Safety and efficacy of vagus nerve preservation technique during minimally invasive esophagectomy

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Background: This study aimed to assess the feasibility, efficacy and safety of McKeown surgery with vagal-sparing using minimally invasive esophagectomy (MIE).

Methods: McKeown surgery with vagal-sparing technique using MIE was adopted on patients diagnosed with resectable esophageal cancer. From June 2020 to January 2021, a total of 20 patients from the Department of Thoracic Surgery of the National Clinical Research Center for Cancer were enrolled.

Results: The study group included 17 (85%) males and 3 (15%) females, with an average age of 62.6 (±7.1) years. The most common tumor location was lower thoracic esophagus (n=9, 45%), followed by middle thoracic esophagus (n=8, 40%) and upper thoracic esophagus (n=3, 15%). Nine (45%) patients had T1b disease, followed by T2 (n=8, 40%), T1a (n=2, 10%), and Tis (n=1, 5%). The average operation time was 221.5 (±61.2) minutes. Postoperative complications were as follow: 2 (10%) with hoarseness, 2 (10%) with pulmonary infection, 1 (5%) with arrhythmia, 1 (5%) with anastomotic leakage, 1 (5%) with delayed gastric emptying, 1 (5%) with pleural effusion, and 1 (5%) with diarrhea. Dumping syndrome, cholestasis, and chylothorax were not observed, and there was no perioperative death.

Conclusions: MIE with vagus nerve preservation is a feasible and safe technique, with the possibility to be an alternative for esophageal carcinoma. Further study is needed to explore the functional outcome of preserving vagus nerve.

Keywords: Esophageal cancer; McKeown; esophagectomy; vagus nerve preservation

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Introduction

After more than a century of esophageal cancer surgery development, increasing attention has been paid to the quality of life (QOL) of patients. With the improvement of people's health awareness and examination methods, the detection rate of early esophageal cancer has increased (1). Owing to the significant probability of lymph node metastasis in esophageal cancer, vagotomy was usually implemented so that lymph nodes could be thoroughly removed (2). As a result, vagal-associated complications

such as chronic diarrhea, dumping syndrome, and delayed gastric emptying were common, seriously impacting the QOL of patients.

The idea of vagal preservation that spares the hepatic and celiac branches as well as the esophageal plexus was first proposed by Akiyama in 1982 for the treatment of benign esophageal stenosis (3). Thereafter, several studies reported vagal-sparing esophagectomy for curative tumor excision with improved functional outcomes as well as attenuated postoperative morbidity (2,4-6). Motoyama *et al.* reported a case of benign esophageal stricture underwent transhiatal esophagectomy using mediastinoscopy with vagus nerve preservation (7). In 2018, Crema *et al.* reported a cohort of 136 patients of megaesophagus treated by subtotal esophagectomy with vagus nerve preservation using laparoscopy (8). More recently, Liu *et al.* tried McKeown surgery utilizing MIE on 48 patients of esophageal cancer (9). However, only pulmonary branch of vagus nerve was reserved in this study. Nearly all existing literatures reporting on the vagal-sparing technique are case reports or case series about early-stage esophageal carcinoma or benign esophageal disease (6-11). Meanwhile, minimally invasive esophagectomy (MIE) has been demonstrated to be a safe and feasible alternative to traditional open esophagectomy, with reduced intraoperative and postoperative complications (12). Theoretically, the combination of MIE and the vagus nerve preservation technique should be able to offer patients fewer surgery-related complications, improved functional outcomes, and better QOL. However, there is a lack of a study combining vagal-sparing technique and MIE in esophageal carcinoma.

We explored the vagus nerve preservation technique using MIE since 2020. In this retrospective study, the safety, efficacy and effect of the vagal-sparing technique with MIE for esophageal cancer were comprehensively evaluated using the data of 20 patients. We present the following article in accordance with the STROBE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-1141/rc).

Methods

Twenty patients with esophageal cancer who received McKeown surgery with the vagal-sparing technique using MIE at the Department of Thoracic Surgery of the National Clinical Research Center for Cancer from June 2020 to January 2021 were enrolled in this study. All patients were pathologically diagnosed with endoscopic biopsy, and were staged according to the 8th edition of the American Joint Commission on Cancer (AJCC) Tumor-Node-Metastasis (TNM) Staging System. Patients with clinical T stage ≥3 or distant metastasis were excluded. The efficacy was assessed based on perioperative parameters including operation time (min), blood loss (mL), number of lymph nodes removed, postoperative hospital-stay (day), first flatus after surgery (day), first defecation after surgery (day), perioperative mortality, postoperative anastomotic leakage and postoperative anastomotic pleural effusion. On the other hand, the safety was assessed based on main postoperative complications including hoarseness, pulmonary infection, arrhythmia, delayed gastric emptying, and diarrhea. The above mentioned essential perioperative parameters, as well as clinicopathological data of this cohort were collected retrospectively. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Approval was acquired from the ethics committee of National Clinical Research Center for Cancer (No. 2014xjs4). Written informed consent was obtained from all patients preoperatively.

