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ORIGINAL RESEARCH

Perioperative Clinical Results of Transcervical and Transhiatal Esophagectomy versus Thoracoscopic Esophagectomy in Patients with Esophageal Carcinoma: A Prospective, Randomized, Controlled Study

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Background: This study assessed the efficacy of transcervical and transhiatal esophagectomy versus thoracoscopic esophagectomy in patients with esophageal carcinoma (EC).

Methods: A total of 80 patients with EC were enrolled in this study, including 40 cases in the observation group that received transcervical combine transhiatal esophagectomy and the rest 40 cases of the group that underwent thoracoscopic esophagectomy. The preoperative, intraoperative, and postoperative data were analyzed between the two surgeries, regarding perioperative bleeding, the total number of dissected mediastinal lymph nodes, operative time, number of lymph nodes in the left para-recurrent laryngeal nerve (para-RLN) or the right para-RLN, time in the intensive care unit (ICU), postoperative pain score, the length of postoperative stay (LOPS), PO_2/fraction of inspired oxygen (PO_2/FiO2), pulmonary infection, and lymphatic metastasis.

Results: The operations were successfully performed in all 80 patients. The results showed that patients who underwent transcervical and transhiatal esophagectomy had shorter operations than those with transthoracic esophagectomy (200 minutes vs 235 minutes, Kruskal–Wallis test [Z] = –3.700, P < 0.001). The number of dissected mediastinal lymph nodes in the left para-RLN in the observation group was higher than in the control group (25.0% vs 2.5%, Z = 2.568, P = 0.010). The postoperative pain score day 1 (0.0% vs 17.5%, Z = –4.292, P < 0.001), postoperative pain score day 3 (12.5% vs 37.5%, Z = –3.363, P < 0.001) and 48-h PO_2/FiO2 (290 minutes vs 255 minutes, Z = 3.747, P < 0.001) were significant between the two groups. The LOPS of patients with EC in the observation group was shorter than the control group (7 vs 8, Z = –2.119, P = 0.034). The number of patients receiving transcervical and transhiatal esophagectomy that developed postoperative pulmonary infections was less than the controls (chi-square [χ^2] = 4.114, P = 0.043). Moreover, the transcervical and transhiatal esophagectomy was an independent protect factor for postoperative pulmonary infection (odds ratio [OR] =7.801, P = 0.037).

Conclusion: The transcervical and transhiatal esophagectomy is a good operation for treating patients with EC, which may offer an opportunity to treat cases who cannot have thoracotomy.

Keywords: esophageal carcinoma, transcervical and transhiatal esophagectomy, thoracoscopic esophagectomy, efficacy, esophagectomy

Background

Esophageal carcinoma (EC) is a common gastrointestinal cancer with a high incidence and mortality in developing countries.[1,2] Studies reported that EC has a poor prognosis with a 5-year survival rate of <20%.[3] To date, esophagectomy

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is the gold standard treatment for the early, intermediate, and locally advanced-stage EC, after which the survival rate was around 50%.[4] The classic surgical method for esophageal cancer is subtotal esophagectomy + lymph node dissection through three incisions in the neck, chest and abdomen, which takes a long time, causes great trauma and has an incidence of postoperative complications as high as 13.4–38.2%.[5,6] In recent years, minimally invasive esophagectomy through thoracic cavity has been gradually applied in the treatment of EC. Compared with classical esophagectomy, minimally invasive esophagectomy has similar lymph nodes removed number and the complication rate is lower.[7–12] However, EC patients with severe thoracic deformities or poor lung function who cannot tolerate the Surgery may lost the opportunities for survival.

Esophageal stripping and transhiatal esophagectomy has been developed to cure EC patients with severe thoracic deformities or poor lung function and cannot tolerate thoracotomy. According to the data from the Society of Thoracic Surgeons Database (2015–2017), more than 1000 operations were reported as transhiatal.[13] However, neither of these two methods can effectively clear mediastinal lymph nodes. We believe that although these treatments can lower cardiopulmonary complications, failure to dissect the chest lymph nodes increases the risk of lymph node metastasis.[14] Transcervical and transhiatal esophagectomy is a novel operation process without thoracotomy, which may dissect the chest lymph nodes and improve the prognosis of EC. We carried out this surgical method since 2014, and preliminarily observed that the number of dissected lymph nodes was similar to that of conventional minimally invasive resection of EC, while pulmonary complications were significantly reduced. To further verify this result, we conducted this study. This study was approved by the Institutional Review Board (IRB) of Chongqing Cancer Hospital, and the approval number was No. 2019 (177).

Methods

This is a 1 year single center, prospective, randomized, open and parallel controlled trial, which aims to compare the perioperative clinical results of transcervical and transhiatal esophagectomy with thoracoscopic esophagectomy in patients with EC. According to the previous transcervical and transhiatal esophagectomy carried out in our department, the incidence rate of lung infection was about 5%. According to the literature, the incidence rate of lung infection in minimally invasive esophagectomy for EC was 24.8%.[15] Choosing α was 0.05, bilateral, β was 0.1, unilateral, and the required sample size was 14 cases. It was planned to select 20 cases in the experimental group and 20 cases in the control group. Considering many factors that need to be compared, 80 cases were finally selected and randomly divided into the observation group and the control group according to 1:1.

Patients

This present study screened 80 patients with EC admitted to the Thoracic Surgery Department at Chongqing Cancer Hospital between September 2018 and November 2019. These cases were divided into the observation group (n = 40) and the control group (n = 40). Patients in the observation group received transcervical and transhiatal esophagectomy, and the control group underwent thoracoscopic esophagectomy. The operation of the experimental group was performed by the medical group with 100 cases experience of transcervical and transhiatal esophagectomy, while the operation of the control group was performed by the medical group with more than 200 cases experience of transcervical and transhiatal esophagectomy.

