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HOW-I-DO-IT ARTICLE

Medial approach for subcarinal lymphadenectomy during thoracoscopic esophagectomy in the prone position

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Abstract

Purpose In esophageal squamous cell carcinoma (ESCC), lymph nodes (LNs) around the subcarina and main bronchi are thought to be highly involved. Therefore, complete dissection of these LNs with preservation of the pulmonary branches of the vagus nerves, which control important pulmonary functions, is recommended. The aim of this retrospective study was to investigate the feasibility of reliable method for lymphadenectomy around the subcarina and main bronchi, named the medial approach, during thoracoscopic esophagectomy in the prone position (TEP).

Methods This was a case-matched control study of patients who underwent TEP for ESCC. The fundamental concept in this method is to first exfoliate the LNs around the subcarina and main bronchi from the pericardium. Developing the operative field contributes to visualizing and preserving the pulmonary branches of the right vagus nerve. Twenty-three patients who underwent the medial approach and 23 patients who underwent the conventional approach were selected by the use of propensity score matching to compare the operative outcomes.

Results The medial approach significantly reduced operative time for procedure (16 ± 3 vs 30 ± 6 min, $p < 0.0001$) and operative blood loss (123 ± 108 vs 207 ± 162 ml, $p = 0.046$) comparing with conventional approach. The incidence of postoperative pneumonia was lower in the medial approach group (4%) than in the conventional approach group (15%) ($p = 0.069$).

Conclusions The medial approach for lymphadenectomy around the subcarina and both main bronchi during TEP is technically safe and feasible in shorting the operative time with possibility to reduce postoperative pneumonia.

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Keywords Thoracoscopic esophagectomy in the prone position · Lymphadenectomy around subcarina and main bronchi · Esophageal cancer · Medial approach · Pulmonary branches of the vagus nerve

Introduction

Subtotal esophagectomy with radical lymphadenectomy remains an effective therapeutic strategy for localized esophageal squamous cell carcinoma (ESCC) [1, 2]. However, it is known to be associated with high morbidity. Pneumonia, a major source of morbidity, is very common and significantly increase postoperative mortality [3, 4].

Since lymph nodes (LNs) around the subcarina and main bronchi are thought to be highly involved in esophageal cancer, complete dissection of these LNs is recommended [5, 6]. On the other hand, pulmonary branches of both vagus nerves run in a complex pattern in this area. Many important pulmonary functions are controlled by the vagus nerve [7–9]. Therefore, complete dissection of these LNs around the subcarina and main bronchi while preserving the pulmonary branches of the vagus nerve is recommended.

In 2006, thoracoscopic esophagectomy in the prone position (TEP) was adopted as a new, minimally invasive surgical approach [10]. Lymphadenectomy with TEP is currently being developed [11–14]. TEP is ergonomic for surgeon leading to perform fine technique such as preserving nerves. The aim of this study was to investigate the feasibility of a reliable method for lymphadenectomy around the subcarina and main bronchi, named the medial approach, during thoracoscopic esophagectomy in the prone position (TEP).

Methods

This was a case-matched control study of 115 patients with ESCC. They underwent TEPs at Kobe University and Hyogo Cancer Center from 2011 to 2017. The diagnosis of esophageal cancer was based on the seventh edition of the Union for International Cancer Control (UICC) tumor node metastasis (TNM) cancer staging system [15]. In this study, inclusion criteria included age 18–75 years; cT1–3, cN0–3 disease [15]; and being able to undergo simultaneous esophagectomy and reconstruction of the gastric conduit.

At both study institutions, the common practice was for all surgical candidates with ESCC to undergo TEP. Depending on the period, the following abdominal procedures were performed: complete laparoscopic surgery, hand-assisted laparoscopic surgery (HALS), or open laparotomy (OL). Three-field (neck, chest, and abdomen) lymph node dissection was performed when clinical supraclavicular node (LN) metastases were diagnosed by preoperative computed tomography (CT). We collected data on 115 curative procedures for ESCC. The type of lymphadenectomy around the subcarina and main bronchi was decided preoperatively. From 2011 to 2013, 35 patients underwent lymphadenectomy using the conventional approach. From 2013 to 2017, 80 patients underwent lymphadenectomy using the medial approach. All procedures were performed by one surgeon (T.O.) who had performed more than 30 TEPs with conventional extended lymphadenectomy prior to this study.

To improve the comparability of each group pair, we performed propensity score matching based on tumor location, depth of tumor invasion, lymph node metastasis status, preoperative chemotherapy, abdominal procedure, and lymph node dissection.

