To describe minimally invasive esophagectomy with a focus on peri-esophageal lacuna anatomy

Nanzheng Chen
The first Affiliated Hospital of Xi'an Jiaotong University
Xiaomei Yang
Hospital 521 of China's Ordnance Industry Group
Haiqi He
The first Affiliated Hospital of Xi'an Jiaotong University
Guangjian Zhang
The First Affiliated Hospital of Xi'an Jiaotong University
Qifei Wu
The First Affiliated Hospital of Xi'an Jiaotong Univesity
Donghong Geng
School of Continuing Education of Xi'an Jiaotong University
Jian Chen
The First Affiiated Hospital of Xi'an Jiaotong University
Junke Fu
The First Affiliated Hospital of Xi'an Jiaotong University
Yong Zhang (823447609@qq.com)
The First Affiliated Hospital of Xi'an Jiaotong University https://orcid.org/0000-0002-9824-303X

Technical innovations

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Abstract

Background: Lacuna anatomy has been studied widely in various organs to improve the operative approach and surgical procedure. However, there are few studies about the peri-esophageal lacuna (PEL). The aim of this study was to describe minimally invasive esophagectomy (MIE) with a focus on PEL anatomy.

Methods: From August 2012 to December 2015, patients with esophageal carcinoma underwent MIE by the same group of surgeons at our institution. A double lumen endotracheal tube was used with left lung ventilation without pneumothorax for patients in group 1. A single lumen endotracheal tube was used with two-lung ventilation and right artificial pneumothorax for patients in group 2. The methods that we used for thoracic esophagus mobilization and modularized lymph node dissection, based on the American joint committee on cancer (AJCC) staging manual, in the peri-esophageal space are described. We evaluated the surgical effect, postoperative complications and follow-up results.

Results: A total of 147 patients (107 men; mean ± standard deviation age 63.1 ± 7.7 years) were enrolled. Among them, 67 were placed in group 1 and 80 in group 2. There was no significant difference between the two groups in terms of age, gender, tumor location, T stage, N stage or comorbidities. The mean operation duration (283±46 vs 307±69 minutes; p=0.007) and blood loss (129±84 vs 260±225 mL; p=0.000) was less in group 2 than group 1. Group 2 also yielded a larger number of lymph nodes compared with group 1 (22.5 ± 11.1 vs 16.4 ± 7.4; p=0.007). Complication rates were similar between the two groups, with hoarseness developing in a significantly smaller number of patients in group 1 than group 2 (1% vs 21%; p=0.000). There was no significant difference between the two groups in one-year (78.3% vs 84.2%; p=0.345) and three-year (52.1% vs 62.7%; p=0.210) survival rates for group 1 (a double lumen endotracheal tube with left lung ventilation without pneumothorax) versus group 2 (a single lumen endotracheal tube with two-lung ventilation and right artificial pneumothorax).

Conclusion: Esophageal mobilization based on PEL and the modularized lymph node dissection based on the AJCC cancer staging manual improves surgical outcomes.

Background

The study of human lacunae involves investigation of their anatomical characteristics as well as their relationships with relevant bodily systems based on traditional parenchymal organ research. Ge et al., [1, 2] suggested that human lacunae consist of space, potential and soft tissue lacunae. Space lacunae can be understood as the visceral organs of traditional human anatomy, such as the bladder, stomach and intestines. Potential lacunae are mostly serous lacunae, such as the pleural, peritoneal and joint cavities. Soft tissue lacunae are usually filled with loose connective tissue, nerves, blood vessels and lymphangion.

Lacuna anatomy has been studied in various human organs and tissues including the cerebral ventricles [3], pericardium [4], articular cavity [5], carpal tunnel [6], tarsal tunnel [7], liver [8], nasolacrimal duct [9], esophageal submucosa [10, 11] and retroperitoneal lacunae [12–14]. These studies were closely related to the operative approach and surgical procedure.

To date, there have been few anatomical studies on the peri-esophageal lacuna (PEL), which is based on the soft tissue lacuna around the esophagus. To obtain the best surgical visual field, there must be full consideration of the lacuna surrounding the esophagus to properly handle the associated nerves, blood vessels and lymphangion. The purpose of this study was to describe the procedure of minimally invasive esophagectomy (MIE) and the method of modularized lymph node dissection with a focus on the PEL anatomy.

Methods

Patient selection

Between August 2012 and December 2015, 147 patients with esophageal cancer were treated with MIE by the same group of surgeons in our department. The esophageal cancers were diagnosed by barium X-rays, esophagogastroduodenoscopy (EGD) and biopsy. Routine enhanced thoracic and abdominal computerized tomography (CT) scan, and cervical ultrasonography were also performed. CT and endoscopic ultrasonography did not indicate any obvious tumor invasion of the surrounding tissues, tumor metastases in distant organs, or enlarged mediastinal lymph nodes. Only patients without severe cardiac or pulmonary dysfunction, assessed by echocardiography and pulmonary function test, were selected for this study. All data were collected retrospectively from the medical records held our hospital.

