



# Outcomes of the Modified Thoracoscopic En-bloc Esophagectomy in Patients with Esophageal Cancer

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## Abstract

**Background:** Esophageal cancer is one of the most prevalent types of cancer and causes of death worldwide. As the mainstream treatment, surgical resection is technically demanding and time-consuming. Therefore, the scope of its application is limited in the clinical setting. A new surgical approach is thus needed for an improved surgical effect and the prognosis of esophageal cancer.

**Objectives:** This study aimed to investigate the effect of a modified thoracoscopic en-bloc esophagectomy on the removal of patients' esophageal cancers and its outcomes.

**Methods:** In this study, a modified en-bloc esophagectomy was developed to remove esophageal cancer. Patients who underwent the modified en-bloc esophagectomy by right thoracoscopic approach or thoracoscope-assisted small incisional approach to have their esophageal cancers removed in Peking University First Hospital (Beijing, China) between January 2014 and January 2017, were screened and retrospectively studied. Cancer recurrence, overall survival, mortality, as well as intraoperative and postoperative outcomes, were reported.

**Results:** A total of 31 patients (22 male and 9 female, mean age: 62.9 years) were included in the study. Out of 30 patients with R0 resection, eight patients had cancer recurrences in the neck, lung, liver, and bone; however, none of the recurrences was identified in the mediastinum. Six patients died during the follow-up period. By the end of December 2020, the five-year survival rate of all patients was 58.3%. The median survival time of N0 patients was 52 months, which was significantly longer than that in N1+2 patients (23 months). Additionally, there was no statistically significant difference between the median survival time of N1 and N2 patients. Moreover, perioperative complications included pneumonia, arrhythmia, hoarseness, and chylous ascites, which were consistent with those reported previously.

**Conclusion:** The modified en-bloc esophagectomy to remove esophageal cancer by right thoracoscopic approach or thoracoscope-assisted small incisional approach was found safe and reliable due to decreased cancer recurrence, increased overall survival rate, and prolonged survival time.

**Keywords:** En-bloc, Esophageal cancer, Esophagectomy, Mortality, Thoracoscopy, Tumor recurrence

## 1. Background

Esophageal cancer is the eighth most frequent cancer and the sixth leading cause of cancer death worldwide (1,3), whose mainstay treatment is surgical resection (4). Postoperative cancer recurrence often happens in the mediastinal area, which could predict the prognosis of the patients (5-7). Therefore, an essential step during surgical esophagectomy is to radically remove the local cancerous tissue to minimize the risk of recurrence (8, 9).

In 1963, Logan *et al.* proposed the en-bloc esophagectomy to remove esophageal cancer with the basic principle of completely resecting the tumor-bearing esophagus, as well as the surrounding soft tissues and lymphatic system (10). This procedure has been shown to improve the outcomes of patients with esophageal cancer (11). However, en-bloc esophagectomy via the transthoracic approach is technically demanding and time-consuming, which limits its application in the clinical setting (12). Other surgical approaches to remove esophageal cancer include the transhiatal route, right thoracotomy with laparotomy, and cervical esophago-gastric anastomosis

(4). However, studies have shown that these approaches have high risks for complications with high mortality rates. As a result, it is crucial to improve the surgical approach for better outcomes in patients with esophageal cancer.

Minimally invasive surgery has been applied successfully to remove gastric and lung cancer (13). The thoracoscopic minimally invasive approach was also reported as a method of esophageal cancer resection (14,15).

## 2. Objectives

This study aimed to investigate the effect of a modified thoracoscopic en-bloc esophagectomy on the removal of patients' esophageal cancers and its outcomes.

## 3. Methods

### 3.1. Study design and patients

In this retrospective study, patients who received the modified en-bloc esophagectomy in Peking University First Hospital (Beijing, China) between January 2014 and January 2017 were reviewed. Their

esophageal cancers were removed either through the right thoracoscopic or the thoracoscope-assisted small incisional approach. All surgical operations were performed by the same team of thoracic surgeons in the hospital, and the resected tissues were sent for pathological examinations to the hospital's pathology laboratory. Postoperatively, all patients were admitted into the surgical intensive care unit for observation and treatment. The study protocol was approved by the hospital's Ethics Committee.