This study was approved by the Institutional Review Board and the Ethics Committee of the Kobe University and Hyogo Cancer Center.

Thoracic procedure

To permit easy retraction of the trachea, a single-lumen tracheal tube was inserted into the trachea and a blocker was inserted into the right main bronchus for one-lung anesthesia before surgery. The patient was initially placed in the prone position. Six 5- or 12-mm ports were inserted into the third intercostal space (ICS) lateral to the midaxillary line, the fifth and seventh ICSs on the posterior axillary line, the sixth and eighth ICSs on the midaxillary line, and the ninth ICS on the scapular line. The chest cavity was inflated via the ports with a CO_2 insufflation pressure of 8 mmHg. The endoscope was usually inserted through the ninth ICS [12].

Surgical technique

Medial approach

Process 1: medial (pericardial) approach

1. First, LNs around the subcarina and main bronchi are exfoliated from the pericardium toward the esophagus (Fig. 1, arrow ①). The landmarks in this field are the pericardium (Fig. 2, *top left*), right and left main bronchi (Fig. 2, *top right* and *bottom left*), carina, and left pulmonary vein (Fig. 2, *bottom right*).

Process 1: right bronchial membranous wall approach

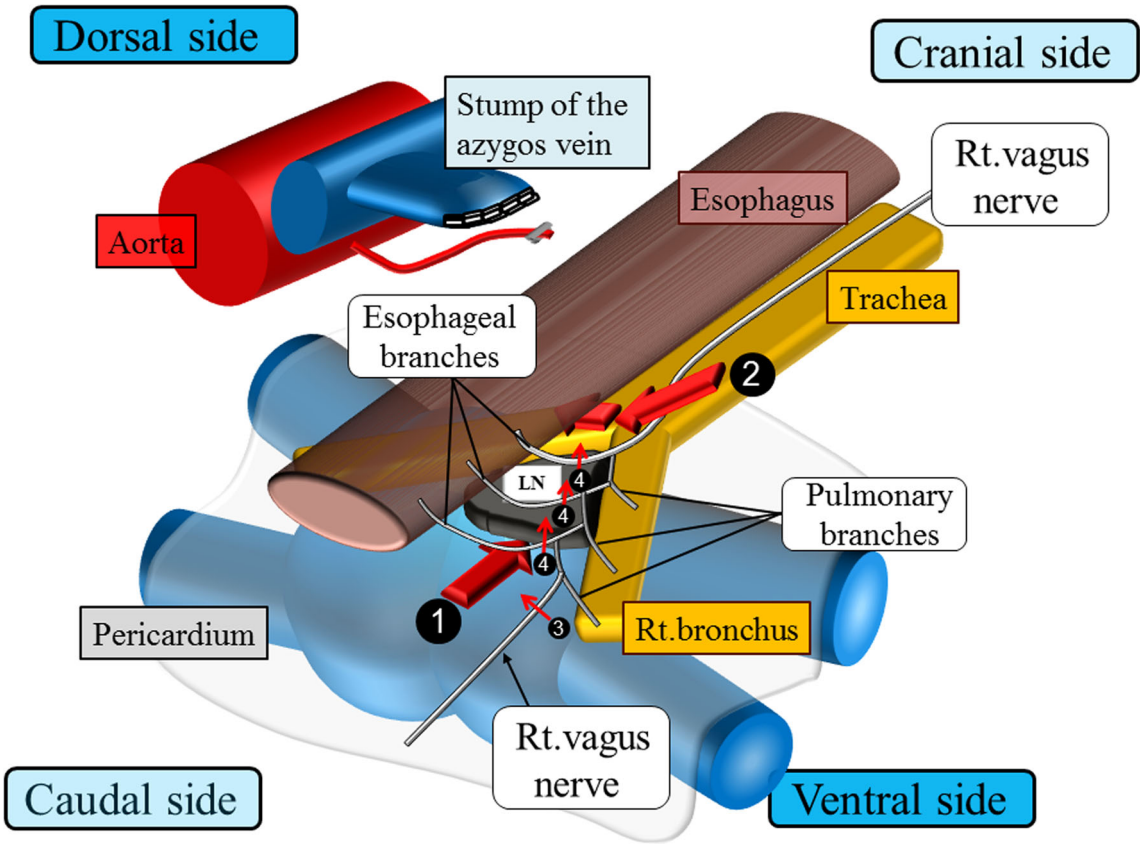

Fig. 1 Lymph nodes around the subcarina and main bronchi are exfoliated from the pericardium toward the esophagus (arrow ①). Next, the azygos vein and right tracheal artery are cut. The left bronchial membranous wall is exposed by exfoliating the esophagus (arrow ②). Subsequently, the right vagus nerve below the level of the last large pulmonary branch (arrow ③) and esophageal branches (arrow ④) are cut in succession but the pulmonary branches are preserved

