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Clinical analysis of minimally invasive McKeown esophagectomy in a single center by a single medical group*

Zi-yi ZHU†, Xu YONG, Rao-jun LUO, Yun-zhen WANG

Department of Thoracic Surgery, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou 310016, China

†E-mail: zhuziyicn@zju.edu.cn

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Abstract: Objective: McKeown esophagectomy followed by cervical and abdominal procedures has been commonly used for invasive esophageal carcinoma. This minimally-invasive operative procedure in the lateral prone position has been considered to be the most appropriate method. We describe our experiences in minimally invasive McKeown esophagectomy (MIME) for esophageal cancer. Methods: Between March 2016 and February 2018, a total of 82 patients underwent MIME by a single group in our department (a single center). All procedure, operation, oncology, and complication data were reviewed. Results: All MIME procedures were completed successfully, with no conversions to open surgery. The median operative time was 260 min, and median blood loss was 100 ml. The average number of total harvested lymph nodes was 20.1 in the chest and 13.5 in the abdomen. There were no deaths within 30 postoperative days. Twenty cases (24.4%) developed postoperative complications, including anastomotic leak in 4 (4.9%), single lateral recurrent nerve palsy in 4 (4.9%), bilateral recurrent nerve palsy in 1 (1.2%), pulmonary problems in 3 (3.7%), chyle leak in 1 (1.2%), and other complications in 7 (including pleural effusions in 4, incomplete ileus in 2, and neck incision infection in 1; 8.54%). Average postoperative hospitalization time was 12 d. Blood loss, operation time, morbidity rate, and the number of harvested lymph nodes were analyzed by evaluating learning curves in different periods. Significant differences were found in operative time (P=0.006), postoperative hospitalization days (P=0.015), total harvested lymph nodes (P=0.003), harvested thoracic lymph nodes (P=0.006), and harvested abdominal lymph nodes (P=0.022) among different periods. Conclusions: Surgical outcomes following MIME for esophageal cancer are safe and acceptable. The MIME procedure for stages I and II could be performed proficiently and reached an experience plateau after approximately 25 cases.

Key words: Minimally invasive McKeown esophagectomy (MIME); Surgical procedure; Learning curve
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1 Introduction

The 2009 incidence and death rates for esophageal cancer in China were the highest in the world, at 22.14 per 100000 and 16.77 per 100000, respectively (Chen et al., 2013). The morbidity and mortality rates for esophagectomy have been persistently high due to the complexity of the procedure. At present, minimally invasive esophagectomy (MIE) is preferred due to fewer respiratory complications, less surgical trauma, and earlier recovery.

Luketich et al. (2003) reported excellent results in 222 patients who underwent MIE. MIE was accepted as an effective alternative to open techniques of esophagectomy, despite the fact that it is technically challenging. Therefore, advanced surgical skills and a suitable learning curve were necessary to achieve the best outcome.

MIE is performed using two approaches: the minimally invasive McKeown esophagectomy (MIME)

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ORCID: Zi-yi ZHU, https://orcid.org/0000-0001-8890-7894

and the minimally invasive Ivor-Lewis esophagectomy operation. MIME involves thoracoscopic esophagectomy, laparoscopic gastric mobilization, and cervical esophagogastric anastomosis.

We report here the analysis of MIME data and learning curves for a single medical group in a single center since March 2016, to avoid bias in analysis. Only a few such studies have been reported. The results of this study will be helpful to local hospitals that are planning to adopt this procedure.

2 Subjects and methods

2.1 Patients

Between March 2016 and February 2018, 238 patients were operated on for esophageal cancer (EC) in our center. Of these, 82 underwent MIME by a single medical group. Patient characteristics are shown in Table 1. According to the Eighth Edition of the Tumor-Node-Metastasis Staging Classification (Amin et al., 2017), the tumor was in the upper esophagus in 13 cases, middle esophagus in 65, and lower esophagus in 4. Patients were classified as clinical Ia (6 patients), Ib (16), IIa (18), IIb (1), IIIa (3), IIIb (33), IIIc (5), and IV (0).

2.2 Operative procedure

Both thoracoscopic and laparoscopic approaches were adopted in our MIME procedure for esophageal and gastric mobilization. Single-lumen endotracheal intubation with artificial pneumothorax using CO_2 insufflation at 6–8 mmHg (1 mmHg=0.133 kPa) was generally used in MIME cases in our center. This method reduced the difficulty and tracheal injury associated with double-lumen endotracheal intubation. Expanded 2-field lymph node dissection was routinely performed, including dissection of bilateral recurrent laryngeal nerve (RLN) lymph nodes. The gastric conduit was passed through the esophageal bed and end-to-side anastomosis with the cervical esophagus.