Inclusion criteria: (1) 65–70 years old; (2) patients with EC whose clinical stage was cT1-3 N0-1 M0. Clinical stage mainly relies on enhanced CT and ultrasound. PET-CT was not used as a routine preoperative examination due to the lack of funding. (3) moderate or severe impairment of lung function; (EV1 accounts for 30–80% of the estimated value) (4) Willing to accept surgical treatment and willing to participate in this experiment.

Exclusion criteria: (1) severe or extensive pleural adhesions; (2) adjacent organs invaded by the tumor; (3) pulmonary function could not tolerate unilateral pulmonary ventilation; (4) patients with other diseases, such as liver failure. (5) Lymph nodes were enlarged and fused into mass with a short diameter greater than 2.5cm. (6) received neoadjuvant chemotherapy or neoadjuvant chemoradiotherapy before.

Clinical Indicators

A number of baseline preoperative, intraoperative, and postoperative indicators were noted, including age, gender, body mass index (BMI), forced expiratory volume in one second (FEV1), maximal voluntary ventilation (MVV), partial pressure of oxygen (PO_2, mmHg,), partial pressure of carbon dioxide (PCO_2, mmHg), Pulmonary complications (respiratory failure, pulmonary infection, and atelectasis)(respiratory failure: the criterion is that oxygen absorption alone cannot guarantee oxygen balance, and non-invasive or invasive ventilator is required to assist ventilation, pulmonary infection diagnosis is based on symptoms and signs, laboratory tests, and CT images, diagnosis of atelectasis is determined by CT), nutrition risk screening 2002 (NRS-2002), T stage, N stage, tumor location, tumor length (cm), perioperative bleeding, the total number of dissected mediastinal lymph nodes, operative time (min), number of lymph nodes in the left para-recurrent laryngeal nerve (para-RLN) or right para-RLN, time in the intensive care unit (ICU, days), postoperative pain score (the highest pain score was selected for the first three days after surgery), the length of postoperative stay (LOPS), 24-h PO_2/fraction of inspired O_2 (PO_2/FiO2), 48-h PO_2/FiO2, fiberoptic bronchoscopy (FOB), and lymphatic metastasis. The primary outcomes were the total number of dissected mediastinal lymph nodes and lymph nodes in the left or right para-RLNs. The flow chart for the trial is shown in Figure 1.

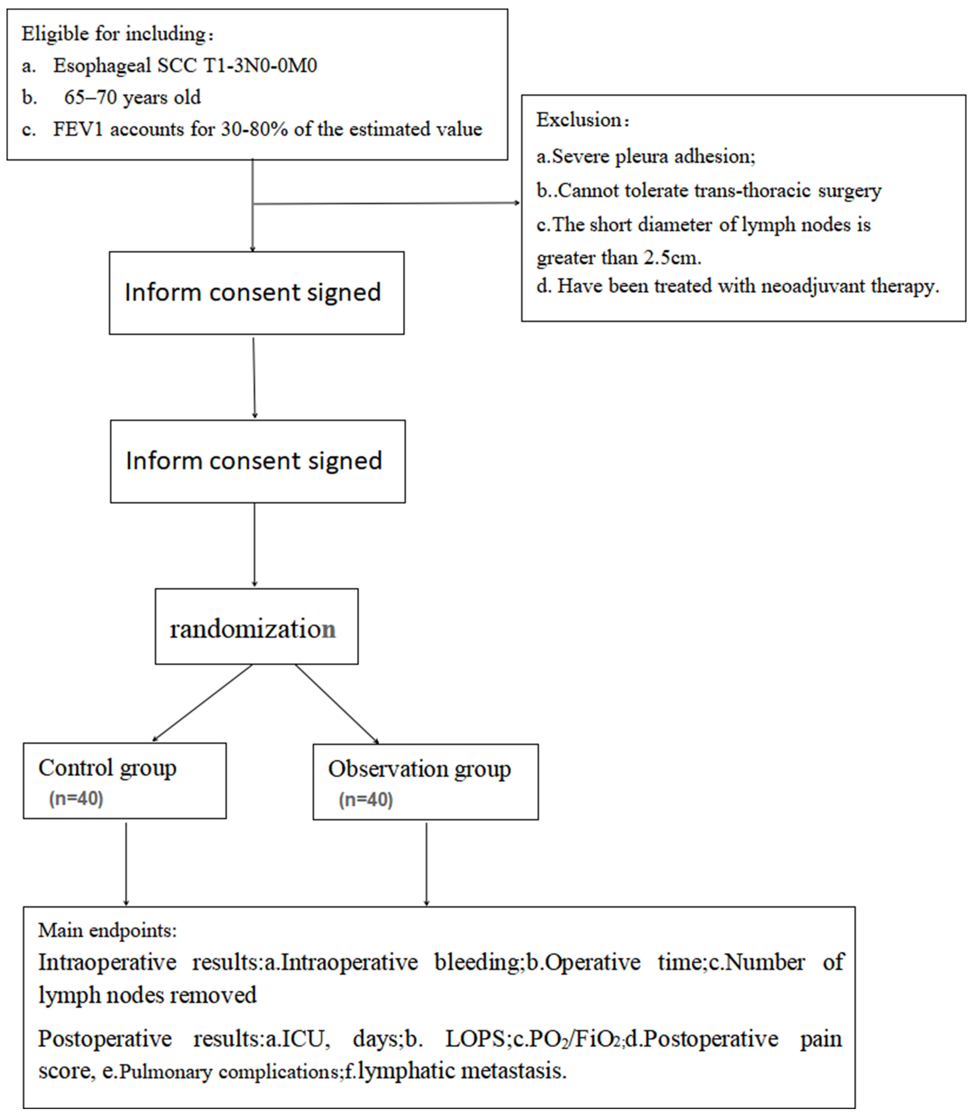

Figure 1 The flow chart for the trial.