2. Next, the right bronchial artery is cut (Fig. 3, *top left*). Subsequently, the left bronchial membranous wall is exposed by exfoliating the esophagus (Fig. 1, arrow ②) (Fig. 3, *top right*).
3. The right vagus nerve and its esophageal and pulmonary branches are exposed (Fig. 3, *bottom left*). Subsequently, the esophageal branches and right vagus nerve below the level of the last large pulmonary branch are cut, but the pulmonary branches are preserved (Fig. 1, arrows ③ and ④) (Fig. 3, *bottom right*).
4. LNs around the subcarina and main bronchi, which are already disconnected from the pericardium and right vagus nerve complex, are disconnected from the right main bronchus (Fig. 4, arrow ⑤, Fig. 5, *top left*), carina, and left main bronchus (Fig. 4, arrow ⑤, Fig. 5, *top right*) in succession. After lymphadenectomy, preservation of structures, including the pulmonary branches of right vagus nerve, can be confirmed visually (Fig. 5, *bottom left and right*).
5. The pulmonary branches of the left vagus nerve are preserved by vagotomy distal to the most caudal pulmonary branch.

Conventional approach

The tissue around the subcarina and both main bronchi is dissected only from the side of the right bronchial membranous wall. With insufficient mobility of the LNs due to the lack of exfoliation from the medial side (from the pericardium), lymphadenectomy around the subcarina and both main bronchi is accomplished with considerable difficulty. Sparing of the pulmonary vagus nerve branches was not performed.

Table 1 summarizes the steps of the medial maneuver.

Abdominal procedure

The abdominal procedure was performed with complete laparoscopic surgery, HALS [16], or OL. After gastric mobilization, abdominal lymphadenectomy around the left gastric pedicle and celiac axis, and excision of the entire isolated thoracic esophageal specimen with dissected LNs through the esophageal hiatus, a gastric conduit of 3–4 cm in width was created outside of the wound and raised via the posterior mediastinal or antethoracic route.

