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ORIGINAL ARTICLE

Single-Port Inflatable Mediastinoscopy Combined With Laparoscopic-Assisted Small Incision Surgery for Radical Esophagectomy Is an Effective and Safe Treatment for Esophageal Cancer

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Abstract

Background We previously developed a novel non-trans thoracic esophagectomy, the single-port inflatable mediastinoscopy combined with laparoscopy for the radical esophagectomy of esophageal cancer. The purpose of this study was to report its therapeutic efficacy and safety.

Methods From May 2016 to August 2017, we have completed 80 cases of radical resection of esophageal carcinoma using this novel surgical technique. The intraoperative findings and postoperative complications were reported.

Results The operation was successfully performed in all patients except for one patient switched from laparoscopic-assisted operation to open surgery. The mean operation duration was 191.4 ± 27 min, and the mean intraoperative blood loss was 147.3 ± 28.9 mL. The mean number of removed lymph node was 21.9 ± 4.1. Five patients (6.4%) who had preoperative type I respiratory failure needed to stay in the intensive care unit for 24 h postoperatively. Postoperative complications included anastomotic leakage (8.9%), anastomotic stricture (21.25%), pleural effusion (9%), and hoarseness postoperative hoarseness (18.8%). The incidence of hoarseness at 3 months postoperation was reduced to 3.8%. All the complications were Clavien-Dindo grades I–III. There were no perioperative death and postoperative cardiopulmonary complications.

Conclusion These results showed that the single-port inflatable mediastinoscopy combined with laparoscopy is feasible for radical esophagectomy and possesses good therapeutic efficacy and safety.

Keywords Esophageal cancer · Esophagectomy · Non-thoracotomy · Inflatable mediastinoscopy · Laparoscopy

Introduction

Esophageal cancer is the eighth most common cancer worldwide,[1] with a higher incidence in less developed and developing countries.[2] It has been reported that more than half of global newly diagnosed esophageal cancer cases occur in China.[3,4] Esophageal cancer has a poor prognosis, with the 5-year survival rate lower than 25%.[5] Currently, radical esophagectomy remains the gold standard treatment for the early and intermediate-stage esophageal cancer.[6] With the development of minimally invasive surgical technique, the mortality of esophagectomy has been dramatically decreased.[7,8] Nevertheless, in minimally invasive esophagectomy, the transthoracic approach is most often adopted. Transthoracic surgery is a crucial independent risk factor for the incidence of postoperative pulmonary complications,[9] the main cause of morbidity and mortality following thoracotomy.[10]

To reduce postoperative pulmonary complications, considerable efforts have been made to develop the non-transthoracic esophagectomy for esophageal cancer. For instance, esophageal stripping and transhiatal esophagectomy are the non-transthoracic operations developed for treatment for esophageal cancer. These methods possess several advantages, including non-thoracotomy, less postoperative pain, less postoperative cardiac and pulmonary complications, and safer for elderly patients. However, these two methods are limited with the poor surgical view, poor mediastinal lymph node dissection (especially upper mediastinal lymph nodes), and high risk of bleeding.[11] Therefore, non-transthoracic

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esophagectomy with effective dissection of mediastinal lymph nodes is challenging for radical resection of esophageal carcinoma.

In 2015 and 2016, Prof. Fujiwara has developed novel surgical methods on the dissection of upper mediastinal lymph nodes using single-port mediastinoscopy through the cervical incision[12] and the lower mediastinal lymph nodes (including the subcarinal lymph nodes) by laparoscopy, respectively.[13] For the first time, non-transthoracic radical resection of esophageal cancer could be achieved along with the dissection of all the mediastinal lymph nodes. Based on the Fujiwara's method, we further improved this surgical method to the "single-port inflatable mediastinoscopy combined with laparoscopy for the radical treatment of esophageal cancer" and has successfully performed this novel surgical method for the first case in March 2016.[14] We have completed 80 cases of radical resection of esophageal carcinoma using this novel surgical technique from May 2016 to August 2017. Therefore, the purpose of this study was to report the therapeutic efficacy and safety of this surgical method in these patients.

