


Single-Stage Surgical Procedure for Patients with Primary Esophageal and Lung Cancers

Jiang Lianyong¹  Hu Fengqing¹ Xie Xiao¹ Zhang Xuefeng² Bi Rui¹

¹ Department of Cardiothoracic Surgery, Xinhua Hospital Affiliated to Shanghai Jiaotong University School of Medicine, Shanghai, China

² Department of Radiology, The First Affiliated Hospital, Naval Medical University, Shanghai, China

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Address for correspondence Zhang Xuefeng, MD, PhD, Department of Radiology, The First Affiliated Hospital, Navy Medical University, Shanghai, China (e-mail: zhangxf0622@126.com).

Bi Rui, MD, Department of Cardiothoracic Surgery, Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, China (e-mail: birui@xinhuaamed.com.cn).

Abstract

Background The aim of this study was to evaluate the safety and feasibility of simultaneous surgery for patients with primary esophageal and lung cancers.

Methods Patients with primary esophageal and lung cancers who underwent simultaneous surgical procedures between January 2016 and January 2022 were retrospectively analyzed. The data of patients who underwent esophagectomy and lobectomy (group EL) were compared with those of patients who underwent esophagectomy and sublobar resection (group ES).

Results A total of 21 patients were included with an average age of 64.62 ± 5.24 years. Group EL contained 8 patients and group ES contained 13 patients. All procedures were completed uneventfully with a mean operative time of 251.19 ± 66.93 minutes. Pulmonary complications occurred in six (28.57%) patients. Other complications included anastomotic leakage in 1 patient, pleural effusion requiring drainage in 8 patients, atrial fibrillation in 2 patients, and incision infection in 1 patient. All patients were followed up for 30.23 ± 21.82 months. During the follow-up period, nine patients had a recurrence of cancer and died of tumor progression, and one patient died of a tracheothoragogastric fistula. Complications and mortality in group EL did not increase when compared to those in group ES.

Conclusion It is safe and feasible to perform a single-stage surgical procedure for patients with primary esophageal and lung cancers. Simultaneous esophagectomy and lobectomy did not increase postoperative complications or mortality compared with esophagectomy and sublobar resection.

Keywords

- esophageal surgery
- lung cancer treatment (surgery medical)
- outcomes (includes mortality morbidity)
- surgery
- complications

Although not a frequently encountered pattern, patients with concomitant primary esophageal and lung cancers are not rare in clinical practice. Fékété et al reported that 3.2% of patients with esophageal squamous cell carcinoma had primary lung carcinoma.¹ A single-stage procedure was reported by some authors for patients with synchronous esophageal and lung cancers, but most of them were

described in case reports or small groups.^{2–4} The literature describing the safety and feasibility of combined resections of synchronous esophageal and lung cancers is limited, especially in patients who underwent esophagectomy and lobectomy.⁵ From January 2015 to January 2022, 1,155 patients with esophageal carcinoma underwent surgical treatment in our center, and 21 (1.8%) of them with primary

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lung cancer received pulmonary resection simultaneously. We retrospectively analyzed the clinical data and follow-up results of these patients and compared the data of patients who underwent esophagectomy and lobectomy with those of patients who underwent esophagectomy and sublobar resection. The aim of this study was to evaluate the safety and feasibility of simultaneous surgery for these patients and to identify appropriate operative procedures.

Patients and Methods

We conducted a retrospective analysis of consecutive patients who underwent simultaneous resection for primary esophageal carcinoma and lung cancer in our center between January 2015 and January 2022. All the patients underwent chest enhanced computed tomography (CT), whole-body positron emission tomography (PET-CT), esophageal endoscopy, electrocardiography, echocardiography, pulmonary function, blood gas analysis, blood classification, and biochemical tests before the operation. Esophageal carcinoma was diagnosed by endoscopy and biopsy preoperatively. Tracheoscopy was performed for patients with central pulmonary nodules. A fine-needle biopsy was conducted when peripheral pulmonary nodules cannot be clearly diagnosed by PET-CT. Angiography of the coronary artery was performed for patients with suspected coronary heart disease. All pathological specimens were examined by two experienced thoracic pathologists. The lesion was diagnosed as primary lung cancer and esophageal carcinoma based on histological findings and immunohistochemical examination. Patients with pulmonary benign or metastatic lesions were excluded. Staging for esophageal carcinoma and lung cancer was classified according to the 8th edition tumor-node-metastasis (TNM) classification defined by the Union for International Cancer Control and American Joint Committee on Cancer. Written informed consent was obtained from the patients. The study was approved by the ethics committee of Xinhua Hospital Affiliated to the Medical College of Shanghai Jiaotong University.