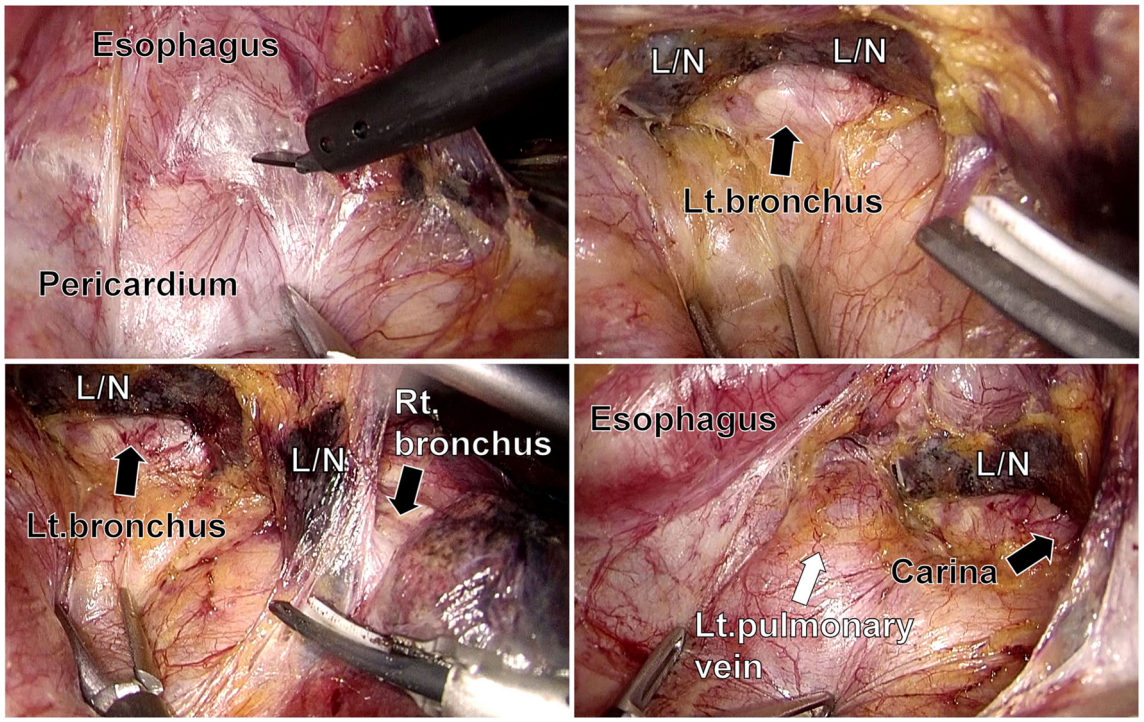

Fig. 2 Images from Fig. 1, arrow ①. Top left: Lymph nodes are exfoliated toward the esophagus. The landmark in this field is the pericardium. Top right: Lymph nodes on the left side are exfoliated first. The left bronchus can be confirmed as the cranial landmark. Bottom left: Subsequently, lymph nodes on the right side are exfoliated from the pericardium. The landmark in this field is the right bronchus. Bottom right: After exfoliation of lymph nodes, the left pulmonary vein and carina can be confirmed

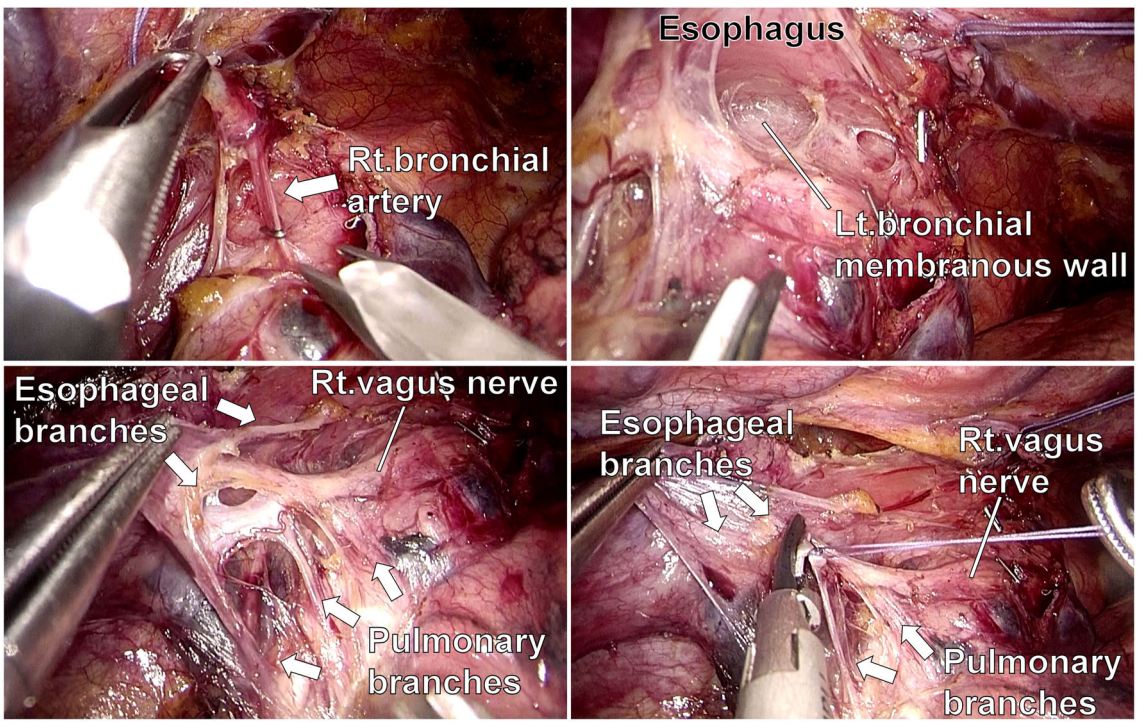

Fig. 3 Top left: After cutting of the azygos vein, the right bronchial artery is cut. Top right: The left bronchial membranous wall is exposed by exfoliating the esophagus (Fig. 1, arrow ②). With this procedure, the surgeon can confirm the position of the carina. Bottom left: Right vagus nerve, with the esophageal and pulmonary branches exposed. Bottom right: Subsequently, the pulmonary branches are preserved by performing the vagotomy distal to the most caudal large pulmonary branch and cutting the esophageal branches in order (Fig. 1, arrows ③ and ④)