2.2.1 Thoracic stage

The left lateral prone position at a 45° angle was used. Endotracheal intubation was performed with a tidal volume of 6–8 ml/kg oxygen. Both the surgeon and assistant surgeon stood at the ventral side of the patient. The monitor was on the opposite side. Four trocar ports with CO_2 pneumothorax (6–8 mmHg) were used in our center. The ports were placed in the fifth (A) and seventh (C) intercostal spaces in the mid axillary line, and the seventh (B) and tenth (D) intercostal spaces in the subscapular line (Fig. 1).

The azygous vein was divided with Hem-o-lok clips (Johnson & Johnson, USA) before opening the superior mediastinal pleura. The right RLN was

Table 1 Patient characteristics

Characteristic	Data
Number	82
Gender	
Man:female	81:1
Mean age (year)	64.2±6.9
Body mass index (BMI) (kg/m^2)	22.2±3.5
Histological type	
Squamous cell carcinoma	80 (97.8%)
Adenocarcinoma	1 (1.2%)
Small cell carcinoma	1 (1.2%)
Location of EC lesion	
Upper esophagus	13 (15.8%)
Middle esophagus	65 (79.3%)
Lower esophagus	4 (4.9%)
Clinical stage	
Ia	6 (7.3%)
Ib	16 (19.5%)
IIa	18 (21.9%)
IIb	1 (1.2%)
IIIa	3 (3.7%)
IIIb	33 (40.2%)
IIIc	5 (6.1%)
IV	0 (0%)
Neoadjuvant chemotherapy	6 (7.3%)

Data are expressed as number, mean±standard deviation, or number (percentage). EC: esophageal cancer

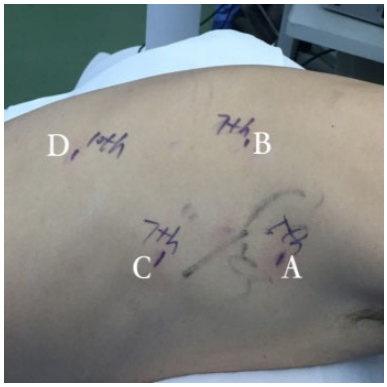

Fig. 1 Four ports placed in the fifth (A) and seventh (C) intercostal spaces of the mid axillary line, and the seventh (B) and tenth (D) intercostal spaces of the subscapular line

exposed near the right subclavian artery by following the right vagus nerve. Lymph nodes around the RLN were dissected (Fig. 2a). The esophagus was mobilized along with soft tissue around the esophagus from azygos arch to diaphragm hiatus, with attention to protection of the thoracic duct and left main bronchus. After being totally mobilized, the esophagus was suspended using a sling fixed at port A (Fig. 1), to dissect the lymph nodes at the carina (Fig. 2c). The trachea was pushed forward to expose the left RLN and dissect the lymph nodes (Fig. 2b). A mediastinal drainage tube though the esophageal bed and a chest tube were routinely placed.

2.2.2 Abdominal stage

The patient was changed to the lithotomy position. The surgeon stood between the patient's legs, and the assistant stood at the patient's right side with the camera holder in the right hand. Four ports were used: right subcostal (A), right abdomen at the midclavicular line (B), left subcostal (C), and umbilicus (D) (Fig. 3). CO_2 pneumoperitoneum (10–15 mmHg) was established through port D.

The gastrocolic ligament was divided along the greater curvature, with protection of the gastroepiploic vascular arch. Proximal gastric mobilization was completed from the splenic flexure of the colon to the short gastric vessel area. Then, the left gastric vessels were divided with the lymphatic tissues around the vessels (Fig. 2d). The gastric conduit was closed with an Endo-GIA stapler (ECR60, Echelon, USA) through a 5-cm mini-incision in the upper abdomen (Fig. 3: port E). Seromuscular layer sewing was routinely preferred. In our experience, the appropriate width of the gastric conduit was 3–4 cm.

2.2.3 Cervical stage

A 5-cm oblique incision was performed at the left anterior border of the sternocleidomastoid muscle (Fig. 3: port F). The cervical esophagus was mobilized and cut down. The gastric conduit was pulled up through the esophageal bed or retrosternal space to the neck incision. An end-to-side esophagogastric anastomosis was performed with a circular stapler (SDH 25A or SDH 21A, Ethicon Endo-Surgery, USA). A nasogastric tube was used in most of our cases.