The operative approach for esophageal carcinoma was modified according to the associated pulmonary operation, and all thoracotomies were made on the same side as the pulmonary operation to limit operative invasion. Esophagectomy was carried out with systematic lymph node dissection in all patients. Reconstruction was performed by a gastric tube through the posterior mediastinal or retrosternal route. All patients who underwent left thoracotomy had intrathoracic esophagogastrostomy, and patients who underwent right thoracotomy adopted intrathoracic or cervical gastroesophageal anastomosis according to the habit of the operator. Lobectomy with regional lymph node dissection is considered a standard procedure for lung cancer. However, wedge resection or segment resection is also considered in patients with peripheral ground-glass nodules ≤ 2 cm.

Postoperative complications were defined as any complication occurring during the hospital stay. Pulmonary complications were defined as the presence of one or more of the following postoperative conditions: initial ventilatory

support for more than 48 hours, reintubation for respiratory failure, need for tracheostomy, pneumonia, or acute respiratory distress syndrome (ARDS).^{6,7} Pneumonia was defined as the presence of new infiltrates upon chest radiography and a positive culture from the bronchoalveolar lavage. ARDS was defined as the existence of a $PO_2:FiO_2$ ratio less than 200 using a positive end-expiratory pressure greater than 5 cm H_2O for more than 24 hours, with bilateral pulmonary opacities but without clinical suspicion of cardiac failure or fluid overload.⁷ Anastomotic leakage was defined as anastomotic dehiscence that was clinically symptomatic (abscess, mediastinitis, externalized drainage of digestive fluid) or clinically asymptomatic but detected by upper gastrointestinal contrast after esophagectomy.

The following clinical characteristics were retrieved from the available medical records: age, sex, body mass index (BMI), history of radiotherapy, chemotherapy and immunotherapy, comorbidity, location of esophageal and lung cancers, diameter of lung cancer, details of esophagectomy and lung resection, postoperative course and complications, histology and pathological stage of lung cancer and esophageal carcinoma, and follow-up.

Postoperative Management and Follow-Up

Patients had scheduled follow-up visits 1, 3, and 6 months postoperatively and then every 6 months thereafter. If the patients did not return to our center, they were asked to undergo examinations in their local hospitals, and the follow-up data were obtained by telephonic interviews with the patients or their family members. The follow-up visits included blood classifications, biochemical tests, abdominal ultrasound, ultrasound of cervical and supraclavicular lymph nodes, and chest CT. Bone scans and brain magnetic resonance imaging (MRI) were performed every year.

Statistical Analysis

The numerical data are expressed as the number of cases (n) and percentage (%). The normal distribution of the data was checked by the Kolmogorov–Smirnov test. Continuous variables with a normal distribution are expressed as the mean \pm standard deviation. Continuous variables with non-normal distributions are expressed as medians and interquartile ranges (IQRs). Comparisons among normally distributed continuous variables were conducted via t -tests. The comparisons among non-normally distributed variables were conducted via the Mann–Whitney U test. The comparisons between enumeration data were conducted by the chi-squared or Fisher's exact method. Analyses were conducted with SPSS Statistics 18 software (IBM Corporation). A p value less than 0.05 was considered statistically significant.

Results

A total of 21 patients were included in this study; there were 20 males and 1 female with an average age of 64.62 ± 5.24 (53–75) years. Twenty patients had one esophageal

carcinoma and one lung cancer, and 1 patient had one esophageal carcinoma and two lung cancers located in the left lower lung and the right upper lung. No patient received preoperative radiotherapy, four patients received preoperative chemotherapy, and two patients received preoperative chemotherapy and immunotherapy. No moderate or above valvular disease was found by echocardiography, and the left ventricular ejection fraction was normal in all patients. Six patients received angiography of the coronary artery, and two patients had mild to moderate coronary stenosis. Atrial fibrillation was diagnosed by electrocardiogram in one patient. Pulmonary function and blood gas analyses were normal in all patients. The patients' baseline characteristics are summarized in ►Table 1.