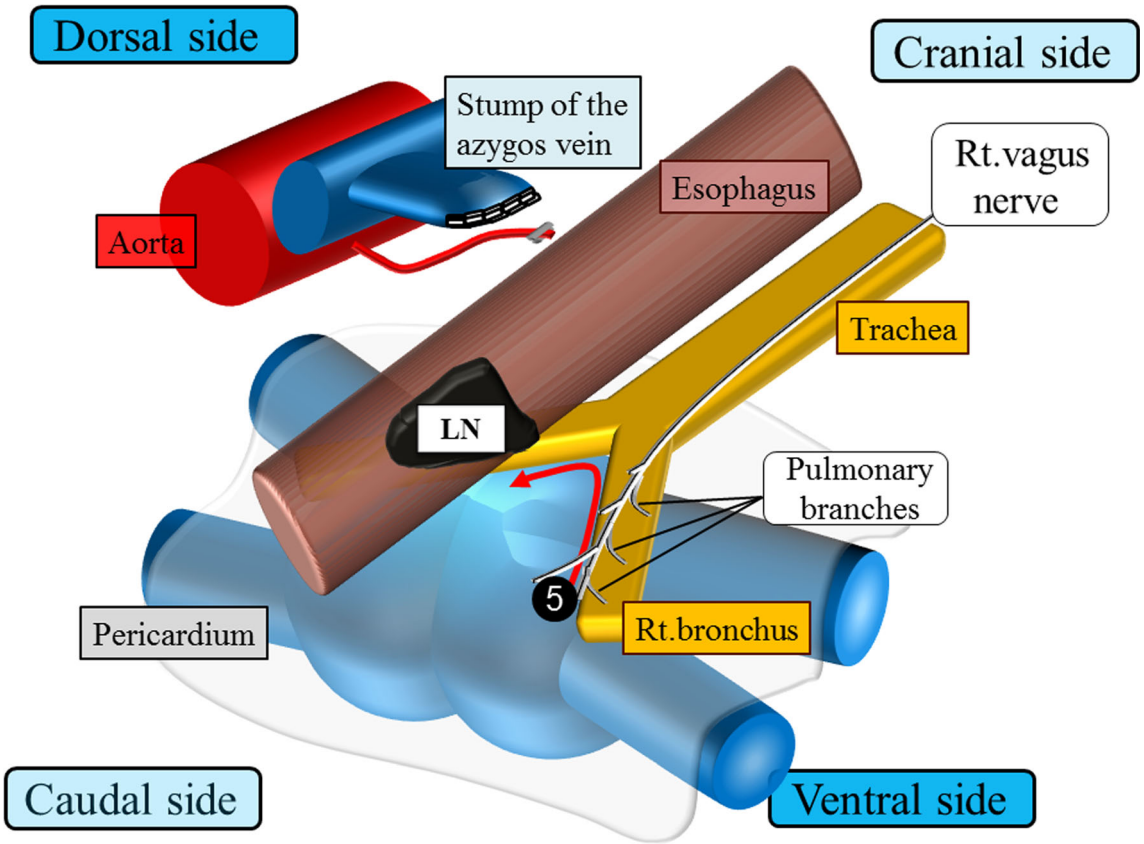

Fig. 4 Lymph nodes around the subcarina and main bronchi are disconnected from the right bronchus, carina, and left bronchus in succession (arrow ⑤)