Surgical procedure

For general anesthesia, two approaches were used. First, a double lumen endotracheal tube was used with left lung ventilation without pneumothorax (Group 1). Second, a single lumen endotracheal tube was used with two lung ventilation. Carbon dioxide (CO2) was used to maintain an insufflation pressure of 6-8 mmHg and a pneumothorax was created to collapse the right lung and to expand the PEL (Group 2). The patients in both groups were initially placed in a left lateral position with the bed inclined forward 30 degrees. A 12-mm trocar for the endoscope was inserted into the 7th/8th intercostal space (ICS) on the midaxillary line. After identifying the right thoracic cavity, three trocars were inserted under endoscopic guidance: a 5-mm trocar in the 3rd/4th ICS and a 12-mm trocar in the 5th/6th ICS behind the anterior axillary line for the surgeon, along with a 5-mm trocar in the 4th/5th ICS behind the posterior axillary line for the assistant (Fig. 1).

The thoracic esophagus dissection consisted of the following four steps (Fig. 2). First, we dissected the posterior esophageal lacuna from the lower edge of the azygos vein arch to the esophageal hiatus. Three to five esophageal nutrient arteries from the descending aorta were then sealed. Second, we dissected the anterior esophageal lacuna from the lower edge of the azygos vein arch to the esophageal hiatus. The pulmonary branches of the vagus nerve were preserved and the esophagocardial branches were divided. The bilateral bronchial arteries were ligated. The middle and lower parts of the paraesophageal lymph nodes, the lymph nodes adjacent to the inferior pulmonary ligament, and the superior phrenic lymph nodes (Module 1, group 8M, 8L, 9R, 10R and 15, AJCC & UICC) [15, 16] were dissected during the first and second steps. Third, we dissected the posterior esophageal lacuna from the lower edge of the azygos vein arch to the top of the thoracic cavity. The azygos vein arch was then transected. Damage to the thoracic duct and left recurrent laryngeal nerve (RLN) should be avoided. However, if thoracic duct injury did occur, it was double ligated at the upper and lower parts of the injury, or ligated above the diaphragm. Fourth, we dissected the anterior esophageal lacuna from the lower edge of the azygos vein arch to the top of the thoracic cavity. Care was taken to avoid damage to the trachea membrane and to both RLNs. The upper part of the paraesophageal lymph nodes, the lymph nodes adjacent to the right side of the trachea (Module 2, group 8U and 4R) and those along the right RLN (Module 3, group 2R) (Fig. 3) were dissected during the third and fourth steps. The free esophagus was then pulled forward to the chest wall using a silk thread for easier dissection of the lymph nodes below the carina (Module 4, group 7) and along the left RLN (Module 5, group 2L) (Fig. 4). It was better to remove the subcarinal lymph nodes (Module 4, group 7) in the anterior part of the peri-esophageal lacuna below the azygos vein arch en bloc after the ligation of branches from the bilateral bronchial arteries. The lymph nodes along the left RLN (Module 5, group 2L) were dissected from the origin of the left RLN below the aortic arch. In the process of exposing and dissecting the bilateral RLN nodes, blunt and sharp separation was used alternatively. Further, dissection with an electrocoagulation hook or harmonic scalpel (Ethicon, Johnson & Johnson, USA) near the RLN was avoided.

The patients were then turned into a supine position and the abdominal phase of the operation was performed with 5 trocars as for the conventional procedure. The resected specimen was removed through a 3 – 5 cm subxiphoid incision, and a 5-cm gastric conduit was pulled up through the posterior mediastinum for mechanical end-to-side esophagogastric anastomosis at the left neck. A naso-jejunal feeding tube or jejunostomy tube was placed for postoperative enteral nutrition.

Post-operative follow-up

All patients underwent follow-up in clinic or by cell phone, every 3 – 6 months for the first 2 years after the operation and then every 6 – 12 months thereafter. The last follow-up time was 20 September 2017.

Statistical analysis

Statistical analyses were performed with SPSS software (version 24.0, IBM SPSS). Continuous variables were expressed as the mean ± standard deviation (SD), and analyzed using Student's t-test. Categorical variables were assessed using Chi-square test or Fisher's exact probability test. Length of survival was determined using the Kaplan-Meier method, and the log-rank test was used for comparisons. A p-value of less than 0.05 was considered significant.

Results

Patient demographics

A total of 147 patients were included in this study. There was a male predominance with 107 men (72.8%) and 40 women (27.2%). The mean (± SD) age was 63.1 (±7.7) years. The most common comorbidities were hypertension, coronary artery disease and diabetes mellitus, which occurred at similar frequencies in the two group patients (p=0.896, 0.591, and 0.117, respectively). There was no statistical difference in the age, gender, tumor location or T (tumor) N (node) M (metastasis) stage between the two groups (Table 1).

Operation features

The thoracic and abdominal stages were performed without conversion to open surgery in all 147 patients. The mean operation time was significantly shorter in group 2 at 283 (±46) minutes, compared with 307 (±69) minutes in group 1 (p=0.007). The total estimated intraoperative blood loss was significantly less in group 2 (129±84 mL) than group 1 (260±225 mL, p=0.000). Postoperatively, the mean duration of chest drainage was shorter in group 1 at 6.2±3.09 days compared with group 2 at 8.6±5.6 days, (p=0.004).

