symptoms or signs of carcinoma and were hospitalized from the outpatient department, and one was diagnosed with paraneoplastic syndrome and hospitalized for further treatment. The tumor in one patient was discovered during a follow-up CT examination for another disease.

Cardiovascular risk factors and relevant past medical history

Thirteen patients had a medical history of hypertension, six had a medical history of diabetes mellitus, six had a smoking index >400, two had anemia, three had hyperlipidemia, two had a medical history of lower extremity edema, one had hypothyroidism, one had bronchial asthma, and one had varicose veins in the lower extremities. Two patients had a definite past medical history of CHD, two had symptoms or signs of discomfort in the precordial area, one had received stent implantation for the treatment of myocardial infarctions, and two were on long-term oral anticoagulants for the treatment of cardiovascular diseases.

Preoperative examinations

The CTCA results for all 14 patients showed moderate to severe coronary artery stenosis: 11 had left anterior descending artery (LAD) stenosis, nine had right coronary artery (RCA) stenosis, six had circumflex coronary artery stenosis, and one had obtuse marginal branch (OM) stenosis. Six cases had single-vessel lesions, three had double-vessel lesions, and five had triple-vessel lesions. Echocardiogram results indicated a mean cardiac ejection fraction of $67.28 \pm 4.70\%$.

Treatment

Coronary angiography and percutaneous coronary intervention (PCI)

The patients underwent CAG under routine local anesthesia. Patients whose CAG results suggested severe stenosis lesions of the local non-proximal LAD branch were required to undergo BMS implantation according to the degree of coronary stenosis.

Lung resection by video-assisted thoracic surgery (VATS)

After general anesthesia and double lumen endotracheal intubation, the patients underwent standard lung resection by VATS.[12] After the pulmonary lobe was resected, the hilar and mediastinal lymph nodes were dissected. A tumor located in the right lobe had a higher tendency to metastasize to the upper paratracheal, prevascular, retrotracheal, lower paratracheal, subcarinal, para-esophageal, pulmonary ligament, and hilar lymph nodes. A tumor located in the left lobe had a higher tendency to metastasize to the upper paratracheal, prevascular, retrotracheal, lower

paratracheal, subaortic, para-aortic, subcarinal, para-esophageal, pulmonary ligament, and hilar lymph nodes. All pulmonary specimens were submitted to the laboratory for further pathological examination.

Anticoagulation methods

Patients were administered loading doses of 300 mg clopidogrel and 300 mg aspirin before PCI treatment.[13,14] During PCI surgery, the patient was first administered 3000 U unfractionated heparin. After the protocol of the PCI treatment was decided, an additional dose of 70–100 U/kg unfractionated heparin was administered.[15] Patients were required to take a daily dose of 100 mg aspirin and 75 mg clopidogrel for three weeks after PCI,[12] and then 100 AXaIU/kg/d low molecular weight heparin (LMWH) for a week to prepare for the subsequent surgery. Approximately 12 hours after pulmonary lobectomy by VATS, patients with no obvious risk of hemorrhage were given an anticoagulation dose of 100 AXaIU/kg/d LMWH. After 72 hours, daily oral administration of 100 mg aspirin and 75 mg clopidogrel resumed.

Results

PCI treatment before VATS surgery

Twenty-four BMSs were implanted during PCI surgery. The vascular distribution was as follows: nine were implanted in the LAD region, seven in the left circumflex coronary artery region, seven in the RCA region, and one was implanted in the OM region. The mean intraoperative dose of heparin was 6464.29 ± 1393.17 U. The recanalization rate of the coronary arteries reached 100%. There was no postoperative residual coronary artery stenosis.

Pulmonary lobectomy by VATS

The period between coronary artery BMS implantation and pulmonary lobectomy in these 14 patients was 30.28 ± 2.84 days. The disease had progressed to T stage in two patients; none had progressed to N stage. Surgical resection was indicated (resectable tumor node metastasis stage) in all patients. Three patients underwent surgical resection of the right upper lobe, two of the right middle lobe, one of the right middle and lower lobes, one of the right lower lobe, two of the left upper lobe, and five underwent surgical resection of the left lower lobe. The mean surgical duration was 125.00 ± 38.33 minutes, the mean intraoperative blood loss was 162.14 ± 98.00 mL, and the mean chest drainage volume within the postoperative 24 hours was 314.64 ± 180.60 mL (hematodes exudate). The mean postoperative drainage was 5.07 ± 2.37 days, which was longer for patients who did not undergo PCI (5.07 ± 2.37 vs. 4.52 ± 1.67 days). After postoperative pathological examination, eight patients were diagnosed with pulmonary adenocarcinoma and six with pulmonary squamous carcinoma (Table 1).

Perioperative complications and death

Two patients suffered postoperative atrial fibrillation (Grade II) but recovered after treatment with cardioversion drugs. One patient suffered from pulmonary infection and atelectasis (Grade II); however, after consultation with the Infectious Diseases Department, a reasonable antibiotic treatment protocol was decided and the infection was controlled. One patient had symptoms or signs of chest tightness and shortness of breath (Grade IIIa). An electrocardiogram (ECG) indicated a decline in the S–T segment. After consultation with the cardiology department, the patient was administered isosorbide dinitrate intravenously for two days, after which the symptoms improved and the ECG results returned to normal.