Operative procedure

Thoracic surgery

The patients were anesthetized and intubation was performed in a single lumen. After placing the patient in a left side-lying position with the trunk tilted ventrad 30°, we established the artificial pneumothorax using carbon dioxide (CO_2). The mediastinal pleura was opened alongside the posterior edge of the right vagal nerve, up to the right subclavian artery level, fully exposing the right recurrent laryngeal nerve. Next, the surrounding lymph nodes and adipose tissues were dissected, and the upper thoracic esophagus and surrounding lymph nodes were dissociated. Subsequently, the azygos vein was divided, and carefulness should be paid to protect the right vagus nerve as well as its pulmonary and cardiac branches (*Figure 1*). The mediastinal pleura in the space between the esophagus and the aorta was then opened, exposing the left vagal trunk (anterior trunk). After that, the left main bronchus was wrapped with an atraumatic strip and pulled to the trocar near the right subscapular angle. The left vagus trunk stem was dissociated from the main bronchus to the diaphragm, and the lymph nodes of the middle lower esophagus, left side of esophagus, left pulmonary ligament, and superior phrenic were dissected. The right vagus trunk was exposed from the inferior edge of the azygos arch to the inferior edge of the

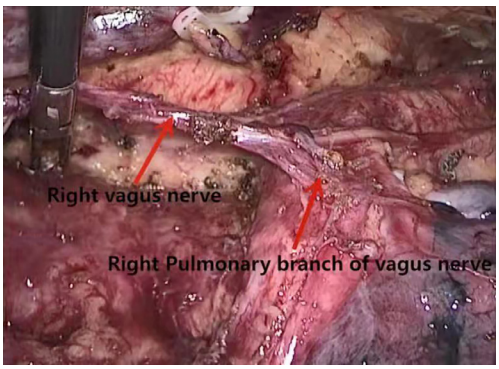

Figure 1 The trunk of right vagus nerve and the pulmonary branch.

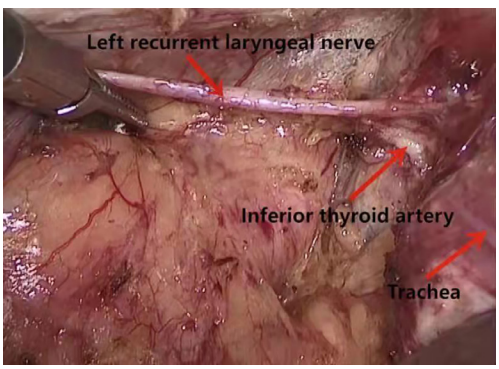

Figure 2 The trunk of left recurrent laryngeal nerve.

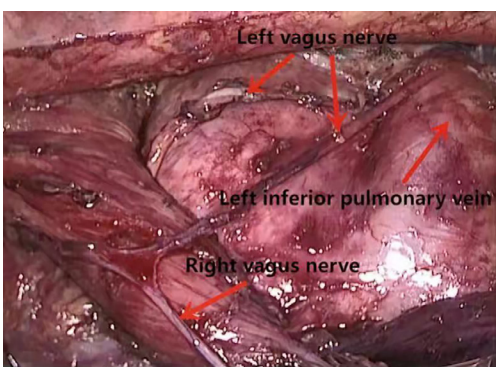

Figure 3 The distribution of left and right vagus nerve.

right main bronchus. The right main bronchus was then wrapped with an atraumatic strip and pulled to the trocar of the fourth intercostal space at the midaxillary line, and the right vagus trunk was dissociated to the diaphragm. Next, the lymph nodes of the middle lower esophagus, right side of esophagus, right pulmonary ligament and superior

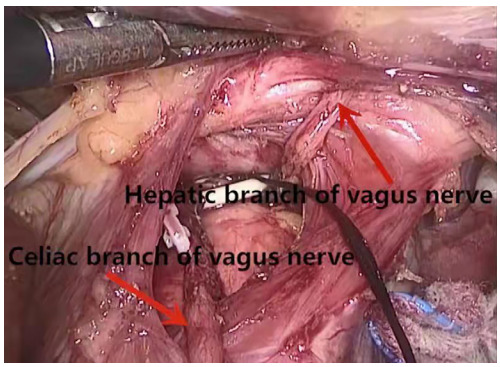

Figure 4 The hepatic and celiac branch of vagus nerve.

phrenic were dissected. Subsequently, the left recurrent laryngeal nerve was dissociated alongside the left rear edge of the trachea, and the lymph nodes and nearby adipose tissue were dissected (*Figure 2*). The subcarinal and hilar lymph nodes were also dissected. The bilateral vagal trunk was exposed, wrapped with atraumatic strips, and placed on the diaphragm (*Figure 3*). Finally, the thoracic cavity was closed, and the patient was placed in the supine position.