In our study, the mean ± SD number of lymph nodes harvested along the left RLN (1.1 ± 1.2 vs 0.5 ± 0.8, p=0.000), during the thoracic stage (13.2 ± 9.0 vs 8.0 ± 5.8, p=0.017), and during both thoracic and abdominal stages (22.5 ± 11.1 vs 16.4 ± 7.4, p=0.007) was significantly higher in group 2 than in group 1. The number of lymph nodes harvested along the right RLN (1.1 ± 1.1 vs 1.3 ± 1.3, p=0.228) and during the abdominal stage (8.2 ± 6.1 vs 9.0 ± 6.0, p=0.91) was similar in both groups (Table 2).

Postoperative complications

There were no deaths during surgery in either group. One patient in group 2 died of sudden death on the 15th postoperative day, and one patient in group 1 died of respiratory failure on the 57th postoperative day. Thus there were two deaths, one in each group, within 90 days of the operation. The most common complication was pneumonia, which occurred at similar frequencies in the two groups (20.9% vs 25%, p=0.557). Hoarseness occurred significantly more commonly in group 2 than in group 1 (26.3% vs 1.5%; p<0.005). There was no difference in the frequency of complications such as chyle thorax (p=0.192), deep venous thrombosis (p=0.075), pulmonary embolism (p=0.209) or delayed gastric emptying (p=0.209) between the two groups. Further, the two groups had a similar proportion of patients experiencing arrhythmia (p=0.268), wound infection (p=0.14), esophageal hiatal hernia (p=0.269), anastomotic stenosis (p=0.81), and anastomotic leakage including cervical and thoracic leakage (p=0.869) (Table 3).

Follow-up results

Only 11 of the 147 cases were not followed-up successfully. For the remaining 136 patients, there was no significant difference between the two groups in terms of one-year survival rate (group1: 78.3% vs group2: 84.2%; p=0.345) and three-year survival rate (group1: 52.1% vs group2: 62.7%; p=0.210) (Fig. 5). The main causes of death were distant metastasis and local metastasis (Table 4).

Discussion

Many studies have described MIE based on traditional parenchymal organ anatomy. This is the first study to describe MIE with a focus on PEL anatomy. Human lacuna anatomical study indicates that the PEL is a kind of soft tissue lacuna that is usually filled with loose connective tissue, nerves, blood vessels and lymphangion. Esophagectomy aims to achieve radical tumor resection and should also guarantee patient safety. For this to occur, the tissues and organs of the PEL should be properly treated during esophageal mobilization. These tissues and organs include the vagus nerve, bilateral RLNs, bilateral bronchial arteries, the azygos vein arch, the thoracic duct and the lymph nodes around the esophagus (group 2R, 2L, 4R, 7, 8U, 8M, 8L, 9R, 10R and 15 (AJCC & UICC)) [15, 16].

Combining published work on human lacuna anatomy with our clinical practice has enabled us to design a practical method for esophagus dissection. First, we chose to use the left lateral decubitus rather than the prone position [17–19], which was based on our experience in open esophagectomy. In the left lateral prone positon, it is difficult to mobilize the esophagus if it is located on the left side of the thoracic aorta, and sheltered by the spine and aorta. In the left lateral position with the bed inclined forward 30 degrees, we had good surgical vision and avoided this esophageal sheltering [20–23]. For clearer exposure of PEL tissues such as the nourishing arteries, nerves and lymph nodes, an artificial pneumothorax was used to expand the PEL facilitating radical resection and improving surgical safety [12, 24–26]. This is consistent with the role of an artificial pneumoperitoneum in surgeries involving the liver, stomach, intestine and kidney [8, 12, 13, 27]. Finally, we designed a sequence for dissection of different parts of the PEL. The middle and lower PEL (below the azygos vein arch) was dissected prior to the upper PEL (above the azygos vein arch), because the middle and lower PEL were bigger than the upper PEL. Several nourishing esophageal arteries in the posterior PEL (between the esophagus and spine) arise from the thoracic aorta. We dissected the posterior PEL before the anterior PEL (between the esophagus and pericardium) to decrease the possibility of bleeding.

After transection of the azygos vein arch, mobilization of the esophagus at its left side became easier while pulling up the gastric conduit in the following steps became safer. After ligation of the bilateral bronchial arteries, bleeding during dissection of the subcarinal lymph nodes and accidental bleeding after surgery would both decrease. We kept the lung branches of the vagus nerve to decrease posterior pulmonary complications. We avoided using electrically powered instruments near the RLNs to decrease posterior hoarseness. We preferred to modularly dissect lymph nodes in the PEL. We dissected some groups of esophageal lymph nodes including group 8M, 8L, 9R and 15 (Module 1) and group 8U and 4R (Module 2), which were easier than other groups of lymph nodes (Module 3, group 2R and Module 4, group 7). The most difficult procedure was to expose the left RLN, so we dissected lymph nodes along the left RLN (Module 5, group 2L) at the last step.

In our series of 147 consecutive patients, thoracoscopic esophagectomy was shown to be feasible with (group 2) or without (group 1) expanding the peri-esophageal space. Most operation features were better in group 2, while most postoperative complications were similar in the two groups. This showed that expanding the peri-esophageal space facilitates mobilization of the esophagus and dissection of the lymph nodes within mediastinum. The higher frequency of hoarseness complications in group 2 was thought to be because more lymph nodes were dissected in this group with the possibility of more nerve injury during lymph node dissection along both RLNs. The survival curve showed that one-year and three-year survival rates were better in group 2 although this was not statistically significant.