Twelve patients with esophageal and right lung cancers underwent esophagectomy in 4 cases and lung resections via right thoracotomy, cervical esophagogastrostomy, and thoracic esophagogastrostomy were performed in 8 cases. All nine patients with left lung cancers underwent esophagectomy and thoracic esophagogastrostomy through left thoracotomy, including the patient with bilateral lung cancers (the patient underwent right upper lobectomy 4 months later). Of the 21 patients, wedge resections were performed in 10 patients, and segment resections and lobectomies were

performed in 3 and 8 patients, respectively. Procedural success occurred in all patients without intraoperative complications. The mean operative time was 251.19 ± 66.93 (160–410) minutes, with a mean intraoperative blood loss of 157.14 ± 100.36 (50–500) mL, and no blood product transfusions occurred during hospitalization. The median duration of mechanical ventilation was 6 hours, and the length of intensive care unit (ICU) stay was 2 days. The mean drainage time was 11.00 ± 6.00 (6–33) days, with a total drainage volume of $3,111.43 \pm 3,304.68$ (850–16,630) mL. Patients were discharged after a mean postoperative hospitalization of 17.71 ± 9.86 (9–47) days. The operative data and pathological stage of cancers are detailed in ►Tables 2 and 3.

Pulmonary complications occurred in 6 patients, including initial ventilation greater than 48 hours in 3 (14.29%) patients, reintubation in 2 (9.52%) patients, and pneumonia in 6 (28.57%) patients. The other complications included anastomotic leakage in 1 patient; pleural effusion requiring drainage in 8 patients, of which 1 occurred on the surgical side and 7 occurred in the contralateral thorax cavity; 2 patients developed atrial fibrillation and recovered sinus rhythm after antiarrhythmic drug treatment; and 1 patient developed incision infection on the third day postoperatively and recovered after debridement. All patients were followed up for 30.23 ± 21.82 (4–77) months. Fourteen patients received adjuvant treatment. Nine patients with lymph node metastasis received chemoradiotherapy, five patients with

Table 1 Baseline characteristics of patients

Variables	Patients (n = 21)
Age (y), mean \pm SD	64.62 \pm 5.24 (53–75)
Gender	
Male	20
Female	1
BMI (kg/m ²), mean \pm SD	21.36 \pm 2.38 (17.1–25.6)
Histology of esophageal carcinoma	
Squamous cell carcinoma	19
Adenocarcinoma	2
Location of esophageal carcinoma	
Proximal esophagus	1
Middle esophagus	12
Distal esophagus	8
Location of lung cancer^a	
Left (upper/lower)	9 (4/5)
Right (upper/middle/lower)	12 (8/1/3)
Diameter of lung cancer (mm), mean \pm SD ^a	14.52 \pm 6.25 (7–30)
Comorbidity	
Hypertension	5
Diabetes	2
Coronary heart disease	2
Atrial fibrillation	1

Abbreviations: BMI, body mass index; SD, standard deviation.

^aThe data of the right lung cancer of the patient with bilateral lung tumors were excluded.

Table 2 Operative and pathological data of patients

Variables	Patients (n = 21)
Surgical approach of esophageal carcinoma	
TLT (thoracotomy/VATS)	9 (9/0)
TART (thoracotomy/VATS)	8 (4/4)
TARTC (thoracotomy/VATS)	4 (3/1)
Route of gastric tube	
Posterior mediastinal	20
Retrosternal	1
Surgical approach to lung cancer	
Wedge (left/right)	10 (3/7)
Segment (left/right)	3 (1/2)
Lobectomy (left/right)	8 (5/3)
Operative time (min), mean \pm SD	251.19 \pm 66.93 (160–410)
Intraoperative blood loss (mL), mean \pm SD	157.14 \pm 100.36 (50–500)
Histology of lung cancer	
Squamous cell carcinoma	1
Microinvasive adenocarcinoma	7
Invasive adenocarcinoma	13

Abbreviations: SD, standard deviation; TART, transabdominal right thoracic esophagectomy; TARTC, transabdominal right thoracocervical esophagectomy; TLT, transleft thoracic esophagectomy; VATS, video-assisted thoracoscopic surgery.