Transcervical and Transhiatal Esophagectomy

Abdominal Operation

(1) A single-lumen endotracheal tube was placed, and the patient was placed in a supine position with a slightly elevated head. (2) The surgeon was on the patient's right side, and an incision about 1 cm in length was made at the lower left side of the umbilicus, which was a laparoscopic observation port. Two holes were made in the ventral midline of the upper abdomen as the main and auxiliary operation holes for the surgeon. The middle point of the lower edge of the left costal arch and the upper right part of the exploration hole were the operation holes for the assistant. (3) Pneumoperitoneum was established with a CO_2 pressure of 8–10 mmHg. (4) The stomach was mobilized from the greater omentum side to the esophageal hiatus, and the splenic artery was exposed, after which the lymph nodes around the splenic artery and the greater curvature under the cardia were dissected. Then the esophageal hiatus was widened, and the left esophagus was mobilized using the descending aorta, posterior border of the pericardium, and left pleura as anatomical landmarks. The mobilization of the left esophagus through the esophageal hiatus was ended when the subcarinal lymph nodes, the left main bronchus, and the carina were exposed. (5) The hepatogastric ligament was incised, and the lesser curvature was mobilized, after which the left gastric artery was cut with a hem-o-lok. Afterward, the lymph nodes of the celiac trunk and the lesser curvature in the subcardia, as well as those along the left gastric and hepatic arteries, were dissected. The right esophageal mobilization was performed using the right pleura, the posterior border of the pericardium, and the descending aorta as anatomical landmarks. The mobilization of the right esophagus was ended after exposure of the right main bronchus. Then, lymph nodes in the upper cardia and adjacent to the left and right lower pulmonary veins were dissected. After the abdominal esophagus was mobilized, the descending aorta, left and right pleurae, tracheal carina, left and right main bronchi, azygos vein, posterior border of the pericardium, and left and right inferior pulmonary veins could be clearly exposed. (6) After the above steps, an incision about 8 cm in length was made in the upper abdomen. The abdominal operation was suspended, and the neck operation was performed.

Neck Operation

(1) An incision about 5 cm in length was made along the anterior border of the left sternocleidomastoid muscle, and the esophagus was mobilized under direct vision, while the left para-RLN was exposed, and the esophagus was transected to create a space for the neck operation. An incision about 1 cm in length was made along the anterior border of the right sternocleidomastoid muscle, and a 5-mm trocar was inserted to connect with the left mobilized cervical esophageal space. (2) A gastric tube was inserted into the distal end of the esophagus as a traction tube. One side of the traction tube was sutured and fixed with the esophagus, and the other side was inserted into the gastric cavity. Then, the stomach was prolapsed from the epigastric incision, and a small incision was made in the gastric wall of the lesser curvature to prolapse the traction tube, after which the small curved side incision was sutured to avoid gastric juice overflow. (3) A self-made inflator was placed in the neck incision to establish an artificial pneumoperitoneum with a CO_2 pressure of 8 mmHg (Figure 2). (4) The assistant pulled the gastric tube from the abdominal side to turn the esophagus in an inverted state and performed the mobilization of the esophagus. Unlike an ordinary mediastinoscopic esophagectomy, we transected the esophagus to create a larger surgical field, which greatly simplified the difficulty of esophageal mobilization through the neck. After the mobilized esophagus met the one in the abdominal cavity, the mobilization ended. The left and right sides of the laryngeal nerve lymph nodes and the carinal lymph nodes were dissected from the neck incision. After mobilization, the left and right para-RLNs, thoracic duct, tracheal membrane, left and right main bronchi, and left and right pleurae could be clearly exposed.

Tubular Stomach Production and Anastomosis

(1) The distal esophagus and stomach were prolapsed from the upper abdominal incision, and a tubular stomach with a width of 3 cm was made with a linear cutting stapler. (2) The tubular stomach was dragged along the esophageal bed to the neck for the "side-to-side, end-to-end, embedded anastomosis" of the esophagus and stomach (Figure 3). The anastomosis process includes four main steps. Step 1. We pull out the gastric tube and esophageal stump were from cervical incision, they should be long enough, generally the extracorporeal stumps of gastric tube and esophagus should be more than 5cm. Suture and fix at the root of gastric tube and esophagus (Figure 3Aa). Step2. We use the linear cut stapler to make a "side-side" anastomosis (Figure 3Bb). Step 3. Using sutures to close the stumps of the esophagus and

Figure 2 A self-made inflator.

gastric tube discontinuously, it is a “end-end” anastomosis (Figure 3Cc). Step 4. Making a “sleeve” anastomosis at last. We perform a semi-pouch suture on the area which is 5cm far away from the junction of esophagus and gastric tube, push the anastomotic stoma into the gastric tube. Fix the anastomotic stoma with inverting suture patterns (Figure 3Dd).

The characteristics of the transcervical and transhiatal esophagectomy are as follows: 1. no incisions on the chest wall; 2. no changes of the intraoperative body position during the operation; 3. single-lumen bronchial intubation used for completing the operation sufficiently.

Statistical Analysis

Statistical analyses were performed using SAS software (version 9.4, IBM Corp.). Continuous data were presented as the mean ± standard deviation ($\overline{X} \pm s$) or [$M(Q_{25}, Q_{75})$] and analyzed by the *t*-test or Kruskal–Wallis test. Categorical data were presented as frequency (N) and percentage (%) and analyzed using χ^2 or Kruskal–Wallis tests. $P < 0.05$ was considered a statistically significant difference.

Results

Preoperative Assessment

A total of 80 patients with EC were enrolled in this study, with a mean age of 70.10 ± 2.95 years. Among these cases, there were 52 males (65%) with an average age of 70.13 ± 2.88 years and 28 females (35%) with an average age of 70.04 ± 3.13 years. The participants were divided into the observation group (n = 40) and the control group (n = 40), with a mean age of 70.30 ± 2.95 and 69.90 ± 2.98 years, respectively.