Methods

Patients

A total of 80 patients with esophageal cancer undergoing single-port inflatable mediastinoscopy combined with laparoscopy for the radical esophagectomy from May 2016 to August 2017 in our hospital. The inclusion criteria were (1) gastroscopic and pathological diagnosis of esophageal squamous cell carcinoma, clinical stage I–IIIA; (2) age of 18 to 80 years; (3) the functions of the main organ system meeting the requirements of radical resection surgery; (4) patients did not receive radiotherapy, chemoradiotherapy, or molecular targeting therapy; (5) patients did not merge with other cancers; and (6) patients voluntarily participate in clinical trials. The exclusion criteria were (1) cervical esophageal squamous cell carcinoma, (2) patients refused surgical treatment, and (3) patients simultaneously participated in other clinical trials. This study was approved by the institutional review board of our hospital. Written informed consent was obtained from the patient.

Surgical Procedure

The preoperative preparations included routine blood tests, electrocardiogram, echocardiography, cervical chest and abdomen enhanced CT, pulmonary function test, and upper gastrointestinal angiography.

The upper mediastinal retractor (Fig. 1) and the lower mediastinal retractor (Fig. 2) were the essential tools (research and development by Suzhou Sagemed Medical Technology Co., Ltd., China) for single-port inflatable mediastinoscopy combined with laparoscopy for esophagectomy. The surgical procedure mainly consisted of left cervical operation and laparoscopic-assisted small incision surgery.

Fig. 1 The upper mediastinal retractor (5-mm width and 35-mm length)

For left cervical operation, a 3-cm incision paralleling the clavicle was made at 2 cm from the supraclavicular region in the left neck. Along the incision, the left recurrent laryngeal nerve was dissected and marked through the muscle of anterior border of the sternocleidomastoid (Fig. 3a). The lymph nodes around the left recurrent laryngeal nerve were then removed. The cervical esophagus was dissected and marked. A 3.5-cm-diameter protective sleeve was placed in the incision to push away the left sternocleidomastoid muscle, blood vessels, and the left thyroid (Fig. 3b) and was then covered by the special protective cover. Three special trocars (diameter of 5 mm) were inserted into the cover (Fig. 3c), and carbon dioxide was injected into the mediastinum with a pressure of 10 mmHg to cause artificial mediastinal emphysema (Fig. 4a–d). Through these three trocars, a 5-mm 30-degree lens, a Maryland forceps (model: endoscopic 1737, Medtronic, Covidien), and a special upper mediastinal retractor were implanted. The special retractor was used to push away the esophagus, trachea, and arteries, so that the Maryland forceps could be easily used to bluntly separate the connective tissue and lymph nodes around the esophagus and then coagulate and cut off them Attention should be paid to protect the thoracic duct. The Maryland forceps was used along the right side of the tracheoesophageal groove of esophagus downwards to make blunt dissection and cut off the esophageal tracheal tissue and peripheral lymph nodes. The separated lymph nodes and surrounding tissues were pushed to the esophageal side. Along the way to the lower edge of the left main bronchus, the lymph nodes behind left main bronchus and trachea tissue were resected. During this procedure, attention should be paid to protect the azygos vein and tracheal membranous part. The left recurrent laryngeal nerve (previously marked) was found, and blunt dissection was performed in the tissues around the esophageal and the left recurrent laryngeal nerve, down to the lower edge of the aortic arch and the origin of left recurrent laryngeal nerve. Along the spinal-esophageal space, blunt

Fig. 2 The lower mediastinal retractor (10-mm width and 45-mm length)

dissection was performed to mobilize the esophagus to the lower edge of the aortic arch. The left recurrent laryngeal nerve was mobilized by sharp dissection, leaving the surrounding tissue and lymph nodes near to the side of the