Our study has some limitations. First, we had a relatively small population in our study. Second, there were more patients with non-squamous carcinoma and more advanced disease staging in group 1. Third, more operations were performed earlier in group 1 than in group 2. Fourth, the surgeons' experience might lead to bias. However, other studies have also shown advantages in terms of visibility and accessibility of the surgical field, with better subsequent surgical outcomes by expanding the PEL [26].

Conclusions

We conclude that esophagus mobilization based on PEL and modularized lymph node dissection based on the AJCC cancer staging manual improves surgical outcomes.

Abbreviations

PEL: Peri-esophageal lacuna; MIE: Minimally invasive esophagectomy; AJCC: American Joint Committeeon Cancer; EGD: Esophagogastroduodenoscopy; CT: Computerized tomography; CO2: Carbon dioxide; ICS: Intercostal space ; UICC: The Union for International Cancer Control; RLN: Left recurrent laryngeal nerve; SD: standard deviation; SPSS: Statistical Product and Service Solutions

Declarations

Ethics approval and consent to participate

This study was conducted with the approval of the Ethics Committee of the First Affiliated Hospital of Xi'an Jiaotong University (Xi'an, CN). It was carried out in accordance with the Declaration of Helsinki.

Consent for publication

Not applicable

Availability of data and materials

The database used and/or analyzed during the current study is not publicly available (to maintain privacy) but can be available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

These authors contributed equally to this work.

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Tables

Table 1 Patients' Demography

Characteristics [a]	Group 1 (n=67)	Group 2 (n=80)	*p Value*
Age, y	61.5±7.4 (42-79)	64.5±7.8 (33-81)	0.986 [b]
Gender			0.406 [c]
Male	51	56	
Female	16	24	
BMI	21.5±2.7	21.5±2.9	0.652 [b]
Smoke	38	36	0.157[c]
Comobidities			
HTN	12	15	0.896 [c]
CAD	2	5	0.591 [c]
DM	1	7	0.117 [c]
Histologic type			0 [c]
Squamous cancer	48	77	
Others	19	3	
Location			0.359 [c]
Upper chest	5	11	
Middle chest	31	40	
Lower chest	31	29	
Stage			0.046 [d]
0	0	4	
I	10	9	
II	24	42	
III	32	25	
IV	1	0	
T			0.286 [c]
Tis	0	4	
T1	10	12	
T2	14	22	
T3	39	37	
T4	4	5	
N			0.069 [c]
N0	34	51	
N1	12	18	
N2	15	9	
N3	6	2	

[a] Continuous data are presented as mean ± standard deviation and categoric data as the number. [b] By the Student *t* test. [c] By the Chi-square test. [d] By the Fisher exact test.

HTN=Hypertension; CAD=Cardiac artery disease; DM=Diabetes mellitus

Table 2 Surgical Features

	Group 1 (n=67)	Group 2 (n=80)	
Variable	Mean±SD	Mean±SD	*p* Value [a]
Total operation time (min)	307±69	283±46	0.007
Total EBL (ml)	260±225	129±84	0
Duration of chest drainage (d)	6.2±3.09	8.6±5.6	0.004
Total LNs	16.4±7.4	22.5±11.1	0.007
Thoracic LNs	8.0±5.8	13.2±9.0	0.017
RRLN	1.1±1.1	1.3±1.3	0.228
LRLN	0.5±0.8	1.1±1.2	0
Abdominal LNs	8.2±6.1	9.0±6.0	0.91

[a] By the Student t test.

EBL=estimated blood loss; Op=operation; RBC=red blood cell; LN=lymph node

Table 3 Postoperative Complications

	Group 1 (n=67)	Group 2 (n=80)	
Variable[a]	No.	No.	p Value
Pneumonia	14	20	0.557 [b]
Hoarseness	1	21	0 [b]
Arrhythmia	2	7	0.268 [b]
Wound infection	5	1	0.140 [b]
Esophageal hiatal hernia	0	1	0.269 [c]
Anastomotic stenosis	4	3	0.81 [b]
Anastomotic leakage	8	9	0.896 [b]
Cervical leakage	5	4	
Thoracic leakage	2	3	
Both cervical and thoracic leakage	1	2	
Chyle thorax	3	0	0.192 [b]
Deep venous thrombosis	2	0	0.075 [c]
Pulmonary embolism	1	0	0.209 [c]
Delayed gastric emptying	1	0	0.209 [c]
Death 90 days postoperation	1	1	0.9 [c]

[a] Categoric data as the number. [b] By the Chi-square test. [c] By the Fisher exact test.