Patients were selected if they met the following inclusion criteria: 1) adult patients with a diagnosis of esophageal cancer based on the published guidelines (16), and 2) no distant metastasis confirmed by a bone scan, computerized tomography, or ultrasound studies. On the other hand, patients with the following features were excluded from the study: 1) incomplete data, 2) a follow-up period of <3 months, 3) other cancer(s) identified during the follow-up period, or 4) neoadjuvant chemo-radiation therapy before the surgery.

### 3.2. Surgical procedures

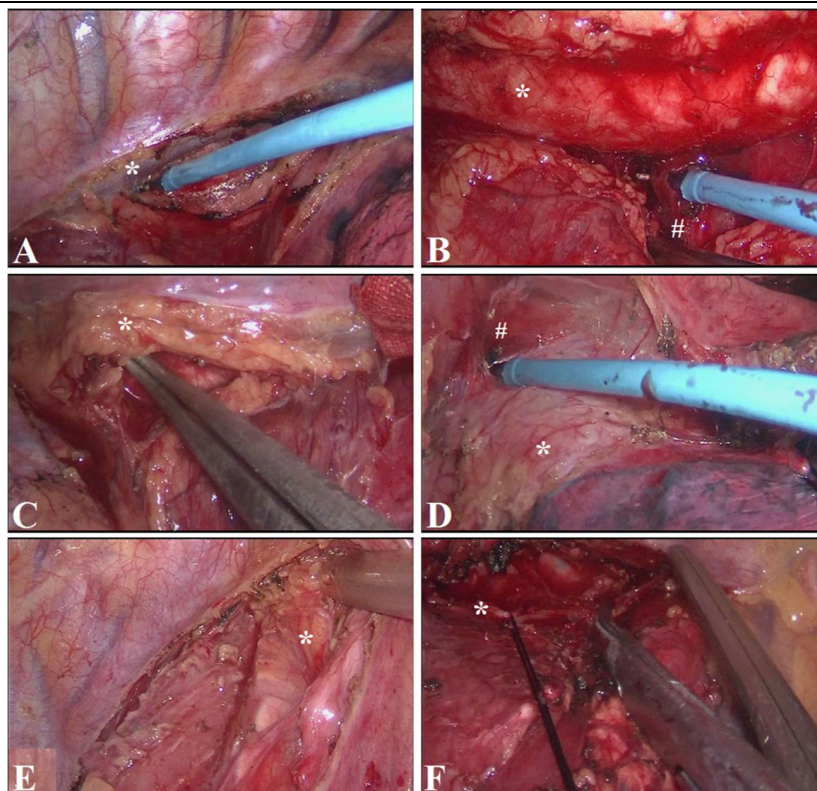
The operation was carried out in three stages following double-lumen endotracheal intubation with general anesthesia:

#### Stage 1: Resection of the thoracic esophagus

The patient was placed in the left lateral decubitus position with single-lung ventilation. To pass the thoracoscope (Storz HD TC300, Karl Storz, Germany), a skin incision was made at the right fourth intercostal space from the posterior axillary line to the middle axillary (4 cm) or the anterior axillary (10 cm). A window for observation was open at the middle axillary line at the right sixth intercostal space.

As for the surgical field, under the arch of the azygos vein, the medial border was the pleural fold at the left hilum. The anterior lateral border was the pleural fold at the right hilum, and the posterior lateral was the azygos vein at the anterior mediastinal pleura. Above the arch of the azygos vein, the anterior border was the right vagus nerve, the posterior was the prevertebral fascia, the superior was the right recurrent laryngeal nerve, and the inferior was the right and left crura of the diaphragm.

First, the mediastinal pleura was incised, accessing the posterior of the azygos vein, and the adipose tissue and the thoracic duct in front of the azygos vein were exposed (Figure 1A). They were then separated from the prevertebral fascia, as well as the thoracic aorta, medially and anteriorly until the left mediastinal pleura was exposed (Figure 1B).