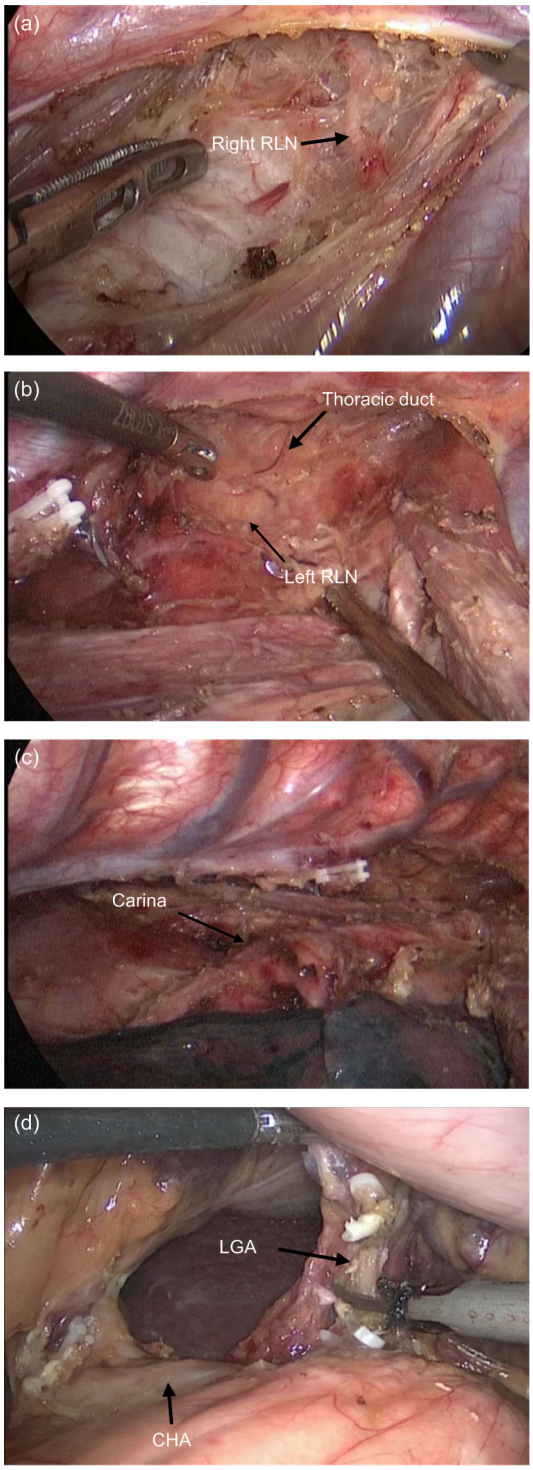

Fig. 2 Thoracoscopic procedure: dissection of lymph nodes around RLN (a); exposure of left RLN area and dissection of lymph nodes (b); dissection of the lymph node on the carina (c); division between left gastric vessel and the lymphatic tissues around vessels dissection (d)
RLN, recurrent laryngeal nerve; LGA, left gastric artery; CHA, common hepatic artery

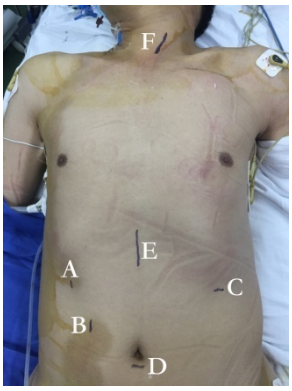

Fig. 3 Four ports used in the right subcostal (A), the right belly on the clavicle midline (B), the left subcostal (C), and umbilicus (D), and two 5-cm incisions in upper abdomen (E) and left neck (F)

2.3 Data

All clinical data of the 82 MIME patients were reviewed. The data included operative time, blood loss, length of postoperative hospital stay, thoracic duct ligation, and the number of harvested lymph nodes. Postoperative short-term outcomes refer to complications that occurred within 30 d after surgery, such as anastomotic leakage, recurrent nerve palsy, pulmonary complications, chyle leak, etc.

2.4 Statistical analysis

The data were analyzed using SPSS Version 19.0. Data fitting normal distribution were expressed as mean±standard deviation, and differences between groups were compared with Student's *t*-test and analysis of variance (ANOVA). Data fitting non-normal distribution were expressed as median (interquartile range), and differences between groups were compared with the Wilcoxon rank-sum test and Kruskal-Wallis *H* test. Categorical variables were expressed as frequency (%) and were analyzed using the chi-square test. ANOVA was used to evaluate differences between data relative and the learning curve. A P value of <0.05 was considered to be significantly different.