Table 4 Causes for death

Variables[a]	Group 1 (n=67)	Group 2 (n=80)
Distance metastasis	13	8
Brain metastasis	1	1
Bone metastasis	4	
Lung metastasis	3	4
Liver metastasis	2	1
Laryngeal metastasis		2
Local metastasis	8	7
Organs failure	6	5
Bleeding of digestive duct	4	3
Haematemesis	3	2
Bloody stools	1	
Pulmonary embolism	1	0
Cardiac infarction	0	1
Esophago-tracheal fistula	1	0
Sudden death	0	2
Hematosepsis	0	1
Unknown	3	3

Figures

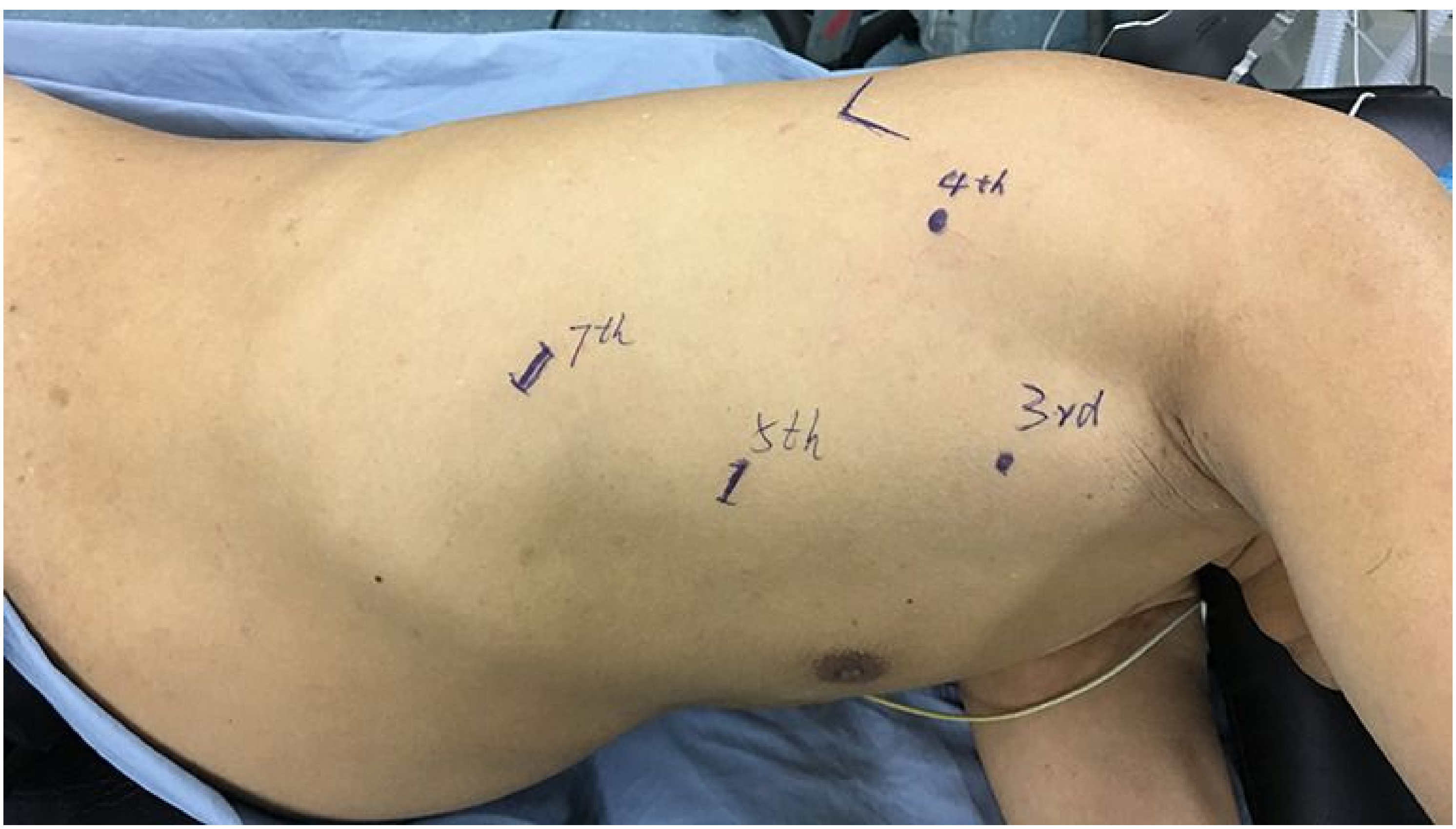

Figure 1

Trocars for thoracic surgery. The camera was inserted into the chest through the 7th intercostal space (ICS). The surgeon operated through the 3rd and 5th ICS most of time and through the 3rd and 4th ICS occasionally.