**Figure 1.** Surgical approach of the modified thoracoscopic en-bloc esophagectomy

A: Dissection along the anterior border of the azygos vein (\*, azygos vein). B: Dissection along the surface of the aorta and removing the contralateral pleura (\*, aorta. #, contralateral pleura). C: Ligation of the thoracic duct above the diaphragm (\*, thoracic duct). D: Dissection along the pericardium surface to expose the crus of the diaphragm (\*, pericardium. #, crus of the diaphragm). E: Right recurrent laryngeal nerve after removing the surrounding lymph nodes (\*, right recurrent laryngeal nerve). F: Removal of lymph nodes next to the left recurrent laryngeal nerve (\*, left recurrent laryngeal nerve)

Resection was then performed in front of the aorta until reaching the pleural fold at the left hilum. Afterward, the thoracic duct was cut and ligated above the diaphragm (Figure 1C). The crura of the diaphragm were then exposed by cleaning anteriorly until reaching the right hilum at the ligament attached to the right lower lung lobe. The mediastinal pleura was incised along the pleural fold at the right hilum, and then it was separated posteriorly and medially. After that, the posterior segment of inferior vena cava, pericardium, inferior pulmonary vein, the right middle segment of bronchus, the right upper lobe bronchus, and the adipose and lymphoid tissues posterior to the right main bronchus were excised until reaching the pleural fold at the left hilum and the inferior border of the left main bronchus. The superior border was the arch of the azygos vein, and the inferior border was the crura of the diaphragm (Figure 1D).

The arch of the azygos vein was excised, accessing the dorsal arch of the azygos vein, and dissection was performed along the aortic arch to separate the adipose tissue from the prevertebral fascia. The thoracic duct was then resected horizontally at the subclavian artery level and reached anteriorly to the pulmonary artery window. Afterward, the mediastinal pleura was incised posteriorly to the vagus nerve and advanced to the lower edge of the subclavian artery. Adipose and lymphoid tissues were then cleaned to reveal the right recurrent laryngeal nerve. The surrounding adipose and lymphoid tissues were then dissected from the surface of the bronchi (Figure 1E). Afterward, the left segment of the recurrent laryngeal nerve looped around the aortic arch was isolated after dissecting the connective tissue left of the trachea. Finally, the surrounding lymphoid tissues were cleaned superiorly to reach the cervical-thoracic junction (Figure 1F).

#### *Stage 2: Operation in the abdominal cavity*

The entire abdominal operation was performed via an incision in the epigastrium. To ensure an en-bloc resection, the stomach was freed superiorly to the esophageal hiatus of the diaphragm and inferiorly to the distal pylorus. Afterward, the dorsal medullary membrane of the upper part of the stomach was completely resected, and the trunk of the celiac artery and its branches were exposed. The surrounding lymph nodes were then completely removed, and the lesser curvature of the stomach and the surrounding lymph nodes were also resected to construct a tubular stomach. Afterward, the right gastric artery was separated and cut off 5 cm above the pylorus. The endo-GIA was used to remove the arcus minor ventriculi and the surrounding lymph nodes, and a 4-cm wide tubular stomach was constructed.

Stage 3: Cervical esophageal resection and the

reconstruction of the digestive tract

An oblique incision was made along the anterior edge of the sternocleidomastoid muscle to free its ligament. Afterward, the lymphoid and the adipose tissues in the triangle formed by the external jugular vein, scapular hyoid muscle, clavicle, and the lateral edge of the internal jugular vein were cleaned. The lymphoid and the adipose tissues surrounding the internal jugular vein and the trachea were also removed after exposing the recurrent laryngeal nerve. Finally, esophagogastric anastomosis was performed through the left side of the neck.