There were no significantly statistical differences in preoperative age ($Z = –0.643$, $P = 0.520$), gender ($\chi^2 < 0.001$, $P = 1.000$), BMI ($t = –1.405$, $P = 0.164$), FEV1% ($t = 0.328$, $P = 0.744$), MVV % ($t = 0.000$, $P = 1.000$), PO_2 ($t = –0.226$, $P = 0.822$), PCO_2 ($Z = 1.078$, $P = 0.281$), the incidence of complications ($\chi^2 = 0.058$, $P = 0.809$), NRS-2002 ($Z = 0.693$, $P = 0.488$), T stage ($Z = 0.922$, $P = 0.357$), N stage ($\chi^2 = 0.205$, $P = 0.651$), tumor location ($\chi^2 = 0.554$, $P = 0.758$), and tumor length ($t = 1.355$, $P = 0.179$) between the two groups (Table 1).

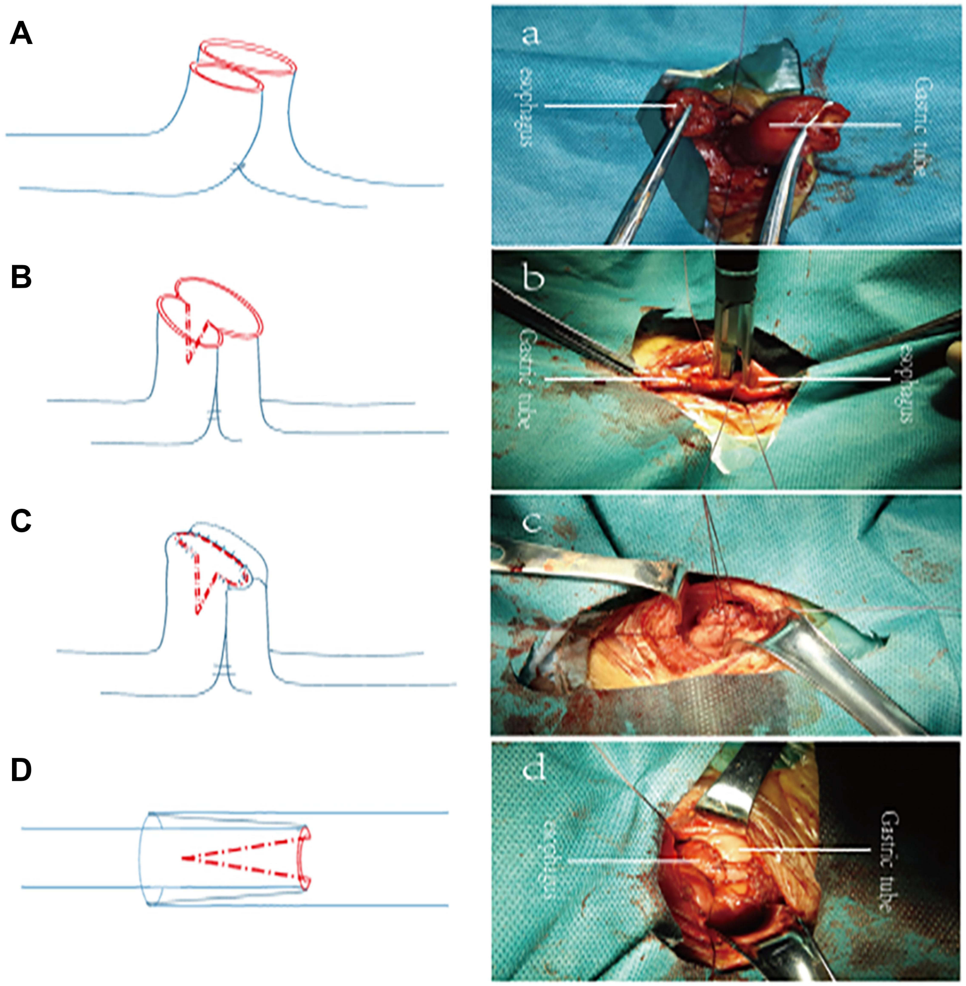

Figure 3 The "side-to-side, end-to-end, embedded anastomosis" of the esophagus and stomach. (**A**)a.Suture and fix at the root of gastric tube and esophagus. (**B**)b "side-side" anastomosis of the gastric tube and esophagus. (**C**)c "end-end" anastomosis of gastric tube and esophagus. (**D**)d "sleeve" anastomosis.

Intraoperative Findings

The parameters containing perioperative bleeding, the total number of dissected mediastinal lymph nodes, operation time, left para-RLN, and right para-RLN were analyzed. The results showed that patients who underwent transcervical and transhiatal esophagectomy had shorter operations than those with transthoracic esophagectomy ($Z = –3.700$, $P < 0.001$). The number of dissected mediastinal lymph nodes in the left para-RLN in the observation group was higher than in the control group (3.65 ± 1.00 vs 3.08 ± 0.80, $t = 2.815$, $P = 0.006$). No differences were discovered in perioperative bleeding ($Z = –1.024$, $P = 0.306$), total number of dissected mediastinal lymph nodes ($Z = –0.620$, $P = 0.535$) and right para-RLN ($Z = –0.932$, $P = 0.352$) between the two groups (Table 2).