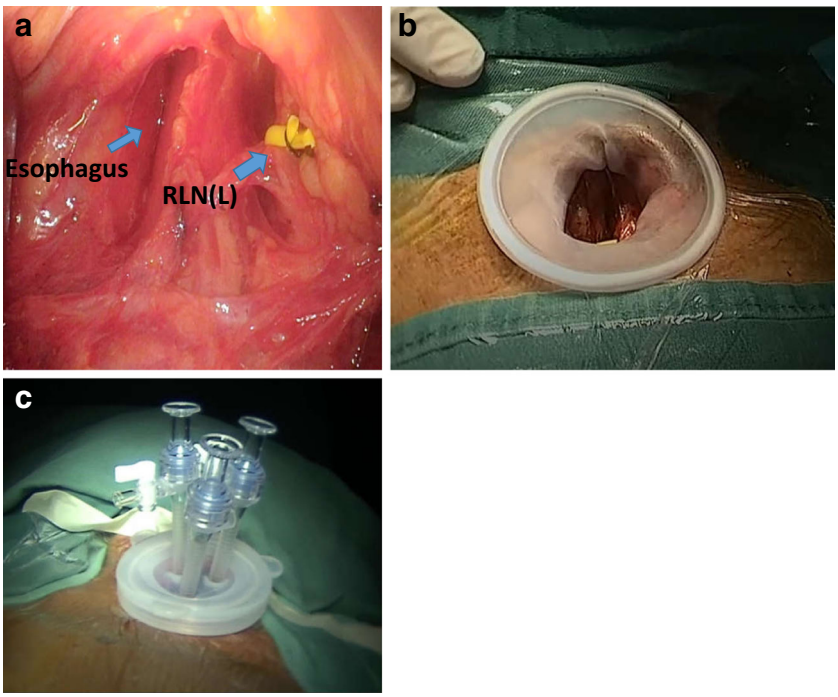

Fig. 3 **a** In the left neck incision, the left recurrent laryngeal nerve was dissected and marked. A 3.5-cm (diameter) protective sleeve was put in the incision (**b**), covered with a special protective cover (**c**). Three special trocars (diameter of 5 mm) were inserted into the cover through the access port, and carbon dioxide was injected into the mediastinum

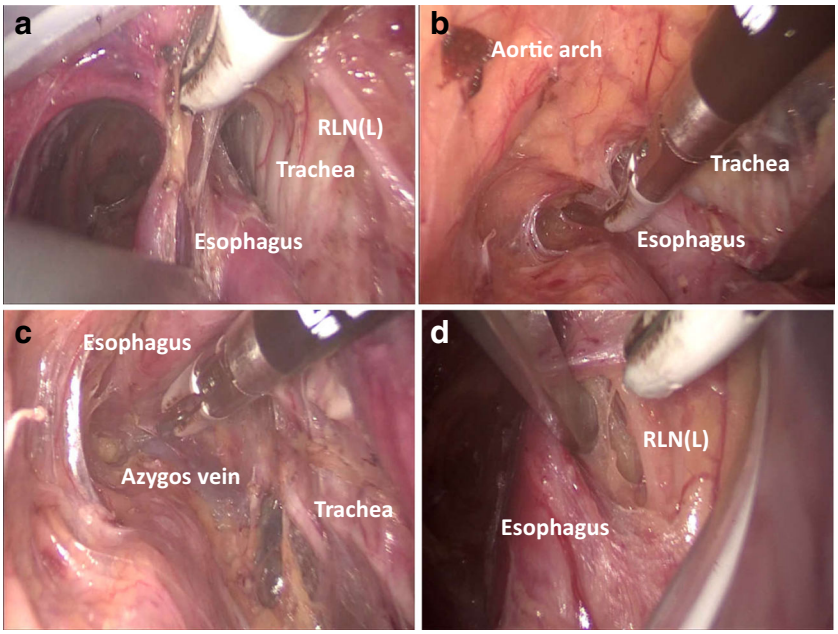

Fig. 4 **a**–**d** Anatomization of the esophagus in the upper mediastinum in the artificial emphysema

esophagus. At the origin of left recurrent laryngeal nerve, the esophagus was completely mobilized until the Maryland forceps cannot further reach.