3 Results

3.1 Clinical data analysis

All procedures were completed with MIME, and no case was converted to an open procedure. The operative and postoperative outcomes are shown in Table 2. The average number of harvested lymph nodes was 20.1 in the chest and 13.5 in the abdomen. The median operative time was 260 min. The median blood loss was 100 ml. No death occurred within 30 d postoperatively. Twenty of 82 patients (24.4%) developed postoperative complications. According to the Clavien-Dindo classification, these included an anastomotic leak in 4 (4.9%), single lateral recurrent nerve palsy in 4 (4.9%), bilateral recurrent palsy in 1 (1.2%), pulmonary problems in 3 (3.7%), chyle leak in 1 (1.2%), and other complications in 7 (including pleural effusion in 4, incomplete ileus in 2, and neck incision infection in 1; 8.5%). The mean postoperative stay was 12 d. The 30-d postoperative hospitalization rate was 76.8%, and patients were mainly re-hospitalized for postoperative chemotherapy.

Table 2 Operative and postoperative outcomes

Outcome	Data
Number	82
Operation time (min)	260.0±61.9
Blood loss (ml)	100 (50)
Harvested lymph nodes	36 (18)
Harvested chest lymph nodes	20.1±9.8
Harvested abdominal lymph nodes	13.5±9.8
Mortality within 30 d	0
Total morbidity (patients)	20 (24.4%)
Anastomotic leakage	4 (4.9%)
Respiratory complications	3 (3.7%)
Vocal cord paralysis	5 (6.1%)
Chyle leak	1 (1.2%)
Other complications	7 (8.5%)
Postoperative stay	12 (3)
Hospitalization 30 d after operation	63 (76.8%)

Data are expressed as number, mean±standard deviation, median (interquartile range), or number (percentage)

3.2 Learning curve data

The 82 cases were divided into three groups by date of surgery (27, 27, and 28 cases), and results for blood loss, operative time, postoperative hospitalization days, harvested lymph nodes, and complications were compared (Table 3). Significant differences were found among the first, second, and third periods in operative time (P=0.006), postoperative hospitalization days (P=0.015), total harvested lymph nodes (P=0.003), harvested thoracic lymph nodes (P=0.006), and harvested abdominal lymph nodes (P=0.022). Blood loss, complications, and the number of harvested lymph nodes were expected to be improved over time.

Table 3 Minimally invasive esophagectomy learning curve

Outcome	First period	Second period	Third period	*P*-value
Number	27	27	28	
Stage				
I+II	14 (51.9%)	9 (33.3%)	19 (67.9%)	0.038[c]
III+IV	13 (48.1%)	18 (66.7%)	9 (32.1%)	
Blood loss (ml)	100 (100)	100 (50)	100 (125)	0.150
Operation time (min)	283.5±62.0	265.6±67.3	232.0±44.9	0.006[a,c]
Complications	7 (25.9%)	8 (29.6%)	3 (10.7%)	0.198
Postoperative hospitalization days	12 (2)	12 (5)	10 (2)	0.015[a,c]
Harvested lymph nodes	24 (14)	35 (21)	36 (22)	0.003[a,b]
Harvested thoracic lymph nodes	16.4±1.7	19.3±1.7	24.5±2.0	0.006[a,c]
Harvested abdominal lymph nodes	10.1±1.5	17.2±2.1	14.8±1.8	0.022[a]
Thoracic duct ligation	9 (33.0%)	15 (55.6%)	9 (32.1%)	0.140
Hospitalization 30 d after operation	7 (25.9%)	7 (25.9%)	5 (17.9%)	0.714

Data are expressed as number, number (percentage), median (interquartile range), or mean±standard deviation. [a] Indicated that there is a significant difference between first period and second period. [b] Indicated that there is a significant difference between first period and third period. [c] Indicated that there is a significant difference between second period and third period

We also analyzed the operative time in all tumor node metastasis (TNM) stages I and II cases. MIME could be performed proficiently and reached an experience plateau after approximately 25 cases (Fig. 4) as suggested by Oshikiri et al. (2017). However, no plateau was found in stages III or IV tumor cases, because of the operative complexity and patient conditions.