Postoperative Outcomes

The operation was successfully performed in all 80 patients. The postoperative outcomes were recorded, including time in ICU, postoperative pain score (days 1, 2 and 3), LOPS, 24-h PO_2/FiO2, 48-h PO_2/FiO2, pulmonary infection, FOB, and lymphatic metastasis. As shown in Table 3, there were no statistical differences for time in ICU ($Z = –1.642$, $P = 0.101$), postoperative pain score day 2 ($Z = –1.367$, $P = 0.172$), 24-h PO_2/FiO2 ($t = 1.811$, $P = 0.074$), FOB ($P = 0.359$), and lymphatic metastasis ($\chi^2 = 1.526$, $P = 0.217$), while the postoperative pain score day 1 ($Z = –4.292$, $P < 0.001$), postoperative pain score day 3 (Z = –3.363, $P < 0.001$) and 48-h PO_2/FiO2 ($Z = 3.747$, $P < 0.001$) were significantly different between the two groups. The LOPS of patients with EC in the observation group was shorter than in the control

Table 1 The Preoperative Assessment for Patients with EC

Variables	Observation (n=40)	Control (n=40)	Statistics	*P*
Age, years, M(Q_{25}, Q_{75})	69.50 (68.00, 72.50)	71.00 (68.00, 72.50)	Z=−0.643	0.520
Gender, n (%)			χ^2<0.001	1.000
Male	26 (65.00)	26 (65.00)		
Female	14 (35.00)	14 (35.00)		
BMI, Kg/m^2, $\overline{X} \pm s$	20.70±2.47	21.41±2.05	t=−1.405	0.164
FEV1, %, $\overline{X} \pm s$	42.23±4.97	41.85±5.25	t=0.328	0.744
MVV, %, $\overline{X} \pm s$	39.03±4.35	39.03±3.58	t=0.000	1.000
PO_2, mmHg, $\overline{X} \pm s$	68.30±3.98	68.50±3.94	t= −0.226	0.822
PCO_2, mmHg, M(Q_{25}, Q_{75})	46.00 (42.00, 48.00)	45.00 (42.00, 47.50)	Z=1.078	0.281
Complications, n (%)			χ^2=0.058	0.809
0	27 (67.50)	28 (70.00)		
1	13 (32.50)	12 (30.00)		
NRS 2002, n (%)			Z=0.693	0.488
1	1 (2.50)	2 (5.00)		
2	14 (35.00)	10 (25.00)		
3	14 (35.00)	25 (62.50)		
4	10 (25.00)	3 (7.50)		
5	1 (2.50)	0 (0.00)		
T-stage, n (%)			Z=0.922	0.357
1	11 (27.50)	12 (30.00)		
2	19 (47.50)	23 (57.50)		
3	10 (25.00)	5 (12.50)		
N-stage, n (%)			χ^2=0.205	0.651
0	16 (40.00)	18 (45.00)		
1	24 (60.00)	22 (55.00)		
Tumor location, n (%)			χ^2=0.554	0.758
Top	13 (32.50)	16 (40.00)		
Middle	20 (50.00)	17 (42.50)		
Bottom	7 (17.50)	7 (17.50)		
Tumor length, cm, $\overline{X} \pm s$	3.41±0.84	3.15±0.89	t=1.355	0.179

Abbreviations: EC, esophageal carcinoma; BMI, body mass index; FEV1, forced expiratory volume in one second; MVV, maximal voluntary ventilation; PO_2, partial pressure of oxygen; PCO_2, partial pressure of carbon dioxide; NRS, nutrition risk screening.

group (Z = –2.119, P = 0.034). The number of patients receiving transcervical and transhiatal esophagectomy developing postoperative pulmonary infections was less than the controls (χ^2 = 4.114, P = 0.043).

The results of logistic regression analysis

A logistic regression model was established to identify independent factors for postoperative pulmonary infection. We identified that the operation route through transcervical and transhiatal was an independent protect factor for post-operative pulmonary infection (Odds ratio [OR] =7.801, P = 0.037) (Table 4).

Discussion

With the development of medical technologies and instruments, the minimally invasive esophagectomy has become an increasingly acceptable surgical treatment for thoracic surgeons. Previous studies have reported minimally invasive surgery has obvious advantages compare open method in postoperative complications, such as less blood loss, rapid postoperative recovery, and earlier discharge.[16–19] Thoracoscopic esophagectomy has been used in clinics for treating EC, which provides better visualization of the operative field and allows a more thorough dissection of the esophagus.[20,21] However, this approach is often linked to high postoperative morbidity and mortality.[22–26] The most important reason for perioperative deaths is pulmonary complications. For those patients who has chronic diseases of the

Table 2 The Intraoperative Assessment for Patients with EC

Variables	Observation (n=40)	Control (n=40)	Statistics	*P*
Perioperative bleeding, M(Q_{25}, Q_{75})	50.00 (50.00, 62.50)	50.00 (50.00, 75.00)	*Z*= −1.024	0.306
Total number of dissected mediastinal lymph nodes, M(Q_{25}, Q_{75})	13.00 (12.00, 14.50)	14.00 (12.00, 15.00)	*Z*= −0.620	0.535
Operative time, min, M(Q_{25}, Q_{75})	200 (175, 220)	235 (195, 250)	*Z*= −3.700	<0.001
Left para-RLN, n (%)	3.65±1.00	3.08±0.80	*t*= 2.815	0.006
2	5 (12.50)	10 (25.00)		
3	14 (35.00)	18 (45.00)		
4	11 (27.50)	11 (27.50)		
5	10 (25.00)	1 (2.50)		
Right para-RLN, n (%)	2.70±0.76	2.88±0.82	*t*= 1.018	0.312
2	19 (47.50)	15 (37.50)		
3	14 (35.00)	16 (40.00)		
4	7 (17.50)	8 (20.00)		
5	0 (0.00)	1 (2.50)		

Abbreviations: EC, esophageal carcinoma; RLN, recurrent laryngeal nerve.

respiratory system with pulmonary dysfunction, the concerns about the risks of high incidence of pulmonary complications may lead doctors and patients to choose non-surgical treatment plan. As a result, this part of patients lost the opportunity of surgical treatment. Herein, we introduced a new minimally invasive esophagectomy surgery that is a transcervical combined with a transhiatal esophagectomy. Our findings showed that this novel operation had a shorter LOPS, lower postoperative pain, and lower pulmonary infection compared with thoracoscopic esophagectomy.