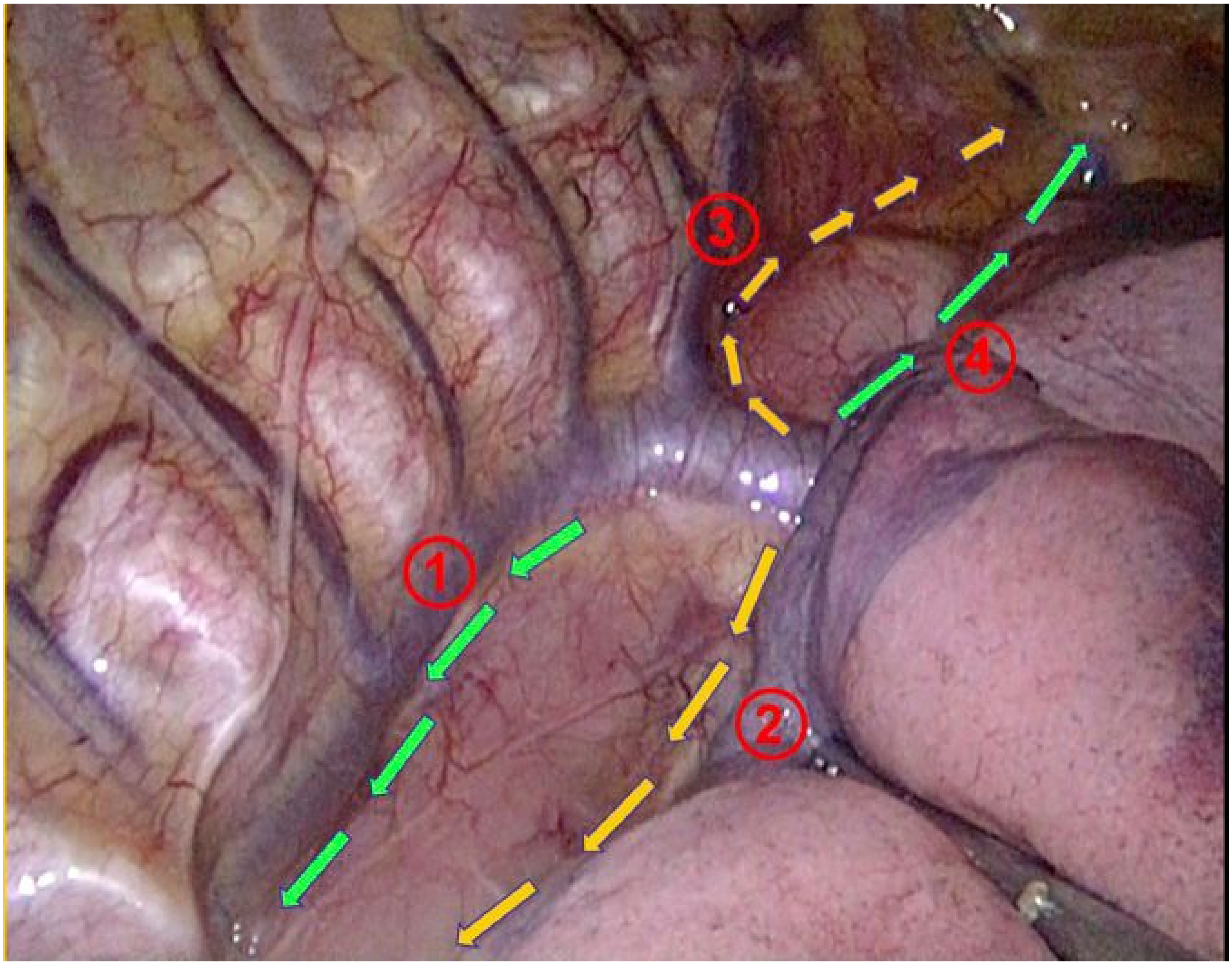

Figure 2

Sequence for dissection of the lacunae around the esophagus. ①The posterior esophageal lacuna from the lower edge of the azygos vein arch to the esophageal hiatus. ②The anterior esophageal lacuna from the lower edge of the azygos vein arch to the esophageal hiatus. ③The posterior esophageal lacuna from the lower edge of the azygos vein arch to the top of the thoracic cavity. ④The anterior esophageal lacuna from the lower edge of the azygos vein arch to the top of the thoracic cavity.