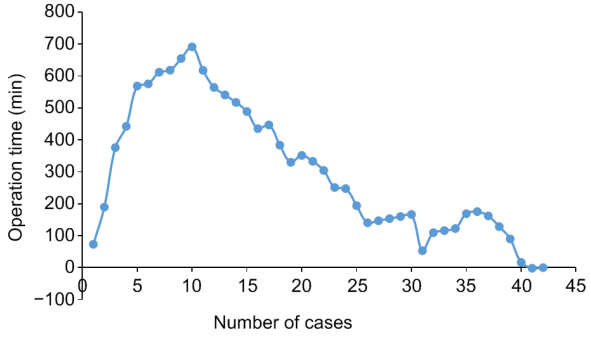

Fig. 4 Learning curve of MIME at I and II stages

4 Discussion

4.1 Operative body position

Three different patient positions were routinely used to mobilize the esophagus when the thoracoscopic procedure was performed: prone, left recumbent, and lateral prone. In the left recumbent position, it was difficult to explore the esophageal bed because of the lungs covering the operative field. Prone position provided good exposure during surgery, but it was inconvenient and dangerous to move the patient to recumbent position for the open portion of the procedure if bleeding occurred. The prone and lateral prone position allowed double-lung ventilation, further reducing operative trauma and improving surgical operability, in contrast to that in the left lateral decubitus position (Bonavina et al., 2012). However, the presence of spine abnormalities was a contraindication to the thoracoscopic approach in the prone position due to technical difficulty in exposing the esophagus because of the interference from the vertebral column or anatomical malformations of the aorta and tracheobronchial tree (Okamura et al., 2016).

In our center, all patients underwent esophageal mobilization with thoracoscopy in the lateral prone position. Combining the advantages of the left recumbent and prone positions, the procedure in lateral prone position could be converted to open surgery in emergency situations (Fabian et al., 2007). Furthermore, left RLN lymph node dissection would also benefit from the lateral prone position (Xi et al., 2016).

4.2 Complications

Due to high morbidity and mortality rates, esophagectomy is regarded as a complex and technically challenging procedure. MIE is associated with fewer pulmonary and cardiovascular complications, a low incidence of chylothorax, an approximately equal incidence of anastomotic leakage, and a slightly increased incidence of RLN palsy (Zhou et al., 2015; Guo et al., 2016).

In our 82 cases, the total complication rate was 24.4%, which was much lower than previously reported for open esophagectomy (OE) (Low et al., 2015) and MIE (Ma et al., 2018). Anastomotic leakage was the major complication of esophagectomy, and occurred in 4.9% of our cases. Previous reports revealed no difference between MIE and OE in anastomotic leakage rate (Zhou et al., 2015). One study reported that laparoscopic gastric mobilization as a part of MIE showed significant reduction of postoperative mortality at both 30 and 90 d (Messager et al., 2015). According to a previous report, anastomosis performed near the vascular arch of the gastric conduit, but not the ischemic area at the tip, resulting in a lower rate of anastomotic leakage (Zhai et al., 2015). To choose the best site for anastomosis, microperfusion assessment with indocyanine green fluorescence angiography was used to identify optimal blood supply (Yukaya et al., 2015).

By reducing both pain and the systemic inflammatory response, MIE decreased the incidence of respiratory complications (Tsujimoto et al., 2012). In addition, double-lung ventilation significantly improved surgical ergonomics by allowing better oxygenation (Cheng et al., 2006), and reduced ischemia-reperfusion injury caused by the one-lung ventilation (Li et al., 2015) and the risk of postoperative pulmonary complications (Noshiro and Miyake, 2013; Ye et al., 2013). The incidence of pulmonary complications was about 3.7% in our center. The low complication rate may have reflected use of a rehabilitation training team in our hospital. The team helped these patients improve lung function before the operation, and encouraged postoperative exercise and sputum mobilization. This may have significantly reduced pulmonary complications, especially in elderly patients.

Only one case of chylothorax was developed in our series. Thoracoscopy provided good operative views and magnification, which was the most important factors in avoiding injury to the thoracic duct. Thoracic duct ligation was not a routine procedure in our group, and ligation was only performed in invasive and obvious injury cases (33 cases).

Lymph node metastasis has been considered one of the most important factors in esophageal cancer prognosis. Thus, lymph node dissection is regarded as an important procedure during esophagectomy. The bilateral RLN chain is a common site for metastasis, in which it is extremely difficult to achieve clearance (Kanemura et al., 2017). In order to attain long-term survival, RLN lymph node dissection was performed, but postoperative hoarseness caused by electrical interference was the greatest barrier (Luketich et al., 2012). As operative experience increased, the rate of hoarseness in our center fell during the second and third periods. Avoiding contact between electrical devices and the RLN and clearly exposing the RLN during lymph node dissection could reduce postoperative hoarseness.