The transhiatal esophagectomy is different from the mediastinoscopic esophagectomy that has been reported.[24–30] In this study, the operation was performed using a standard thoracoscopic lens instead of a traditional mediastinoscope. The esophagus was cut off during the operation and the stump of dorsal esophagus is introversive during the dissociation, which was not the same as the mediastinoscopy. Routine thoracoscopic energy instruments such as an ultrasonic knife and a suction device for the endoscope were used in the dissociation process. Our results showed that the LOPS of patients with EC who underwent transcervical and transhiatal esophagectomy was shorter than those who had thoracoscopic esophagectomy. Due to the small diameter and low localization requirements of endotracheal intubation, single-lumen intubation was adopted in the transcervical and transhiatal esophagectomy, with an intubation time that was significantly shorter than double-lumen intubation. During the whole surgery, patients maintained double-lung ventilation without single-lung ventilation; thereby, the stability of the intraoperative blood gas was better. Thoracoscopic esophagectomy requires double-lumen intubation or single-lumen intubation plus artificial pneumothorax, and the double-lumen intubation has a thicker diameter, deeper intubation location, and higher requirement and repeated adjustment of the position, easily leading to more serious endotracheal injury. The lung tissues of patients undergoing thoracotomy have conducted traction to better expose the esophagus in the posterior mediastinum, which may inevitably cause mechanical damage to lung tissues. In our study, transcervical and transhiatal esophagectomy has no thoracic incision, lower pulmonary infection, and lower postoperative pain of cough and sputum excretion, leading to better cooperation with medical staff to complete respiratory nursing.

Squamous cell carcinoma (SCC), a primary histologic type of EC, usually occurs in the thoracic esophagus, extensively spreads to the mediastinal lymph nodes, especially along the bilateral RLNs.[27] At present, the mediastinal lymphadenectomy is an essential part of radical esophagectomy for esophageal SCC or thoracic EC.[28,29] Fujiwara et al reported a single-port mediastinoscope- assisted transhiatal esophagectomy (MATHE) for the treatment of thoracic EC.[31] Okumura et al explored the clinical significance of MATHE among 67 patients with EC and found the lymph node metastasis and blood loss were independent prognostic factors.[32] Although the pleural lymph node dissection under the thoracoscopic esophagectomy has been widely applied, the visual range of surgery is relatively small. It is difficult during thoracoscopic surgery to remove the lymph nodes near the para-RLN, which are not often visualized clearly.[30] In our study, the transcervical esophagectomy was performed in the upper mediastinum, and the transhiatal esophagectomy was

Table 3 The Postoperative Assessment for Patients with EC

Variables	Observation (n=40)	Control (n=40)	Statistics	P
Time in ICU, n (%)			$Z= -1.642$	0.101
1	20 (50.00)	14 (35.00)		
2	20 (50.00)	23 (57.50)		
3	0 (0.00)	3 (7.50)		
Postoperative pain score Day1, n (%)			$Z= -4.292$	<0.001
3	12 (30.00)	5 (12.50)		
4	12 (30.00)	4 (10.00)		
5	16 (40.00)	14 (35.00)		
6	0 (0.00)	10 (25.00)		
7	0 (0.00)	7 (17.50)		
Postoperative pain score Day2, n (%)			$Z= -1.367$	0.172
3	19 (47.50)	13 (32.50)		
4	9 (22.50)	13 (32.50)		
5	12 (30.00)	9 (22.50)		
6	0 (0.00)	5 (12.50)		
Postoperative pain score Day3, n (%)			$Z= -3.363$	<0.001
2	14 (35.00)	4 (10.00)		
3	21 (52.50)	20 (50.00)		
4	5 (12.50)	15 (37.50)		
5	0 (0.00)	1 (2.50)		
LOPS, days, M(Q_{25}, Q_{75})	7.00 (7.00, 8.00)	8.00 (7.00, 8.50)	$Z= -2.119$	0.034
24-h PO_2/FIO_2, $\overline{X} \pm s$	296.50±33.71	282.75±34.19	$t=1.811$	0.074
48-h PO_2/FIO_2, M(Q_{25}, Q_{75})	290.00 (265.00, 315.00)	255.00 (245.00, 280.00)	$Z=3.747$	<0.001
Pulmonary infection, n (%)			$\chi^2=4.114$	0.043
No	38 (95.00)	32 (80.00)		
Yes	2 (5.00)	8 (20.00)		
FOB, n (%)			-	0.359
No	39 (97.50)	36 (90.00)		
Yes	1 (2.50)	4 (10.00)		
Lymphatic metastasis, n (%)			$\chi^2=1.526$	0.217
No	9 (22.50)	14 (35.00)		
Yes	31 (77.50)	26 (65.00)		

Note: Using Fisher test.
Abbreviations: EC, esophageal carcinoma; ICU, intensive care unit; LOPS, the length of postoperative stay; PO_2/FIO_2, partial pressure of oxygen /fraction of inspiration oxygen; FOB, fiberoptic bronchoscopy.

conducted in the middle and lower mediastinum. The left and right para-RLNs could be completely exposed during the dissection, which completes the lymph node dissection and protects the RLN.