Abdominal surgery

Under the direct vision of the laparoscope, the greater curvature of the stomach was dissociated to the left diaphragmatic crus, and then the lesser curvature was dissociated to the cardia alongside the inferior edge of the hepatic branch of the vagus (*Figure 4*). Next, the esophageal hiatus was cut from the right front, and the atraumatic strips were located and pulled down to the abdominal cavity so as to probe and protect the celiac branch. The short gastric vessels were then cut off, and the lymph nodes of the short gastric vessels, celiac trunk, common hepatic artery, and splenic artery were then dissected. Two videos with the critical steps are presented in the supplementary files (Video S1 and Video S2).

Postoperative management

On the first day after the operation, the patients were encouraged to engage in off-bed activity under the guidance of doctors and nutritionists.

Statistical analysis

Clinicopathological data of patients included were collected, including operation time (min), blood loss (mL), number

Table 1 Baseline characteristics of patients included in this study

Characteristics	Vagus nerve sparing (N=20)
Gender	
Male	17 (85%)
Female	3 (15%)
Age (years), mean ± SD	62.6 (±7.1)
Comorbidities	
Hypertension	6 (30%)
Diabetes	3 (15%)
Other	2 (10%)
Tumor location	
Upper	3 (15%)
Middle	8 (40%)
Lower	9 (45%)
Clinical T staging	
Tis	1 (5%)
T1a	2 (10%)
T1b	9 (45%)
T2	8 (40%)

SD, standard deviation.

Table 2 Intraoperative and postoperative characteristics of patients

Characteristics	Vagus nerve preservation (N=20)
Operation time (min), mean ± SD	221.5±61.2
Blood loss (mL), mean ± SD	68.6±42.0
Number of lymph nodes removed, mean ± SD	28.5±13.1
Postoperative hospital-stay (day), mean ± SD	8.9±3.5
First flatus after surgery (day), mean ± SD	2.2±0.7
First defecation after surgery (day), mean ± SD	3.3±1.1
Postoperative complications	
Hoarseness	2 (10%)
Pulmonary infection	2 (10%)
Arrhythmia	1 (5%)
Anastomotic leakage	1 (5%)
Delayed gastric emptying	1 (5%)
Pleural effusion	1 (5%)
Diarrhea	1 (5%)
Perioperative mortality	0

SD, standard deviation.

of lymph nodes removed, postoperative hospital-stay (day), first flatus after surgery (day), first defecation after surgery (day), perioperative mortality, main postoperative complications. Counted variable were presented as mean and standard deviation (SD), and categorical data were listed as counts and percentages, where applicable. The statistical calculations were performed using SPSS 17.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results

In this study, McKeown surgery with vagal-sparing technique using MIE was applied to 20 patients. The clinicopathological data of this cohort are listed in *Table 1*. The group included 17 (85%) males and 3 (15%) females, with average age of 62.6 (±7.1) at the time of surgery. T stage was routinely assessed by endoscopic ultrasonography and distant metastasis was excluded through positron emission tomography-computed tomography (PET-CT). Eleven (55%) patients had comorbidities, with hypertension (6, 30%) being the most frequent, followed by diabetes (3, 15%). The most common tumor location was lower thoracic esophagus (9, 45%), followed by middle thoracic esophagus (8, 40%) and upper thoracic esophagus (3, 15%). Nine (45%) patients had T1b disease, followed by T2 (8, 40%), T1a (2, 10%) and Tis (1, 5%).

In terms of the safety-associated parameters, the average operation time was 221.5 (±61.2) minutes, 95.6 (±32.3) minutes for the thoracic portion and 35.2 (±18.6) minutes for the abdominal portion. The average blood loss during surgery was 68.6 (±42.0) mL. The average number of lymph nodes removed was 28.5 (±13.1). The average postoperative hospital-stay was 8.9 (±3.50) days. The time of first flatus and first defecation after surgery was 2.2 (±0.7) and 3.3 (±1.1) days, respectively. Besides, there was 1 (5%) with anastomotic leakage, 1 (5%) with pleural effusion. On the other hand, efficacy-associated postoperative complications were as follow: 2 (10%) with hoarseness, 2 (10%) with pulmonary infection, 1 (5%) with arrhythmia, 1 (5%) with delayed gastric emptying, and 1 (5%) with diarrhea. Dumping syndrome, cholestasis, and chylothorax were not observed, and there was no perioperative death. The details are presented in *Table 2*.