Discussion

In patients with a combination of NSCLC and CHD, the main severe complication of surgery is the occurrence of ACS during the perioperative period. According to the literature, the postoperative risk of cardiac complications is as high as 4.2% in patients who have undergone pulmonary lobectomy and have a medical history of myocardial infarction or myocardial ischemia.[3,4] In high-risk surgical patients aged >60 years or with a medical history of myocardial ischemia, our CTCA results indicated that 32.5% (93/286) had different degrees of coronary artery stenosis, 4.9% (14/286) of which required PCI intervention. This

Table 1 Clinical data on 14 patients diagnosed with NSCLC combined with CHD who underwent selective pulmonary lobectomy by VATS in the early period after PCI

Item	Data
Single coronary intervention	9/14
Double coronary intervention	5/14
Operative time (minutes)	125.00 ± 38.3
Blood loss (mL)	162.14 ± 97.99
Chest drainage in the first 24 hours (mL)	314.64 ± 180.60
Change in hemoglobin (preoperative/12 hours after surgery)	–0.78 ± 0.79
Drainage days (days)	5.07 ± 2.36
Complications	4/14
TNM stage progression	2/14
Squamous cell carcinoma	6/14
Adenocarcinoma	8/14

CHD, coronary heart disease; NSCLC, non-small cell lung cancer; PCI, percutaneous coronary intervention; TNM, tumor node metastasis; VATS, video-assisted thoracic surgery.

study retrospectively reviewed the clinical data of these patients to provide further information for future treatment in clinical practice.

For NSCLC patients with a surgical indicator for radical resection, surgical treatment was recommended and was considered to be the main factor that influenced their prognosis; however, there was disagreement about the timing of the surgery and the safety of antithrombotic therapy after PCI. Previous studies have shown that surgical treatment within two to four weeks after PCI intervention could significantly increase the occurrence of perioperative death and cardiac ischemic events.[10,11,16] It is recommended that antithrombotic therapy after PCI treatment is prolonged within one tumor doubling period (about 33 days) to reduce the risk of stent thrombosis and ACS.[7,8]

Control of tumor progression

According to preoperative thoracic CT, two patients showed T stage progression; however, none of the patients progressed to N stage. Fourteen patients in stages IA–IIB underwent surgical treatment after receiving anticoagulant therapy for 30.28 ± 2.84 days after PCI treatment. This indicated that the progression conditions of patients with early NSCLC within one doubling period (33 days) were clinically acceptable; however, rapidly growing tumors could still cause patients to lose their opportunity for surgical treatment.

Hemorrhage risk

During evaluation of the data on acute hemorrhage, two patients were observed with a postoperative 24 hour drainage volume >600 mL. Because the patients had no obvious uncomfortable symptoms and their postoperative hemoglobin level was >10 g/dL, it was presumed that this drainage was related to increased pleural effusion induced by the dissociation of extensive adhesion; however, when LMWH anticoagulation was administered 12 hours after pulmonary lobectomy surgery, statistical results indicated that the drainage volume from the thoracic cavity gradually decreased 72 hours after surgery. The drainage tube was removed in most patients (13/14) between the third and seventh day after surgery when the daily drainage volume was <100 mL. The drainage tube in one patient with prolonged air leaks was removed on the 12th day after surgery. Thus, it was considered that this treatment strategy could be clinically acceptable to control perioperative hemorrhage risk.

Risk of coronary heart disease

A previous study reported that the occurrence of perioperative stent-related myocardial infarction was 6.2% (2/32) in patients who underwent pulmonary lobectomy within three months after PCI intervention,[17] while for those who underwent non-cardiac surgery within two to four weeks after PCI intervention, the occurrence of perioperative myocardial infarction was 20% (8/40).[10] However, another study showed that the occurrence rates of perioperative myocardial infarction and myocardial ischemia were 0.6% (10/1383) and 13.3% (184/1383), respectively, in patients who waited six weeks after PCI.[17] In our study, one patient (7.1%) suffered postoperative chest tightness and an ECG ST–T segment change, which was considered to be postoperative ACS. After two days of vasodilation, the patient achieved complete remission, and the possibility of myocardial infarction was excluded.

In patients diagnosed with a combination of NSCLC and CHD who underwent selective pulmonary lobectomy by VATS during the early postoperative period after PCI treatment, operation stress and intermittent anticoagulant therapy resulted in ~6–7% of patients suffering postoperative complications, such as acute coronary artery occlusion and stent thrombosis. For these high-risk patients, under the conditions of active antithrombotic therapy, ECG should be continually monitored during the perioperative period. When ECG results show abnormalities, the patient should undergo a timely and dynamic myocardial enzyme spectrum test as soon as possible to assess and treat perioperative ACS and myocardial infarction. When there is no risk of hemorrhage within 12 hours after surgery, the patients should receive LMWH treatment as early as possible to ensure the continuity of the antithrombotic therapy and greatly decrease the risk of coronary stent restenosis.

In patients who also have pleural adhesions or bronchiectasis, the drainage volume induced by the dissociation of extensive adhesion is always higher, and anticoagulant therapy could further increase exudation. In such patients, intraoperative hemostasis needs to occur before postoperative anticoagulant therapy can be administered. Meanwhile, ECG and myocardial enzyme spectrum changes should be monitored simultaneously.

Study limitations

Because of the small sample size, all possible complications in patients with NSCLC and CHD treated with PCI intervention were not observed in our study. Further studies using larger sample sizes are required to obtain accurate statistical data. Our research only indicates the safety of pulmonary lobectomy by VATS in the early postoperative PCI period and we have little evidence of the long-term effect.

For patients diagnosed with a combination of NSCLC and severe CHD, PCI intervention is recommended as soon as possible, followed by three weeks of dual antiplatelet therapy, a week of LMWH antithrombotic therapy, and

lung resection by VATS. LWMH antithrombotic therapy should be resumed within 12 hours after surgery and dual antiplatelet therapy within three days after surgery. This treatment strategy could not only advance the timing of surgery, but may also control perioperative hemorrhaging and CHD event risks to within acceptable ranges, which could allow more patients the opportunity to undergo surgical treatment.

Disclosure

No authors report any conflict of interest.

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