If the preoperative PET-CT, ultrasound endoscopy, and chest-enhanced CT showed lymphadenopathy in the lymph nodes around the recurrent laryngeal nerve, the right cervical operation would be performed to dissect the lymph nodes around the right recurrent laryngeal nerve. Briefly, a 3-cm incision corresponding to the left side was made in the right neck. Along the right incision of the anterior border of the sternocleidomastoid muscle, the right recurrent laryngeal nerve was identified, around which the lymph nodes and soft tissue were removed. It is not necessary to dissect the esophagus from the right cervical incision due to the previous work done in the left incision. However, in the last ten patients of this new operation, we successfully dissected the lymph nodes around right recurrent laryngeal nerve through the single left cervical incision. We used the upper mediastinal tractor to push trachea for exposing the lymph nodes around the right recurrent laryngeal nerve.

For laparoscopic-assisted small incision surgery, the incisions of five ports for the laparoscopic operation were made as follows: two 1-cm incisions were made at 3 cm from the paraumbilical region and used as the main operative ports. One 1-cm incision below the right costal margin and another 5-mm incision under xiphoid were made and used as the assisting ports. A 2-cm incision was made exteriorly and a little higher than the left main operative port and used as the laparoscopic port (Fig. 5). The stomach was dissected and the lymph nodes in the abdominal cavity were removed using the conventional method. After opening the esophageal hiatus with an ultrasonic scalpel, two special mediastinal retractors were placed to expose the lower mediastinal esophagus. Blunt dissection was performed in the tissues by Maryland forceps, and lymph nodes around the subcarinal and inferior pulmonary vein were removed. The inferior esophagus was completely immobilized so that perforation with upper mediastinum could be achieved.

The esophagus was resected in the neck and a pouch was made in the proximal end. A nail anvil was inserted into the pouch, and then the purse-string suture was tightened and

Fig. 5 Five-port laparoscopic surgery

fixed in preparation of anastomosis. The distal end of the esophagus was sewed with a long line for the traction of the tubular stomach. A 5-cm subxiphoid incision was made and through which the esophagus and stomach were pulled out. Using cutting and stitching instruments, a tubular stomach with a width of about 4 cm was reconstructed. The tubular stomach was lifted up to the neck with a prefabricated long line through the esophageal bed of mediastinum. The stomach wall was cut at the highest point of the tubular stomach, and a circular stapler (EEA 24 or EEA 26, internal diameter = 15 mm or 17 mm, respectively; Jiangsu Milon Medical Device Technology Co., Ltd., China) was inserted to anastomose the greater curvature side of the tubular stomach and the cervical esophageal. Then, a linear cutting stapler was used to close the proximal end of the tubular stomach at 2 cm from the anastomotic site. The reconstructed stomach tube was then correspondingly inserted, forming the new esophageal tract. The jejunum was exposed through the subxiphoid incision, and a nutrition tube was placed and fixed in the jejunum. Each incision was closed with appropriate sutures and the operation was concluded. After surgery, a gastric tube was routinely used for 5 to 7 days, At the seventh day, postoperatively anastomotic leaks were evaluated by oral meglumine diatrizoate esophagogram and subsequent neck and chest CT scan. Postoperative pain was assessed by the visual analogue scale (VAS) score on the first 3 days after surgery.

Statistical Analysis

Continuous data were presented as the mean ± standard deviation (SD). Categorical data were expressed as number (percentage). All statistical analyses were performed using IBM SPSS Version 20 (SPSS Statistics v22, IBM Corporation, Somers, NY, USA).