Discussion

Esophagectomy is still essential in the current combined modality therapy for esophageal cancer (13). Traditional open esophagectomy is accompanied by a high incidence of postoperative complications, and MIE has been shown to be a safe and feasible alternative that does not compromise the prognosis of patients (12,14). Some common but severe postoperative complications, such as dumping syndrome, diarrhea, and abdominal distension are considered to be associated with the truncal vagotomy (15,16). Thus, a vagal-sparing esophagectomy using MIE would theoretically be a better and promising technique.

We found that the vagal nerve trunk, pulmonary branch, hepatic branch, and celiac branch could be preserved together under direct vision, and lymph node dissection could also be comprehensively carried out. Given the high incidence of vagus nerve variation, careful and elaborate dissociation with sophisticated skills is indispensable to perform a vagal-sparing esophagectomy. During the operation, under the magnifying effect of the endoscope, the vagus nerve trunk at the protuberance level was easily identifiable. Through the traction of a non-invasive skin strap, the bilateral vagal trunk was dissociated in a top-down manner. Dissociation of the vagus nerve should be carried out before lymph node dissection so that the difficulty caused by nerve variation can be minimized. Also, the procedure is more difficult for obese patients due to a greater amount of adipose tissue. Since the subcarinal lymph nodes and the lymph nodes near the initial part of the left recurrent laryngeal nerve are especially close to the vagus nerve trunk, more attention should be paid during lymph node dissection in these areas to avoid injury.

The anterior trunk of the vagus nerve is located in the front-left of the abdominal esophagus, and sends out hepatic branches above the level of the cardia and runs straight to the right, travelling through the thicker part of the lesser omentum near the liver. The path of the hepatic branches was generally easy to identify and not susceptible to injury. The posterior trunk of the vagus nerve is mainly located in the right and posterior-right part of the abdominal esophagus. The celiac branch originates from the posterior trunk below the level of the cardia and runs to left gastric artery trunk in front of the right diaphragmatic crus. The course and branching of the celiac branch vary greatly and is prone to injury when the exposure is not clear enough. According to the distribution of the vagus trunk, the front-right area of the esophageal hiatus can be cut open relatively safely to enter thoracic cavity. When entering the thoracic cavity, two strips placed on the diaphragm are conspicuous after opening the esophageal hiatus. The left and right vagus nerves can be wrapped using two strips of different lengths, making it convenient for surgeons to distinguish between them. By pulling the strips, the route of the hepatic and celiac branches can be identified.

Through careful dissociation and sophisticated skills, esophagectomy with preservation of the vagal trunk and its main branches using MIE was feasible. However, radical tumor excision and complete lymph node dissection is always an essential prerequisite for the adoption of this technique.

As for the effect of preserving the vagus nerve, this cohort showed that the incidence of key postoperative complications including hoarseness, pulmonary infection, arrhythmia, anastomotic leakage, delayed gastric emptying, pleural effusion, and diarrhea were lower compared to ordinary MIE or traditional open esophagectomy (12,14,15). Also, there was no perioperative death. Although our cohort was relatively small, some initial signs of improvement regarding the effectiveness and safety of the vagus nerve preservation technique using MIE could be seen. Further study with larger sample size and longer follow-up was need to explore the functional outcome of preserving vagus nerve.

As for the completeness of lymph node dissection, pathological examination revealed an average of 28.5 (±13.1) lymph nodes removed, which was sufficiently large compared to ordinary MIE or traditional open esophagectomy (17).

The retrospective nature and relatively small sample size were the two main limitations of this research. Furthermore, we explored the vagus nerve preservation technique only in patients with a T stage ≤ T2. Whether this indication should be expanded or not still requires further investigation with a larger sample in the future.

Conclusions

MIE with vagus nerve preservation is a safe and feasible technique, with the possibility to be an alternative for esophageal carcinoma. Further study is needed to explore the functional outcome of preserving vagus nerve.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-1141/rc

Data Sharing Statement: Available at https://atm.amegroups.com/article/view/10.21037/atm-22-1141/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-1141/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are 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. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Approval was acquired from the ethics committee of National Clinical Research Center for Cancer (No. 2014xjs4). Written informed consent was obtained from all patients preoperatively.

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