#### *3.3. Evaluation of the outcomes*

All patients included in this study were followed up after the third month postoperatively and up to five years. The primary outcome was cancer recurrence during the follow-up period, which was examined by a repeated bone scan, computerized tomography, or ultrasound study. The secondary outcomes included death, intraoperative measurements (such as the operation time and the volume of hemorrhage), length of postoperative hospitalization, and complications (including pneumonia, arrhythmia, hoarseness, and chylous ascites). The Kaplan-Meier survival analysis was conducted based on the data collected between April 2014 and December 2020.

#### *3.4. Statistical analysis*

Continuous data and categorical data were presented as mean±SD and percentages, respectively. The difference between different groups was analyzed by the Chi-squared test, and a two-tailed P-value of less than 0.05 was considered statistically significant. All statistical analyses were performed using the SPSS software (version 16.0, IBM, USA).

## **4. Results**

Thirty-one patients were included in the study, 22 (71.0%) of whom were male, and their mean age was 62.9 years. All patients had squamous cell carcinoma. Their demographic characteristics and the clinical characteristics of their esophageal cancers are presented in Table 1.

Thirty patients had R0 resection. Eight of them experienced cancer recurrence during the follow-up period: four patients in the neck and four in the abdomen. None of the recurrences occurred in the mediastinal area. Five out of those eight patients with cancer recurrences died. However, none of the R0 resection patients without cancer recurrence died during the follow-up period. Only one patient with non-R0 resection had a cancer recurrence in the mediastinum who died due to a thoracic stomach-tracheal fistula six months after the surgery (Table 2). No death was observed during the perioperative

**Table 1.** Demographic and clinical characteristics of the patients in esophageal cancer

Parameters	Level	N (%)	P-value
<b>Gender</b>	Female	9 (29.0)	0.031
	Male	22 (71.0)	
<b>Age, year</b>	>60	18 (58.1)	0.472
	≤60	13 (41.9)	
<b>Length of cancer (cm)</b>	≤3	14 (45.2)	0.303
	3~	10 (32.2)	
	>5	7 (22.6)	
<b>Location of cancer</b>	Superior segment	17 (54.8)	0.001
	Middle segment	13 (41.9)	
	Inferior segment	1 (3.2)	
<b>T staging of cancer</b>	T1	6 (19.4)	0.295
	T2	5 (16.1)	
	T3	12 (38.7)	
	T4	8 (25.8)	
<b>N staging of cancer</b>	N0	13 (41.9)	0.007
	N1	12 (38.7)	
	N2	4 (12.9)	
	N3	2 (6.5)	

**Table 2.** Recurrence of esophageal cancer in patients treated with modified thoracoscopic en-bloc esophagectomy

Cancer recurrence	N (%)
<b>R0 resection (n=30)</b>	
Cervical lymph node	4 (13.3)
Abdominal lymph node	1 (3.3)
Pulmonary	1 (3.3)
Liver	1 (3.3)
Bone	1 (3.3)
<b>Non-R0 resection (n=1)</b>	
Mediastinum	1 (1/1)

period. Intraoperative outcomes are shown in Table 3. The overall postoperative complication rate was only 9%. Pneumonia, arrhythmia, hoarseness, and chylous ascites were the complications observed in patients. The incidence rate of pneumonia (5/31, 16.1%) was the highest among them (Table 4).

The results of the Kaplan-Meier analysis of the overall survival of all patients are shown in Figure 2. By the end of December 2020, the median survival time of N0 patients with non-lymphatic metastasis