The strength of our study was that transcervical and transhiatal esophagectomy, a novel concept of minimally invasive surgery for EC, does not change the body position and requires no thoracotomy, which provides opportunities for patients

Table 4 Independent Factors for Postoperative Pulmonary Infection Based on Logistic Regression Analysis

	OR (95% CI)	P value
Operation route through transcervical and transhiatal	7.801(1.13–53.731)	<0.001
Operation time	1.002(0.981–1.024)	0.83
Perioperative bleeding	1.004(0.972–1.037)	0.81
Left para-RLN	2.154(0.87–5.33)	0.10
Right para-RLN	1.071(0.439–2.614)	0.88

Abbreviations: OR, odds ratio; CI, confidence interval; RLN, recurrent laryngeal nerve.

who cannot tolerate thoracotomy. The application of single-lumen bronchial intubation can reduce the risk of anesthesia and the incidence of perioperative pulmonary infection. However, some limitations should be warranted as a caution for the explanation of the data. This surgery has a small operating space for the surgeons and a high requirement for assistants to help the surgeons expose the surgical field in the small space as much as possible. Using the current energy platform is prone to smoke generation that interferes with the operative vision, so it is necessary to continuously apply the suction device for smoke extraction, which may affect the smoothness of the operation. Patients who underwent surgery needed the complete data of preoperative CT or ultrasound diameter. Compared with thoracoscopic esophagectomy, the transcervical and transhiatal esophagectomy shows no significant advantage in lymph node dissection because of the immaturity of the technology and the imperfection of equipment, which may result in an increase of the recurrence rate. Thus, this surgery may currently serve as a supplement and is unable to replace thoracoscopic esophagectomy. Operation skills and standardized surgical procedures should be further improved in future clinical work. Meanwhile, the corresponding surgical instruments are needed, such as a lens and separating pliers with radians and energy platforms with less smoke.

The limitations of the study are as follow: 1) this was a non-randomized control investigation with a small sample size that may have an impact on the statistical power of our results. More studies with well-designed, large samples and randomized controlled trials should be considered to further assess the therapeutic efficacy of this surgery. 2) Due to the difficulty of the operation, we selected patients with clinical stage cT1-3 N0-1 M0. Some patients with later stage or with enlarged and fused lymph nodes may not be suitable for this operation. According to the latest guidelines, neoadjuvant therapy is recommended for patients with clinical stage T3 and above or N+[33] and it is not clear whether this surgical method is safe and feasible for patients after neoadjuvant therapy. 3) This is a clinical study on the surgical method of EC, the surgical method is completely different from the conventional minimally invasive esophagectomy through thoracic cavity. The surgical method is very difficult, and the surgeons need a re-learning process. Moreover, there are not many cases that have to choose this surgical method, so it may be difficult to repeat this study.

Conclusion

In this study, we developed a new minimally invasive esophagectomy surgery (transcervical and transhiatal esophagectomy) and assessed the therapeutic efficacy of this operation among patients with EC. Our results showed that the transcervical and transhiatal esophagectomy. Tumor resection rate and lymph node dissection rate can achieve the same surgical effect as thoracoscopic esophagectomy, which is safe and feasible. Postoperative pulmonary complications are reduced, and it can be used for EC patients whose clinical stages were cT1-3 N0-1 M0 with chronic lung disease, low lung function, or difficult thoracic surgery.

Data Sharing Statement

We declared that materials described in the manuscript, including all relevant raw data, will be freely available to any scientist wishing to use them for non-commercial purposes, without breaching participant confidentiality.

Ethics Approval and Consent to Participate

This study was conducted with approval from the Ethics Committee of Chongqing University Cancer Hospital. This study was conducted in accordance with the declaration of Helsinki. Written informed consent was obtained from all participants.

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Disclosure

The authors declare that they have no competing interests.