Results

Patients

A total of 80 patients (51 males and 29 females) with esophageal cancer were included. The demographic and clinical characteristics of the 80 patients were summarized in Table 1. The mean age was 62.9 ± 6.5 (median, range 77–46) years. The tumor location included upper thoracic (n = 24), middle thoracic (n = 35), and lower thoracic areas (n = 21). The tumors were mainly at stage IIA (n = 36, 45%) and in ASA II (n = 43, 53.8%) classification.

As for the preoperative cardiopulmonary function, except for five cases with mild to moderate respiratory function failure, all patients had normal pulmonary and cardiac functions.

Table 1 Demographic and clinical characteristics of the 80 patients

Parameters	Case (n)	%
Sex		
Male	51	63.8%
Female	29	36.3%
Tumor location		
Upper thoracic area	24	30.0%
Mid-thoracic area	35	43.8%
Lower thoracic area	21	26.3%
Clinical stage		
IA	9	11.3%
IB	10	12.5%
IIA	36	45.0%
IIB	19	23.8%
IIIA	6	7.5%
ASA classification		
1	31	38.8%
2	43	53.8%
3	6	7.5%
Preoperative neoadjuvant chemotherapy		
No	65	82.3%
Yes	14	17.7%

Intraoperative Findings

The operation was successfully performed in all 80 patients. The mediastinoscopy was successfully performed in all 80 patients, while one case was switched from laparoscopy to open surgery as the patient had serious peritoneal adhesion due to previous treatment for colon cancer therapy.

The mean operation duration was 191.4 ± 27 min and the mean intraoperative blood loss was 147.3 ± 28.9 mL. The mean number of removed lymph nodes was 21.9 ± 4.1 (median = 21.5, range 15–33). In all patients, the postoperative pathological examination showed no evidence of residual tumor at the surgical margin. The R0 resection rate was 100%. The mean length of hospital stay was 17.8 ± 8.1 days.

Postoperative Outcomes

The incidences of postoperative complications were listed in Table 2. All the complications were Clavien-Dindo grade I–III. Five patients who had preoperative type I respiratory failure needed to stay in the ICU for 24 h postoperatively and then returned to the general wards. There was no perioperative death or postoperative cardiopulmonary complications. The 30- and 90-day mortality rates were both 0%. Seven cases (8.9%) developed anastomotic leakage, which was resolved by adequate drainage and nutritional treatment. Seventeen cases (21.25%)

Table 2 Postoperative complications

Complications	Cases (*n*)	Clavien-Dindo grade			%
		I	II	III	
Anastomotic fistula	7		7		8.9%
Anastomotic stricture	17	9		8	21.25%
Pleural effusion	7	7			9.0%
Breast milk chest	0				0.0%
Atelectasis	0				0.0%
Postoperative hoarseness	15	15			19.2%
Hoarseness at 3 months postoperation	3	3			3.8%

ICU intensive care unit

with anastomotic stricture, 8 of them with moderate (5–9 mm) or serious (< 5 mm) stricture received endoscopic balloon dilatation. Pleural effusion was found in 7 cases (9%), which were treated with adequate chest tube drainage.

Recurrent laryngeal nerve injury caused hoarseness in 15 cases (18.75%) and cough after drinking water in 2 cases (2.5%), respectively. The recurrent laryngeal nerve injury was treated with intravenous infusion of ganglioside (40 mg/day) for 3 days and gradually recovered within 1 to 2 months because the nerve injury was temporary and reversible. At 3 months postoperation, only 3 patients still had hoarseness.

The mean VAS score during the first 3 days after surgery for all patients was 4.09 ± 0.57.