Less than 5% postoperative mortality has been reported by other centers. However, advances in the surgical approach and anastomotic technique showed no significant correlation with the complications related to anastomotic leakage or respiratory infection (Okamura et al., 2016). Meanwhile, our center had mortality and morbidity rates similar to those of other specialty centers.

4.3 Learning curve

All 82 esophagectomy cases were performed successfully with the MIME procedure. Operative time was 260 min and blood loss was 100 ml, which were similar to the results in other studies (Meng et al., 2014; Ma et al., 2018). A previous study reported that blood loss during MIE was less than that during OE, but the operative time was not shorter than that in OE (Lv et al., 2016). However, when compared with OE cases, the MIME procedure was shorter in our center, with fewer postoperative hospitalization days.

MIME is preferred by many as their first choice, but surgical familiarity with the procedure requires a long period of training and experience. In our center, some early cases were excluded from the procedure due to tumor invasion or other operative challenges. However, with the accumulation of cases and operative experience over time, we were capable of performing some advanced cases safely and successfully. In our group, the operative time decreased significantly in the second and third periods, indicating that surgical performance improved with the number of procedures performed. In addition, an upward trend in the number of harvested lymph nodes was related to surgical experience. However, there were no significant differences in blood loss or postoperative morbidity among three periods. After performing 25 cases

of MIME, this technique may reach a plateau in our center.

Another key element of success was the excellent cooperation and support from different team members, including surgeons, nurses, and rehabilitation trainers. This collaboration has also played a decisive role in helping choose the surgical method and modifying our operative strategy, which eventually led us to success.

5 Conclusions

Surgical outcomes following MIME for esophageal cancer were safe and acceptable. MIME for stages I and II could be performed proficiently and reached an experience plateau after approximately 25 cases in one medical group.

Compliance with ethics guidelines

Zi-yi ZHU, Xu YONG, Rao-jun LUO, and Yun-zhen WANG declare that they have no conflict of interest.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5). Informed consent was obtained from the patients for inclusion in the study.

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中文概要

题　目：单中心单医疗组全腔镜食管癌切除的临床分析

目　的：颈胸腹联合三切口食管癌切除术（McKeown）被广泛应用于食管癌的治疗。侧俯卧位的全腔镜食管癌切除术目前被认为是合适的治疗方式。本文回顾性分析了本中心的食管癌全腔镜手术的经验。

创新点：目前全腔镜食管癌手术在国内仍是少数大的医疗中心开展，对于多数医院仍未能开展。本研究单中心单医疗组全腔镜食管癌病例分析以及学习曲线，目前国内类似经验总结尚不多，对于该术式推广有一定指导意义。

方　法：在 2016 年 4 月至 2018 年 2 月之间，共 82 例食管癌病人在我中心由单医疗组进行全腔镜食管癌切除手术，手术方式、临床资料、手术、病理、并发症等资料被回顾性分析。全部的腔镜手术全部被成功完成，无一例术中转为开放手术。手术时间为 260 分钟，术中出血 100 毫升。胸部和腹部的淋巴结清扫枚数分别为 20.1 和 13.5 枚。术后 30 天内未出现死亡病例。总并发症率为 24.4%，包括吻合口瘘 4 例（4.9%），喉返神经损伤 5 例（6.1%），肺部感染 3 例（3.7%），乳糜胸 1 例（1.2%），胸腔积液 4 例（4.9%），不全肠梗阻 2 例（2.5%），颈部切口感染 1 例（1.2%）。术后平均住院天数 12 天。根据学习曲线，我们分析了不同阶段的出血量、手术时间、并发症率、淋巴结清扫数量等数据。不同阶段的手术时间（P=0.006）、术后住院天数（P=0.015）、总淋巴结清扫数（P=0.003）、胸腔内淋巴结清扫数（P=0.006）和腹腔内淋巴结清扫数（P=0.022）均有统计学差异。

结　论：全腔镜食管癌切除手术被认为是安全的、合适的。对于 I 期、II 期的食管癌病人，随着手术例数的积累手术技巧会更熟练，并在 25 例左右到达平台期。

关键词：全腔镜食管癌切除术（McKeown手术）；手术技巧；学习曲线