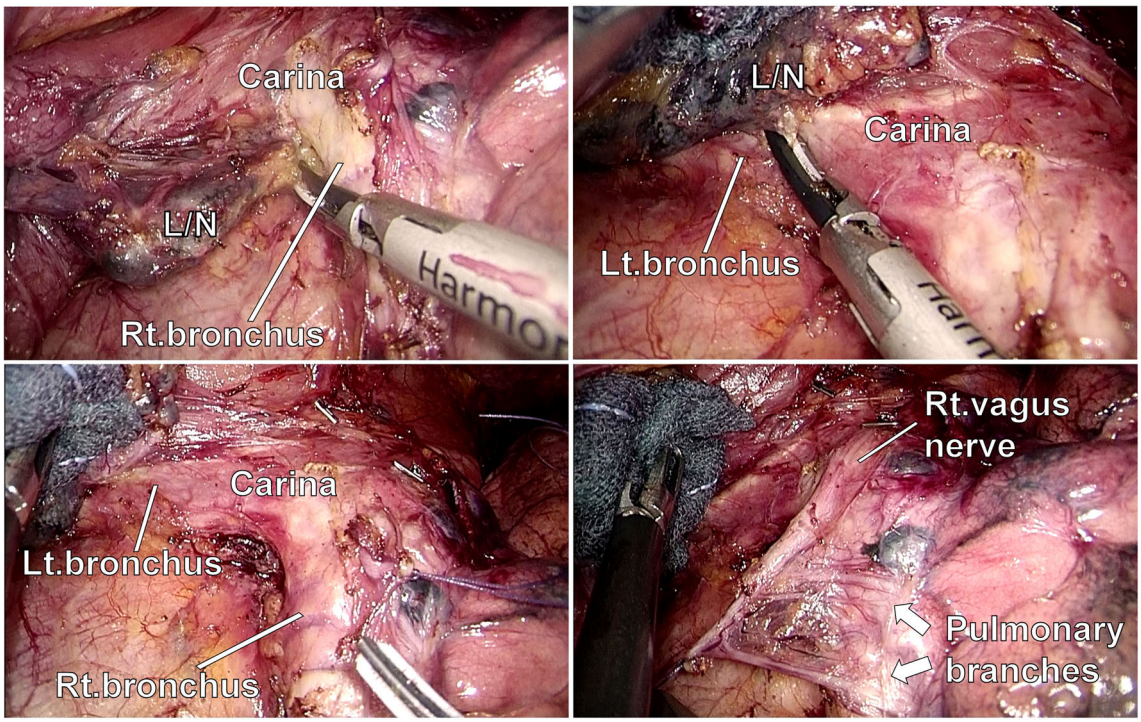

Fig. 5 Top panels: Lymph nodes are disconnected from the right bronchus, carina, and left bronchus in succession (Fig. 4, arrow ⑤). Bottom left: An intact bifurcation can be confirmed visually after lymphadenectomy. Bottom right: Preserved pulmonary branches of the right vagus nerve can be confirmed

Table 1 Summary of the medial approach

Process	Steps
Process 1	Medial (pericardial) approach
	① Lymph nodes on the left side are exfoliated from the pericardium.
	② The left pulmonary vein and left main bronchus are exposed.
	③ Lymph nodes attached to the right main bronchial cartilage are exfoliated from the pericardium.
Process 2	Right bronchial membranous wall approach
	④The right bronchial artery is cut.
	⑤ The left bronchial membranous wall is exposed by exfoliating the esophagus.
	⑥ Esophageal branches of the right vagus nerve and the right vagus nerve distal to the most caudal large pulmonary branch are cut, but the pulmonary branches are preserved.
	⑦ Lymph nodes are disconnected from the right main bronchus, carina, and left main bronchus in succession.

Cervical procedure

The left neck was the site of the anastomosis. For three-field lymphadenectomy, supraclavicular nodes in upper or middle esophageal tumors or LNs preoperatively diagnosed as metastatic based on enhanced computed tomography were dissected through a collar incision.

Evaluation of the technique

The operative time for the entire thoracic procedure and for lymphadenectomy around the subcarina and both main bronchi, operative blood loss, rate of conversion to open surgery, number of dissected LNs during the entire thoracic procedure and around the subcarina and both main bronchi, intraoperative morbidity related to the air duct, rate of pneumonia, time to resumption of ingestion, and duration of postoperative hospital stay in the two groups were compared.

Propensity score matching

A key issue in any case–control study is the matching of cases to controls. The propensity score is the conditional probability of being assigned to a particular treatment given a vector of observed covariates. Both large- and small-sample theory show that adjustment for the scalar propensity score is sufficient to remove bias from all observed covariates [17]. In this retrospective study, we used propensity score matching to assemble two comparable groups.

After estimating the propensity score of patients treated with conventional approach, we matched each patient sequentially to the patient treated with medial approach who had the closest propensity score, using simple 1:1 nearest-neighbor matching. We imposed a caliper of 0.20 of the standard deviation of the logit of the propensity score. We included tumor location, depth of tumor invasion, lymph node metastasis status, preoperative chemotherapy, abdominal procedure, and lymph node dissection as covariates.

Statistical analysis

Differences between the two groups were analyzed using the χ^2 test, Mann–Whitney U test, or Student's t test, as appropriate. p values < 0.05 were considered statistically significant.

Results

From 2011 to December 2017, we collected data on 46 (medial approach group $n = 23$; conventional approach group $n = 23$) curative procedures for esophageal cancer by using the propensity score method to achieve a valid comparison of outcomes between the medial approach and conventional approach groups. Patient and tumor characteristics are shown in Table 2. There were no significant differences between the two groups in gender distribution, age, tumor location and depth, lymph node metastasis, stage, histology, preoperative therapy, abdominal procedure, conduit and route for reconstruction, and LN dissection (Table 2) in matched cohort. The duration of the thoracic procedure (287 ± 36 vs 325 ± 49 min, $p = 0.005$) and the operative time for dissection around the subcarina and both main bronchi (16 ± 3 vs 30 ± 6 min, $p < 0.0001$) were significantly shorter in the medial approach group. Estimated blood loss was also significantly lower in the medial approach group (123 ± 108 vs 207 ± 162 ml, $p = 0.046$). On the other hand, there was no significant difference in the number of dissected LNs around the subcarina and both main bronchi between the two groups. The rate of pneumonia was lower in the medial approach group than in the conventional approach group although there was no significant difference ($p = 0.069$). None of the other operative results were significantly different between the two groups (Table 3).