Discussion

The surgical method described in this study was improved based on the methods described by Prof. Fujiwara,[12,13] Affiliated Hospital of Kyoto Prefectural University of Medicine, Japan. The operation was performed by two operation teams. One team made the cervical incision and performed the single-port mediastinoscopy for the dissection of upper mediastinal lymph nodes and upper esophageal. Simultaneously, another team performed laparoscopy for the dissection of lower mediastinal lymph nodes and lower esophageal segment (Fig. 6). Carbon dioxide was simultaneously pumped into the mediastinum and abdominal cavity to maintain the pressure at about 10 mmHg. The novel inflatable mediastinoscopy ensured an excellent surgical view in the mediastinal and abdominal operative field, markedly elevating the surgical safety and reducing the difficulty for the resection of the whole mediastinal lymph nodes and dissection of the whole esophagus. Thus, this surgical method overcomes the defects of the conventional non-transthoracic esophagectomy. In addition, the clear surgical view can effectively reduce the operation duration and intraoperative blood loss as compared with the thoracic-abdominal endoscopic or conventional open transthoracic esophagectomy of esophageal cancer radical surgery.[15,16] Moreover, the total esophageal excision and lymph nodes dissection can be appropriately performed.

Compared to transthoracic surgery, non-transthoracic surgery can effectively relieve postoperative pain and reduce the perioperative cardiopulmonary complications, thus expanding the surgical indications in the patients unable to receive transthoracic surgery, such as severe thoracic adhesions, chest abnormalities, and poor cardiopulmonary function.

During the operation, there are some issues which should be paid special attention. Identification of the recurrent laryngeal nerve via the left neck incision is crucial for a successful surgery. It should be avoided to excessively dissect and expose the left recurrent laryngeal nerve excessively as the excessive dissection would cause nerve demyelination, thus leading to nerve damage and hoarseness postoperation. Before surgery, it should be determined whether the right neck incision and nerve lymph node resection around the right recurrent laryngeal are needed based on the preoperative radiological findings. In the last ten patients of our study, we successfully resected the right recurrent laryngeal nerve lymph nodes via the left neck incision.

Some shortcomings of this surgical method should be pointed out. First, the surgical field is smaller in the mediastinum than in the thorax. Successful surgery in the narrow surgical field highly depends on the experience of the surgeon. We found that the operation was very difficult in the first few cases. It was easy to injure the recurrent laryngeal nerve or other important tissues causing bleeding. Consequently, there were 15 cases of postoperative hoarseness and 2 cases of cough upon drinking water in our patients. There was no major bleeding event in this study. It is important to use special upper and lower mediastinal retractors in the narrow operative spaces. In our procedure, Maryland forceps was used to separate and cut tissue. Even though the use of Maryland forceps produced a few smokes during operation, which did not affect the view of the surgical field. Second, this procedure used