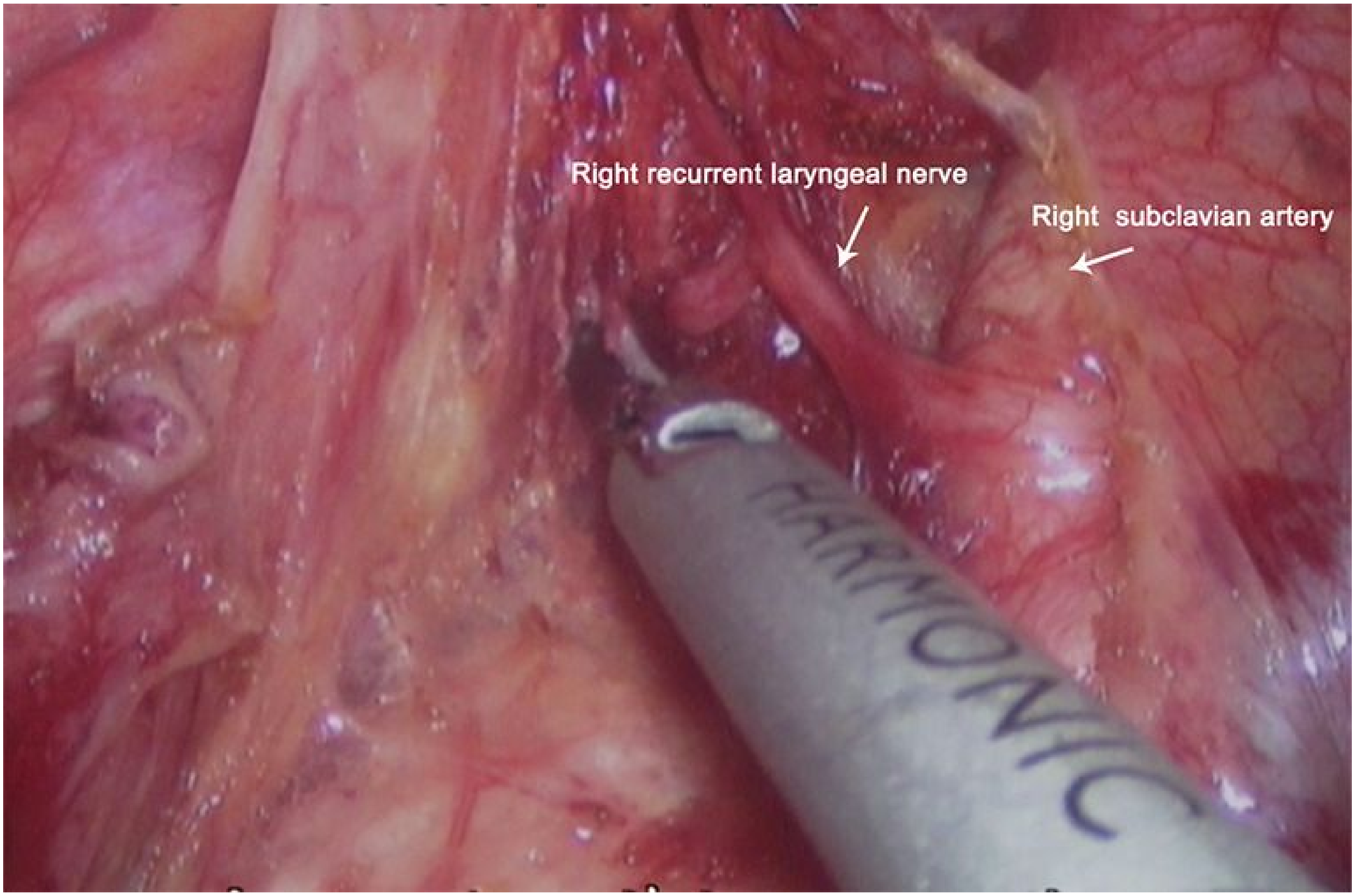

Figure 3

Dissection of the lymph nodes along the right recurrent laryngeal nerve

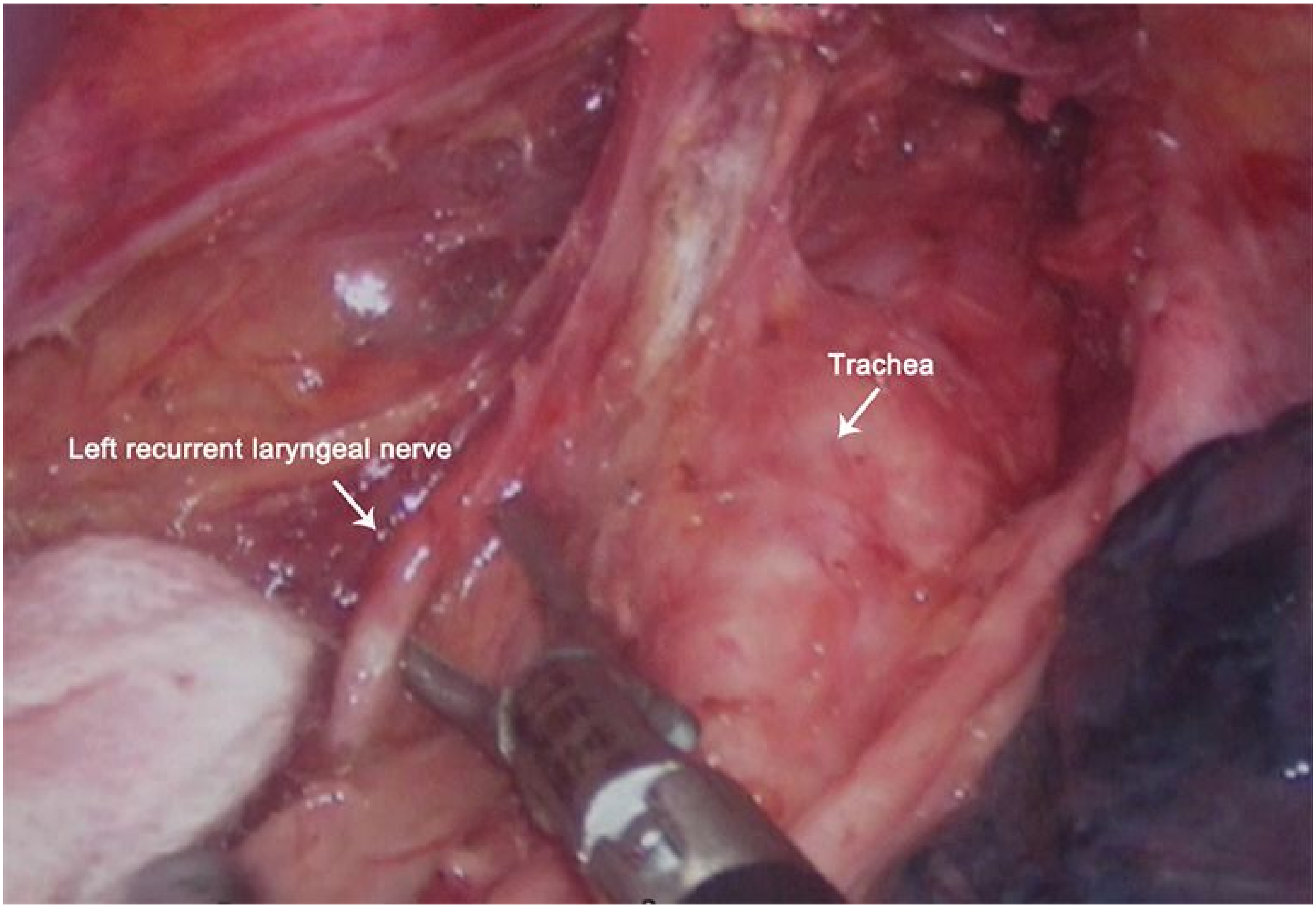

Figure 4

Dissection of the lymph nodes along the left recurrent laryngeal nerve

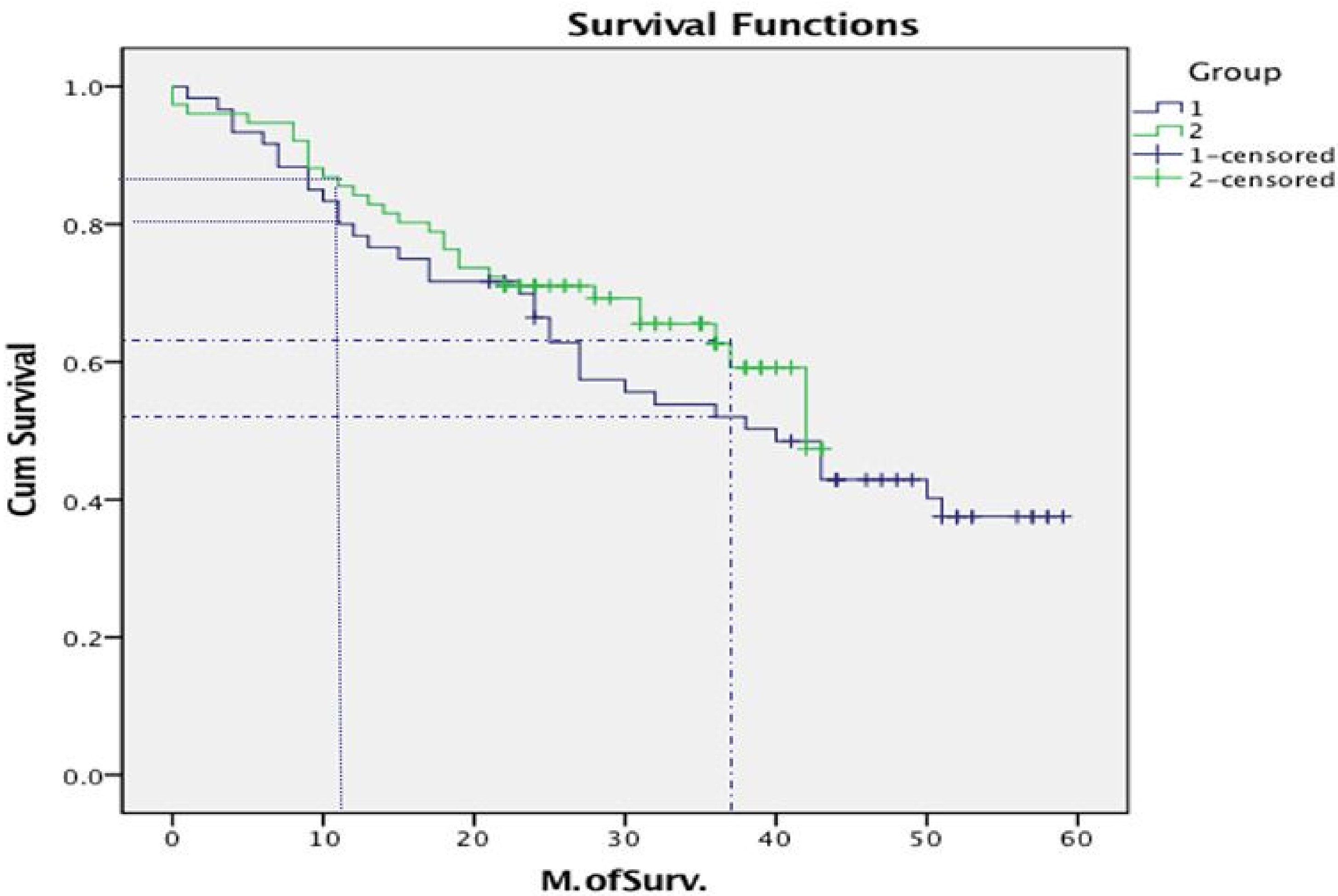

Figure 5

Survival curve for the two groups (p=0.343). Group 1 stands for the patients received a double lumen endotracheal tube with left lung ventilation without pneumothorax. A single lumen endotracheal tube was used with two-lung ventilation and right artificial pneumothorax for patients in group 2.