Table 2 Clinicopathologic characteristics of patients who underwent lymphadenectomy using the medial approach or conventional approach

	Whole cohort			Matched cohort		
	Medial approach group ($n = 80$)	Conventional approach group ($n = 35$)	p	Medial approach group ($n = 23$)	Conventional approach group ($n = 23$)	p
Gender (male/female)	68/12	30/5	0.921	20/3	20/3	1.000
Age (years)	64.9	65.3	0.834	66.8	64.0	0.204
Tumor location (upper/middle/lower esophagus)	19/36/25	12/8/15	0.079	5/8/10	8/8/7	0.543
Depth of tumor invasion (cT1/T2/T3/T4)	33/11/36/0	9/15/11/0	0.003	6/7/10/0	6/7/10/0	1.000
Lymph node metastasis (cN0/N1–3)	41/39	17/18	0.792	10/13	9/14	0.765
UICC c-stage (I/II/III/IV)	32/19/23/6	15/10/10/0	0.408	6/11/3/3	7/7/9/0	0.073
Histology (scc/others)	80/0	35/0	1.000	23/0	23/0	1.000
Preoperative chemotherapy (yes/no)	44/36	20/15	0.832	15/8	14/9	0.760
Abdominal procedure (laparoscopy/HALS/open)	23/51/6	0/19/16	< 0.001	0/18/5	0/16/7	0.502
Conduit (stomach/others)	80/0	35/0	1.000	23/0	23/0	1.000
Reconstruction route (posterior mediastinum/others)	75/5	33/2	0.912	20/3	21/2	0.636
Lymph node dissection (extended two-field/three-field)	53/27	18/17	0.132	11/12	10/13	0.767

UICC Union for International Cancer Control, *scc* squamous cell carcinoma

Discussion

The sympathetic nervous system and vagus nerve complex run across the mediastinum. To preserve organ function, branches of these nerves should be spared, even though not sparing them makes it easy to ensure a radical and complete lymphadenectomy. Pulmonary branches of the vagus nerve run over the subcarinal and main bronchial lymph nodes in a complex pattern [18]. These branches exert an important regulatory role in inflammation and many pulmonary functions such as the cough reflex, bronchial diameter regulation, and mucous production [7–9]. Thus, sparing the entire vagus nerve during esophagectomy improves recovery [19]. One clinical study has suggested that sparing the pulmonary branches of the vagus nerve during open transthoracic esophagectomy reduces the incidence of pulmonary complications and even mortality [20]. Consequently, subcarinal and main bronchial LN dissection with sparing of the pulmonary branches of the vagus nerve is very important. Technically, the pulmonary branches could be preserved by transecting the vagus nerve below the level of the last large

Table 3 Surgical outcomes of patients who underwent the medial or conventional approach

	Medial approach group ($n = 23$)	Conventional approach group ($n = 23$)	p
Operative time for entire thoracic procedure (min)			
Chest	287 ± 36	325 ± 49	0.005
Dissection around the subcarina and main bronchi	16 ± 3	30 ± 6	< 0.0001
Operative blood loss (ml)	123 ± 108	207 ± 162	0.046
Conversion to open surgery	0	0	1.000
Number of dissected lymph nodes			
Chest	29 ± 10	28 ± 13	0.804
Around the subcarina and main bronchi	7 ± 5	8 ± 6	0.351
Intraoperative morbidity related to the air duct	0	0	1.000
Occurrence of pneumonia[a] (more than grade II)	1 (4%)	5 (15%)	0.069
Time to resumption of ingestion (days)[b]	7 (5–49)	6 (4–24)	0.105
Postoperative hospital stay (days)[b]	22 (13–117)	17 (9–157)	0.382

Data are expressed as means ± SD unless otherwise indicated. Data are expressed as medians

[a] Postoperative morbidity were analyzed according to the Clavien–Dindo classification