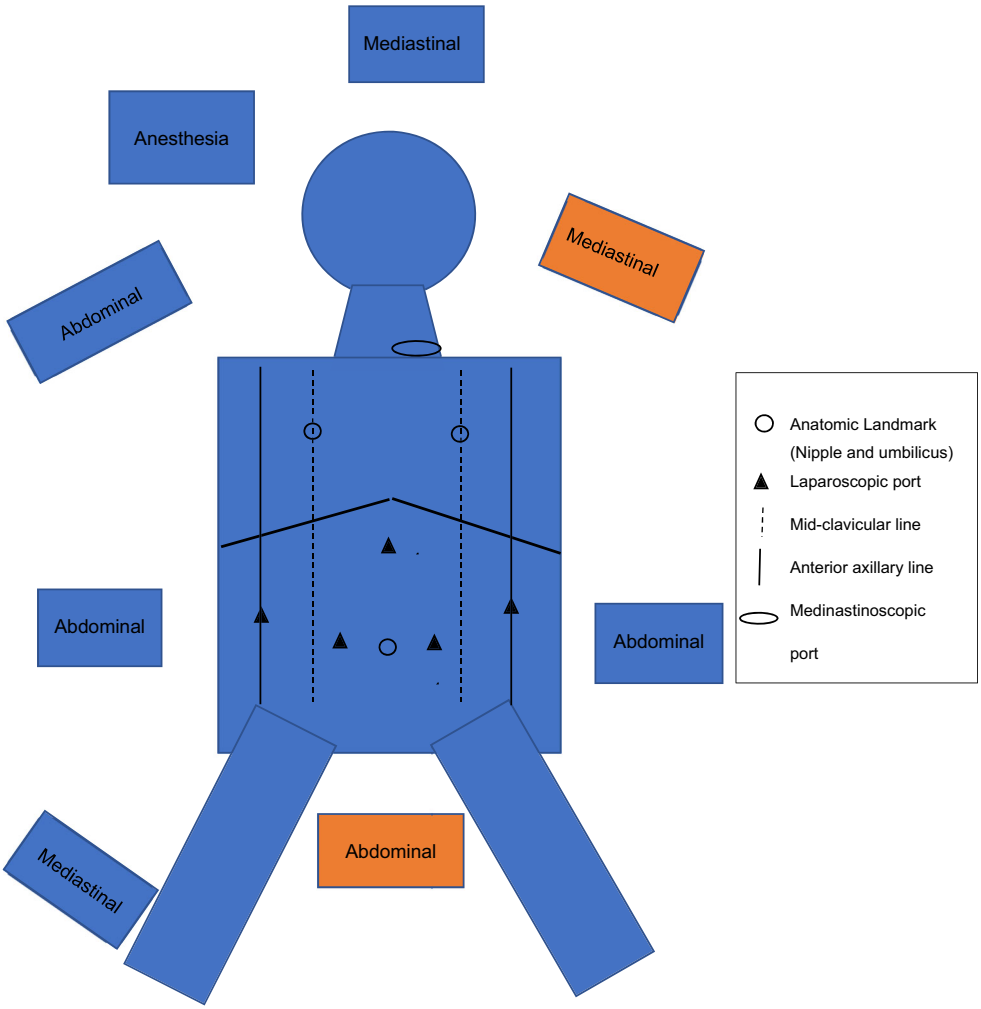

Fig. 6 The location of surgeon and assistants

inflatable mediastinoscopy and laparoscopy simultaneously so that the pressure of carbon dioxide insufflation was higher than that of mediastinoscopy or laparoscopy. High-pressure carbon dioxide insufflation is a risk factor for cardiopulmonary or cerebral complications. Therefore, the inflated pressure of artificial mediastinal emphysema should be strictly maintained within 10 mmHg, which can effectively expose the surgical field but not cause serious accumulation of carbon dioxide. Moreover, arterial blood gas analysis was performed every half hour during the operation.

There are still some limitations of this study. First, this surgical method was started to be performed in March 2016; hence, only short-term follow-up result was obtained. Nevertheless, all the patients are still being followed up for the long-term results. In addition, this study was a retrospective study, and we did not include patients receiving other methods for esophagectomy as the control group. In the following study, a well-designed, randomized controlled trial should be conducted to comprehensively evaluate the therapeutic efficacy and safety of this new surgical method. Furthermore, we did not assess the postoperative quality of life of the patients. All these limitations should be addressed in the following study.

Conclusion

In summary, our results showed that the single-port inflatable mediastinoscopy combined with laparoscopy possesses good therapeutic efficacy and safety for the radical esophagectomy in esophageal cancer, which is a feasible non-transthoracic treatment option for esophageal carcinoma.

Authors' Contributions

Xiaojin Wang: drafting and revising manuscript.
Xiaojian Li and Bin Zhang: acquisition
Hua Cheng: analysis

Hongcheng Zhong and Ruiqi Wang: interpretation of data
Beilong Zhong: coordination
Qingdong Cao: design and approval

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Compliance with Ethical Standards

Conflicts of Interest The authors declare that there are no conflicts of interest.

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