**Table 3.** Results of perioperative and postoperative measurements

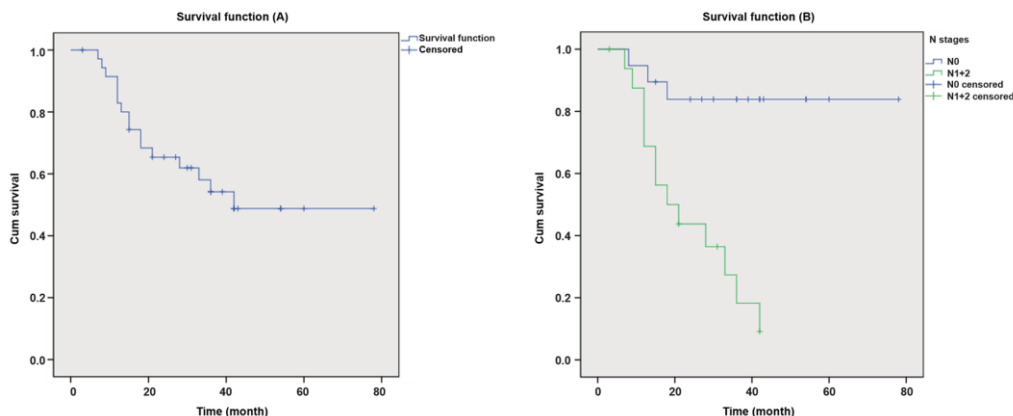
Parameter	Mean±SD
<b>Operation duration (min)</b>	420.52±124.73
<b>Intraoperative hemorrhage (ml)</b>	287.96±188.82
<b>Number of lymph nodes removed</b>	27.48±14.64
<b>Hospital stay after operation (day)</b>	12.68±5.00

SD: standard deviation

was 52 months (Figure 2A), and the median survival time of N1+2 patients with lymphatic metastasis was 23 months (Figure 2B). Additionally, there was a

**Table 4.** Postoperative complications in patients with esophageal cancer

Complications	N (%)
<b>Pneumonia</b>	5 (16.1)
<b>Arrhythmia</b>	3 (9.7)
<b>Hoarseness</b>	3 (9.7)
<b>Chylous ascites</b>	1 (3.2)



**Figure 2.** Kaplan-Meier analysis of the overall survival of patients  
 Survival function A: The overall survival of all patients with esophageal cancer who underwent modified thoracoscopic en-bloc esophagectomy from January 2014 and January 2017. Data shown in the survival curve were concluded by December 2019.  
 Survival function B: The comparison of the overall survival of all patients in stage N0 and stage N1+2 esophageal cancer who underwent modified thoracoscopic en-bloc esophagectomy between January 2014 and January 2017. Data shown in the survival curve were concluded by December 2019

statistically significant difference in the survival time between the two groups ( $P=0.001$ ).

## 5. Discussion

Postoperative recurrence is a substantial cause of surgical failure for patients with esophageal cancer. The most common location for cancer recurrence was the mediastinal lymph nodes. (5,7) Therefore, a surgical technique was essential to completely remove the lymphoid tissue in the mediastinal area and improve surgical outcomes. No recurrence was found in the mediastinal area in patients under study, who received a modified thoracoscopic en-bloc technique to remove their esophageal cancer, suggesting that the modified technique can improve postoperative outcomes.

In 1963, Logan *et al.* proposed the en-bloc technique to treat esophageal cancer located in the distal esophagus or the gastroesophageal junction. (10) Later, Skinner *et al.* applied this technique to patients with thoracic esophageal cancer. (17) The reported five-year survival rate was 16%, with an improved survival rate of 53% in patients with localized cancer. (10) The basic principle of the en-bloc esophagectomy technique is to resect the tumor mass around the membrane enveloping the surrounding tissues, which include the bilateral pleural surfaces, the pericardium in the front, and the lymphatic tissue between the esophagus and the spine. In addition, the thoracic duct, which follows the course of the esophagus, is resected during the en-bloc procedure. All the soft tissue between the esophagus and the vertebral spine, including the thoracic duct, the azygos vein, the segment of the right intercostal artery, and the bilateral intercostal veins in front of the vertebral body, were removed together with the esophagus.

Clinical anatomy showed that the adventitia of the esophagus could be divided into three segments: cervical, thoracic, and abdominal. (18,19) The cervical esophageal adventitia has two lobes, with the root extending out from the left and right inferior thyroid arteries. The recurrent laryngeal nerve and regional lymph nodes are distributed along the inferior thyroid artery in the adventitia. The upper and middle thoracic esophageal sections share the adventitia with the trachea, which also includes the mediastinal left and right recurrent laryngeal nerves, bronchial arteries, and draining lymph nodes. The lower thoracic esophageal section has its root in the esophageal artery. The adventitia of the abdominal esophageal section has its base in the inferior phrenic and celiac arteries. The en-bloc technique could remove the adventitia in the thoracic and abdominal esophageal sections but not the cervical esophageal due to its location in the two lobes.