[b] Data are given as medians

pulmonary branch [17, 21]; however, it is difficult because the pulmonary branches are attached to the subcarinal and main bronchial LNs. It is also more difficult on the right side due to the direction of the surgical approach. Usually, esophagectomy is performed via the right thoracic approach; thus, the right vagus system exists on the same side as the subcarinal and main bronchial LNs. To avoid pulmonary branch injury, there should be some ingenuity in lymphadenectomy technique. In patients with conventional approach without sparing of the pulmonary vagus nerve branches, occurrence of pneumonia had not been so rare. Thus, we standardized medial approach with sparing of the pulmonary vagus nerve branches for the contribution to reducing the pneumonia. Even though en bloc subcarinal lymphadenectomy by mobilizing lymph nodes from the pericardium has been performed from more than 20 years ago [22], there was few technical reports in TEP. So we described the knack and pitfall of this procedure in detail at this article.

The key feature of our medial approach is mobilization of the subcarinal and main bronchial LNs before dealing with the vagus nerve system. Doing so makes it easy to develop the operative field, which contributes to recognizing the pattern of the right vagus nerve arborization into pulmonary branches and ensuring that the right vagotomy is distal to the most caudal large pulmonary branch. This approach allows surgeons to perform reproducible lymphadenectomy with sparing of the right vagus nerve branches. Unexpectedly, the feasibility of our method was confirmed by significant shortening of operative time for dissection comparing to the conventional approach. Additionally, reduction of estimated operative blood loss was also seen. In conventional approach, bleeding of subcarinal LNs had occurred frequently because LNs attached to the pericardium were fragile for external pressure by forceps. Acquirement of flexibility of the subcarinal LNs by first mobilization from the pericardium might contribute to prevent LNs breaking that lead to the bleeding. Hemostatic procedure should prolong the operation time. Necessity of astriction around subcarina after lymphadenectomy, which needed about 10 to 15 min and was not included in the time of dissection around the subcarina and main bronchi, is the other reason of the prolonged operative total time in the conventional group. Concerning the decreasing of the postoperative pneumonia, sparing of the right vagus nerve branches might make any contribution although there was no significant difference. Occurrence of pneumonia is multifactorial so not just sparing of the right vagus nerve branches around the subcarina and main bronchi but many other factors affect to the reduction of the pneumonia. But feasibility of medial approach by sparing of the right vagus nerve branches was verified. We previously reported that at least 30 cases were needed to reach a plateau in the TEP procedure [23]. Surgeon (T.O.) had performed more than 30 TEPs with conventional extended lymphadenectomy prior to this study. So it is certain that these results are not due to learning curve.

Concerning the left side, it is easy to preserve the pulmonary branches by finding the most caudal large pulmonary vagus nerve branch and performing vagotomy distal to this branch orthodromically, because the left vagus nerve system is posterior to the subcarinal LNs.

The major limitations of this study relate to its retrospective, small size, and single-surgeon design. Furthermore, the study periods were different between two procedures. Minimally invasive esophagectomy including TEP consists of complex procedures so that not just medial approach but multi-factories as well may affect the changed outcomes. After consideration of these limitations, our results indicate that medial approach for subcarinal and main bronchial lymphadenectomy with sparing of the pulmonary branches of the vagus nerve is a reliable, reproducible method. Since no definitive conclusions can be drawn from this study, a randomized prospective trial of this technique is desirable.

Conclusion

The medial approach for subcarinal and main bronchial lymphadenectomy sparing of the right vagus nerve branches in TEP is technically safe and feasible procedure that reduces operative time in the subcarinal field and entire thoracic procedure, and shows the possibility to decrease the postoperative pneumonia.

Authors' contributions (1) Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work. Conception or design of the work: Taro Oshikiri, Susumu Miura, Gosuke Takiguchi, Hiroshi Hasegawa. Acquisition of data: Taro Oshikiri, Yasuhiro Fujino, Gosuke Takiguchi, Masahiro Tominaga, Masashi Yamamoto, Kimihiro Yamashita, Yoshihiro Kakeji. Interpretation of data for the work: Taro Oshikiri, Gosuke Takiguchi, Yoshihiro Kakeji. (2) Drafting the work or revising it critically for important intellectual content. Drafting the work: Taro Oshikiri, Susumu Miura, Yoshihiro Kakeji. Revising the work critically for important intellectual content: Taro Oshikiri, Masashi Yamamoto, Shingo Kanaji, Takeru Matsuda, Tetsu Nakamura, Satoshi Suzuki, Yoshihiro Kakeji. (3) Final approval of the version to be published. All authors. (4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the study.

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