Table 3 Histology and pathological stage of lung cancer and esophageal carcinoma

No.	Group	Location of esophageal carcinoma	Histology of esophageal carcinoma	Pathological stage of esophageal carcinoma	Histology of lung cancer	Pathological stage of lung cancer
1	ES	D	SCC	T3N1M0	MIA	T1aN0M0
2	ES	M	SCC	T3N0M0	IA	T1bN0M0
3	ES	M	SCC	T3N0M0	IA	T1bN0M0
4	EL	D	SCC	T2N0M0	IA	T1cN0M0
5	ES	M	SCC	T1bN0M0	IA	T1bN0M0
6	ES	D	AC	T3N2M0	MIA	T1aN0M0
7	ES	D	SCC	T3N2M0	IA	T1bN0M0
8	ES	P	SCC	T3N0M0	IA	T1bN0M0
9	EL	M	SCC	T3N2M0	IA	T1bN0M0
10	ES	M	SCC	T3N1M0	MIA	T1aN0M0
11	EL	M	SCC	T2N1M0	IA	T1aN0M0
12	EL	M	SCC	T3N1M0	IA	T2aN0M0 ^a
13	ES	M	SCC	T1bN0M0	MIA	T1aN0M0
14	ES	M	SCC	T2N0M0	MIA	T1aN0M0
15	ES	M	SCC	T3N0M0	IA	T1bN0M0
16	EL	D	SCC	T3N0M0	IA	T1aN0M0
17	EL	M	SCC	T3N2M0	SCC	T2aN2M0
18	ES	D	AC	T3N2M0	MIA	T1aN0M0
19	ES	D	SCC	T2N0M0	MIA	T1aN0M0
20	EL	M	SCC	T1bN0M0	IA	T1cN0M0
21	EL	D	SCC	T3N0M0	IA	T2aN1M0 ^a

Abbreviations: AC, adenocarcinoma; D, distal esophagus; EL, esophagectomy combined with lobectomy; ES, esophagectomy combined with sublobar resection; IA, invasive adenocarcinoma; M, middle esophagus; MIA, microinvasive adenocarcinoma; P, proximal esophagus; SCC, squamous cell carcinoma.

^aTumor invading the pleura.

T3N0M0 cancer received chemotherapy, and seven patients did not receive adjuvant treatment due to early staging or physical conditions. During the follow-up period, eight patients had a recurrence of esophageal carcinoma, and one patient had a recurrence of T2aN2M0 lung cancer (no. 17 in ►Table 3). Death occurred in 10 patients; 9 of them died of tumor progression of esophageal carcinoma, and the other patient developed a tracheothoracogastric fistula 3 months postoperatively and finally died of pulmonary infection 1 month later (no. 21 in ►Table 3).

A comparison of surgical outcomes between patients who underwent esophagectomy combined with lobectomy (group EL) and patients who underwent esophagectomy combined with sublobar resection (group ES) is summarized in ►Table 4. Patients in group EL were older and had larger tumor diameters than those in group ES. The average operating time, blood loss, duration of ventilation, length of ICU stay, duration of drainage, and postoperative hospital stay did not differ between the two groups, but patients in the EL group had a larger total drainage volume than those in the ES group. There was also no difference in complications or mortality between the two groups.

Discussion

Surgical resection is the most effective treatment for both resectable esophageal and lung cancers but represents a special challenge in the setting of patients with two synchronous tumors. A two-stage operation can minimize the risk of simultaneous occurrence of major pulmonary complications and anastomotic failure; it is conducive to the short-term rehabilitation of patients, but it also has some disadvantages, as tumors progress in the blank period, leading to prolonged overall hospital stays and increased cost, and two operations within a short period are also a burden to patients.^{8,9} Considering the above situation, thoracic surgeons and patients always hope to treat two kinds of tumors in one operation. However, performing two different operations simultaneously results in more extensive resection and greater surgical trauma, which may be adverse to the rehabilitation of patients. Therefore, we are most concerned about whether a single-stage operation will increase the incidence of perioperative complications and mortality.