References

1. Pakzad R, Mohammadian-Hafshejani A, Khosravi B, et al. The incidence and mortality of esophageal cancer and their relationship to development in Asia. *Ann Transl Med*. 2016;4(2):29. doi:10.3978/j.issn.2305-5839.2016.01.11
2. Chen WQ, Zheng RS, Baade PD, et al. Cancer statistics in China, 2015. *CA Cancer J Clin*. 2016;66(2):115–132. doi:10.3322/caac.21338
3. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. *CA Cancer J Clin*. 2019;69(1):7–34. doi:10.3322/caac.21551
4. Ajani JA, D'Amico TA, Bentrem DJ, et al. Esophageal and esophagogastric junction cancers, version 2.2019, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw*. 2019;17(7):855–883. doi:10.6004/jnccn.2019.0033
5. Takeuchi H, Miyata H, Gotoh M, et al. A risk model for esophagectomy using data of 5354 patients included in a Japanese nationwide web-based database. *Ann Surg*. 2014;260(2):259–266. doi:10.1097/SLA.0000000000000644
6. Zingg U, Smithers BM, Gotley DC, et al. Factors associated with postoperative pulmonary morbidity after esophagectomy for cancer. *Ann Surg Oncol*. 2011;18(5):1460–1468. doi:10.1245/s10434-010-1474-5
7. Luketich JD, Pennathur A, Awais O, et al. Outcomes after minimally invasive esophagectomy review of over 1000 patients. *Ann Surg*. 2012;256 (1):95–103. doi:10.1097/SLA.0b013e3182590603
8. Biere S, Henegouwen MIV, Maas KW, et al. Minimally invasive versus open oesophagectomy for patients with oesophageal cancer: a multicentre, open-label, randomised controlled trial. *Lancet*. 2012;379(9829):1887–1892. doi:10.1016/S0140-6736(12)60516-9
9. Müller-Stich BP, Probst P, Nienhüser H, et al. Meta-analysis of randomized controlled trials and individual patient data comparing minimally invasive with open oesophagectomy for cancer. *Br J Surg*. 2021;108(9):1026–1033. doi:10.1093/bjs/znab278
10. Canet J, Gallart L, Gomar C, et al. Prediction of postoperative pulmonary complications in a population-based surgical cohort. *Anesthesiology*. 2010;113(6):1338–1350. doi:10.1097/ALN.0b013e3181fc6e0a
11. Van Haren RM, Mehran RJ, Mena GE, et al. Enhanced recovery decreases pulmonary and cardiac complications after thoracotomy for lung cancer. *Ann Thorac Surg*. 2018;106(1):272–279. doi:10.1016/j.athoracsur.2018.01.088
12. Gillinov AM, Heitmiller RF. Strategies to reduce pulmonary complications after transhiatal esophagectomy. *Dis Esophagus*. 2017;11(1):43–47. doi:10.1093/dote/11.1.43
13. The Society of Thoracic Surgeons. STS general thoracic surgery database; 2018; Available from: https://www.sts.org/registries-research-center/sts-national-database/sts-general-thoracic-surgery-database. Accessed August 02, 2020.
14. Donohoe CL, O'Farrell NJ, Ravi N, Reynolds JV. Evidence-based selective application of transhiatal esophagectomy in a high-volume esophageal center. *World J Surg*. 2012;36(1):98–103. doi:10.1007/s00268-011-1307-0
15. Liu G, Peng L, Liu B, Wang K, Han Y. Analysis of risk factors for pulmonary infection in patients with minimally invasive esophagectomy. *Oncol Lett*. 2019;17(3):3283–3288. doi:10.3892/ol.2019.9987
16. Takeuchi H, Miyata H, Ozawa S, et al. Comparison of short-term outcomes between open and minimally invasive esophagectomy for esophageal cancer using a nationwide database in Japan. *Ann Surg Oncol*. 2017;24(7):1821–1827. doi:10.1245/s10434-017-5808-4
17. Smithers BM, Gotley DC, Martin I, Thomas JM. Comparison of the outcomes between open and minimally invasive esophagectomy. *Ann Surg*. 2007;245(2):232–240. doi:10.1097/01.sla.0000225093.58071.c6
18. Nagpal K, Ahmed K, Vats A, et al. Is minimally invasive surgery beneficial in the management of esophageal cancer? A meta-analysis. *Surg Endosc*. 2010;24(7):1621–1629. doi:10.1007/s00464-009-0822-7
19. Ben-David K, Sarosi GA, Cendan JC, Howard D, Rossidis G, Hochwald SN. Decreasing morbidity and mortality in 100 consecutive minimally invasive esophagectomies. *Surg Endosc*. 2012;26(1):162–167. doi:10.1007/s00464-011-1846-3
20. Watson DI, Davies N, Jamieson GG. Totally endoscopic Ivor Lewis esophagectomy. *Surg Endosc*. 1999;13(3):293–297. doi:10.1007/s004649900969
21. Nguyen NT, Follette DM, Lemoine PH, Roberts PF, Goodnight JE. Minimally invasive Ivor Lewis esophagectomy. *Ann Thorac Surg*. 2001;72 (2):593–596. doi:10.1016/S0003-4975(00)02261-X
22. Schlottmann F, Strassle PD, Patti MG. Transhiatal vs. transthoracic esophagectomy: a NSQIP analysis of postoperative outcomes and risk factors for morbidity. *J Gastrointest Surg*. 2017;21(11):1757–1763. doi:10.1007/s11605-017-3572-1
23. Mertens AC, Kalff MC, Eshuis WJ, et al. Transthoracic versus transhiatal esophagectomy for esophageal cancer: a nationwide propensity score-matched cohort analysis. *Ann Surg Oncol*. 2020;28:175–183. doi:10.1245/s10434-020-08760-8
24. Wei MT, Zhang YC, Deng XB, Yang TH, He YZ, Wang ZQ. Transthoracic vs transhiatal surgery for cancer of the esophagogastric junction: a meta-analysis. *World J Gastroenterol*. 2014;20(29):10183–10192. doi:10.3748/wjg.v20.i29.10183
25. Hulscher JB, van Sandick JW, de Boer AG, et al. Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the esophagus. *N Engl J Med*. 2002;347(21):1662–1669. doi:10.1056/NEJMoa022343
26. Hulscher JB, Tijssen JG, Obertop H, van Lanschot JJ. Transthoracic versus transhiatal resection for carcinoma of the esophagus: a meta-analysis. *Ann Thorac Surg*. 2001;72(1):306–313. doi:10.1016/S0003-4975(00)02570-4
27. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. *CA Cancer J Clin*. 2015;65(2):87–108. doi:10.3322/caac.21262
28. Tachimori Y, Ozawa S, Numasaki H, et al. Efficacy of lymph node dissection by node zones according to tumor location for esophageal squamous cell carcinoma. *Esophagus*. 2016;13:1–7. doi:10.1007/s10388-015-0515-3
29. Udagawa H, Ueno M, Shinohara H, et al. The importance of grouping of lymph node stations and rationale of three-field lymphadenectomy for thoracic esophageal cancer. *J Surg Oncol*. 2012;106(6):742–747. doi:10.1002/jso.23122
30. Ikeda Y, Niimi M, Kan S, Takami H, Kodaira S. Thoracoscopic esophagectomy combined with mediastinoscopy via the neck. *Ann Thorac Surg*. 2002;73(4):1329–1331. doi:10.1016/S0003-4975(01)03593-7
31. Fujiwara H, Shiozaki A, Konishi H, et al. Perioperative outcomes of single-port mediastinoscope-assisted transhiatal esophagectomy for thoracic esophageal cancer. *Dis Esophagus*. 2017;30(10):1–8. doi:10.1093/dote/dox047
32. Okumura H, Uchikado Y, Matsumoto M, et al. Clinical significance of mediastinoscope-assisted transhiatal esophagectomy in patients with esophageal cancer. *Langenbecks Arch Surg*. 2015;400(6):699–706. doi:10.1007/s00423-015-1330-y
33. Kitagawa Y, Uno T, Oyama T, et al. Esophageal cancer practice guidelines 2017 edited by the Japan Esophageal Society: part 1. *Esophagus*. 2019;16(1):1–24. doi:10.1007/s10388-018-0641-9