With the widespread use of thoracoscopy and further improvements in esophageal surgical techniques, thoracoscopic resection of esophageal

cancer has shown satisfactory results in patients with early-stage esophageal cancer, which significantly improved the quality of their life. (20) However, it is worth noting that the current thoracoscopic technique to remove esophageal cancer frees the esophagus first and then cleans the lymph nodes. This is contrary to the concept of en-bloc resection and limits its application in patients with advanced esophageal cancer. Therefore, the authors developed the modified thoracoscopic en-bloc resection with the anterior border of resection being the pericardium (partial or complete), the posterior border being the spine, and the lateral borders being the bilateral pleura. In addition, a 180- to 270-degree excision was performed to remove tissues around the aorta. The length of the esophagus to be resected was usually from the diaphragm to or above the arch of the azygos vein, which depended on the location of cancer or the choice of surgical approach. The thoracic duct was also removed. In this surgical approach, the posterior resection should be performed close to the surface of the descending aorta, and the resection of the esophageal and bronchial arteries should be performed at the root of these vessels, as close as possible to the aortic surface. Furthermore, the anterior resection should be performed on the surface of the pericardium and the tracheobronchial membrane. It is also crucial to remove the entire tissue inside the boundaries within the mediastinum, not only around the esophagus.

In this study, the port hole was extended to an 8-10 cm incision to facilitate the removal of difficult tumors with traditional instruments. The resection of the azygos vein and the pericardium greatly reduced the intraoperative hemorrhage and decreased the disturbance to cardiac function, which made the operation relatively simple and ensured the complete resection of esophageal cancer.

In the present study, 30 out of 31 patients (96.8%) had R0 resection. Eight of them experienced cancer recurrence; however, none of the recurrences happened in the mediastinal area. Moreover, none of the patients without cancer recurrence died during the follow-up period, which indicated the advantages of the current modified technique to reduce the tumor recurrence rate in the mediastinum and potential benefits for long-term survival in patients. On the other hand, the present study showed a high rate of cancer recurrence in the cervical area (13.3%), which could be because most patients had cancers localized in the middle or upper parts of the esophagus. Therefore, a better surgical technique to reduce the rate of tumor recurrence in the cervical area for these patients requires further investigations.

There was no perioperative death, the volume of intraoperative blood loss, and the length of hospital stays were similar to previous findings. (21) However, the operation duration in this study was

longer than what had been reported previously, (21) which might be due to the more time spent removing more lymph nodes, compared to previous studies. (21) The overall rate of postoperative complications was also low, with the most common complication being pulmonary involvements, which was similar to those reported before, (21,23) which suggested the reliability and safety of this modified technique.

The limitations of this study include conducting a single-center study, a small number of patients, and a short follow-up period. The retrospective nature of the study could have introduced biases into the results. In addition, the authors did not perform any outcome comparisons between patients with different cancer locations or stages due to the small sample size.

## 6. Conclusion

In summary, a modified thoracoscopic en-bloc esophagectomy by right thoracoscopic approach or thoracoscope-assisted small incisional approach was developed. This surgical technique could decrease the likelihood of cancer recurrence in the mediastinal area, with potential benefits of long-term survival for patients. A larger sample size and a multi-center study are necessary to validate and optimize its treatment effects.

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## Footnotes

**Conflicts of Interest:** The authors declare that they have no conflict of interest.

**Author's contributions:** ZL contributed to the study design, all authors collected the data and performed the data analysis, and all authors prepared the manuscript.

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**Consent for publication:** Not applicable.

**Availability of data and material:** The datasets collected and analyzed in the present study are available by the corresponding author upon reasonable request.

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