Pulmonary complications are one of the most common postoperative complications of esophagectomy, with an

Table 4 Comparison of surgical outcomes between group EL and group ES

Variables	Group EL (n = 8)	Group ES (n = 13)	p value
Gender (male/female)	8/0	12/1	1.000
Age(y), mean \pm SD	68.38 \pm 4.03	62.31 \pm 4.59	0.006
BMI (kg/m ²), mean \pm SD	20.73 \pm 2.29	21.75 \pm 2.44	0.353
Diameter of lung cancer (mm), mean \pm SD	19.25 \pm 6.90	11.62 \pm 3.64	0.003
Surgical approach of esophageal carcinoma			
TLT	5	4	0.163
TART	1	7	
TARTC	2	2	
Operative time (min), mean \pm SD	265.63 \pm 83.77	242.31 \pm 56.11	0.452
Intraoperative blood loss (mL), mean \pm SD	206.25 \pm 139.99	126.92 \pm 52.50	0.078
Duration of ventilation (h), median (25 and 75%)	15.5 (4.75 and 124.5)	5 (1 and 15.5)	0.161
Length of ICU stay (d), median (25 and 75%)	3 (1 and 11)	2 (1 and 2.5)	0.456
Duration of drainage (d), mean \pm SD	13.75 \pm 8.71	9.31 \pm 2.75	0.100
Total drainage volume (mL), mean \pm SD	4,940 \pm 4,887.31	1,986.15 \pm 816.87	0.043
Postoperative hospital stays (d), mean \pm SD	18.63 \pm 10.10	17.15 \pm 10.07	0.749
Follow-up time unit is month (m)	22.25 \pm 20.69	35.15 \pm 21.79	0.195
Complications			
Initial ventilation >48 h	2	1	0.531
Reintubation	2	0	0.133
Pneumonia	4	2	0.146
Anastomotic leak	1	0	0.381
Pleural effusion requiring drainage	4	4	0.646
Atrial fibrillation	2	0	0.133
Incision infection	0	1	1.000
Deaths	3	6	1.000

Abbreviations: BMI, body mass index; EL, esophagectomy combined with lobectomy; ES, esophagectomy combined with sublobar resection; SD, standard deviation; TART, transabdominal right thoracic esophagectomy; TARTC, transabdominal right thoracocervical esophagectomy; TLT, trans-left thoracic esophagectomy.

incidence of 7 to 38%.^{10–12} Several risk factors have already been reported for the occurrence of pulmonary complications, and they vary among studies due to the definition of pulmonary complications and the type of surgery.^{7,13} However, most previous studies have shown that impairment of pulmonary function is an independent risk factor.^{11,14,15} Lung resection results in a persistent reduction in postoperative pulmonary function of 10 to 40%, which may contribute to functional impairments.^{16,17} Esophagectomy combined with lung resection, especially lobectomy, may further increase the incidence of pulmonary complications and may lead to high mortality, so some doctors choose a two-stage surgical procedure or even an entirely nonsurgical approach for high-risk patients.⁹ Several studies reported their experience of simultaneous resection of esophageal and lung cancers, but most of them reported no pulmonary complications. Wang and colleagues reported only one respiratory failure in their 14 patients who underwent esophagectomy and lobectomy. This low incidence of pulmonary complica-

tions may be related to their limited cases and the patients' good condition.^{2–5} In our study of 21 patients, pulmonary complications occurred in 6 (28.57%) patients, and most of them had a prolonged ICU stay and postoperative length of stay. The results are comparable to the postoperative pulmonary complications of patients who underwent esophageal resection alone reported in the literature.¹²

Anastomotic fistula is a serious postoperative complication of esophageal cancer, with an incidence of 8.2 to 15%.^{18–20} The occurrence of anastomotic leakage is related to the anastomotic mode, tension of the anastomotic site, and nutritional status of the patient before the operation. Anastomotic leakage is less frequent with thoracic anastomosis than cervical anastomosis. In our study, anastomotic leakage occurred in one patient (4.76%), and the low incidence of anastomotic leakage may be attributed to the high application rate of intrathoracic anastomosis. Thoracic fistula is considered to be more life-threatening because thoracic anastomotic fistula can lead to pleural membrane pollution

and sepsis. For patients who undergo simultaneous esophagectomy and lung resection, once anastomotic fistula occurs, it may also cause tracheal fistula because the naked tracheal stump is easily vulnerable to inflammation and gastric acid. Therefore, some scholars advocate neck anastomosis for patients undergoing simultaneous surgery and even staged procedures in high-risk patients.^{5,9} Some doctors use pedicled flaps to cover the bronchial stump, and they believe that pedicled flaps can promote the healing of bronchial stumps and reduce the occurrence of bronchial fistula.^{2,5} In our study, considering simplifying the operation and reducing the surgical trauma, most of the patients underwent thoracic anastomoses, no pedicled flap was used, and there was no occurrence of bronchial fistula.

Other complications in our study included pleural effusion requiring drainage, atrial fibrillation, and incision infection. Pleural effusion requiring drainage was the most common postoperative complication in this cohort, accounting for 38% (8/21) of patients, which may be related to extensive resection and lymph node dissection. It can also explain the large amount of pleural drainage in this group, especially in patients with esophagectomy and lobectomy. This deserves our attention because a large amount of pleural effusion may result in atelectasis or infection of the lung and affect the recovery of pulmonary function. Atrial fibrillation is one of the most common complications after thoracic surgery and may increase the length of stay and the incidence of complications. There are many reasons related to postoperative atrial fibrillation, and the extent and type of thoracic surgery were reported to affect the likelihood of developing atrial fibrillation. According to these studies, pneumonectomies and lobectomies generally carry a greater risk than wedge resection (>15 vs. 5–15%).^{21,22} In our study, two patients (9.52%) in group EL developed atrial fibrillation, and there was no difference in the incidence between the EL and ES groups. The simultaneous procedure did not seem to increase the incidence of postoperative atrial fibrillation in our limited cases, even in patients who underwent esophagectomy and lobectomy.

Lobectomy with regional lymph nodes has been considered a standard resection for non-small-cell cancer (NSCLC).²³ Several studies in recent years have shown that sublobar resection and lobectomy may have equivalent survival for patients with early-stage lung cancer.^{24,25} Other studies have shown that sublobar resection is beneficial to the protection of lung function and is especially suitable for some high-risk patients with pulmonary insufficiency or other combined diseases.^{26,27} A recent prospective study conducted by Saji and coworkers showed that segmentectomy contributes to the protection of lung function, but it is not as effective as we expected; the differences in the proportions of median forced expiratory volume in first second (FEV1) reduction between the segmentectomy and lobectomy groups were 2.7% at 6 months and 3.5% at 12 months postoperatively.²⁸ In our study, 8 patients received lobectomy, and compared to the 13 patients who received wedge resection or segmentectomy, there was no difference in the duration of ventilation, length of ICU stay, postoperative hospital stay, or complications. Our data showed that esophagectomy combined with lobectomy did

not increase the postoperative risk of patients when compared with esophagectomy combined with sublobar resection.

Conclusion

In summary, it is safe and feasible to perform esophagectomy and lung resection simultaneously for patients in good condition, and simultaneous esophagectomy and lobectomy did not increase postoperative complications or mortality compared with esophagectomy and sublobar resection. Of course, this study has many limitations. First, this is a retrospective study with limited cases. We only selected patients with good conditions for surgical treatment, but patients who chose nonsurgical treatment were not included in this study, which may affect the incidence of postoperative complications. Second, most patients who underwent lobectomy underwent left thoracotomy, and most patients who underwent right thoracotomy underwent sublobar resection. This selection bias may affect our results. Third, we did not compare the results with those of patients who underwent esophagectomy alone, so it is not clear whether combined surgery will increase complications. Finally, most patients in this group died of esophageal cancer progression, but due to too many confounding factors and limited cases, it is not clear whether the modified left thoracotomy procedure will affect the prognosis of patients.

Conflict of Interest

None declared.

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