Comparison of short-term therapeutic efficacy between minimally invasive Ivor-Lewis esophagectomy and Mckeown esophagectomy for esophageal cancer.

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Abstract

Objective: Minimal Invasive Esophagectomy (MIE) has become the main radical treatment for esophageal cancer. However, there are still many controversies on MIE. This paper compared the short-term therapeutic efficacy between minimally invasive Ivor-Lewis esophagectomy and McKeown esophagectomy for esophageal cancer.

Methods: The clinical data of patients with esophageal cancer treated by MIE from November 2014 to May 2016 in the PLA General Hospital (Beijing, China) were analysed retrospectively. The baseline and intraoperative data and postoperative outcomes were compared.

Results: There were 185 patients in total, including 120 patients in Ivor-Lewis group and 65 patients in McKeown group. There was no significant difference in baseline data between two groups. However, the location of tumors in the Ivor-Lewis group was mainly located in the middle-lower thoracic region, while the position of tumors in the McKeown group was mainly located in the middle-upper thoracic region. The operation time of the Ivor-Lewis group (314 ± 45 min) was slightly longer than that of the McKeown group (303 ± 37 min). The incidence of anastomotic leakage and recurrent laryngeal nerve injury in Ivor-Lewis group was significantly lower than that in McKeown group (2.5% (3/120) *vs.* 12.3% (8/65), 0.8% (1/120) *vs.* 9.2% (6/65)).

Conclusions: Compared with minimally invasive McKeown esophagectomy, Ivor-Lewis esophagectomy has lower incidence of anastomotic leakage and recurrent laryngeal nerve paralysis, but can complete thorough lymph node dissection and accurate staging.

Introduction

Esophageal cancer is one of the most common malignant tumors that seriously affect the health of Chinese residents. Surgery is the most important method for the radical treatment of esophageal cancer [1]. However, the traditional open radical resection of esophageal cancer usually causes big traumas and high risk, and its efficacy is not satisfactory [2,3]. In recent years, the Minimally Invasive Esophagectomy (MIE) has been gradually promoted to clinical practice; it has obtained the universal approval for its outstanding advantages of less trauma, fewer complications, as well as rapid postoperative recovery [4-6]. However, in clinical practice, the surgeons of different hospitals usually adopt different operative method of MIE, that the selection of technical principle and operative method is still controversial. The selection of the anastomotic stoma location is one of the controversies [7]. In recent years, on the basis of MIE techniques, our hospital (Chinese PLA General Hospital) treated esophageal cancer patients with two operative methods, some patients were treated with minimally invasive Ivor-Lewis esophagectomy with thoracic anastomosis, and some were treated with minimally invasive McKeown esophagectomy with cervical anastomosis. To compare the short-term therapeutic efficacy of the two operative method, we made a retrospectively analysis on the clinical data of patients and reported as follows.

Materials and Methods

General information

The clinical data of all patients with esophageal cancer who received MIE treatment in Chinese PLA General Hospital from November 2014 to May 2016 were retrieved by electronic medical record system. The case selection criteria include: 1) patients of pathologically confirmed thoracic esophageal squamous cell cancer; 2) aged 18 to 75; 3) the stomach as the substitute organ for the esophagus; 4) minimally invasive Ivor-Lewis esophagectomy or minimally invasive McKeown esophagectomy as the operative method. The exclusion criteria include: 1) patients who received preoperative radiotherapy or (and) chemotherapy; 2) patients who received previous right

thoracotomy or abdominal surgery; 3) hybrid MIE (laparoscopy+right thoracotomy+open surgery). The gender, age, Body Mass Index (BMI), general status of PS score, pathological diagnosis, TNM stage, primary tumor location, and lesion length were collected.

From November 2014 to May 2016, our hospital have received and cured 307 cases of esophageal cancer patients, among whom 246 patients were treated with MIE. There were 120 cases of minimally invasive Ivor-Lewis esophagectomy (Ivor-Lewis group) and 65 cases of minimally invasive McKeown esophagectomy (McKeown group) after screening. The basic data of the two groups of patients was shown in Table 1. The patients enrolled in minimally invasive Ivor-Lewis group were mainly with middle-lower esophageal cancer, while the patients in minimally invasive McKeown group were mainly with middle-upper esophageal cancer. In addition, there was no significant difference in baseline date between the two groups.

Operative methods

All the minimally invasive esophagectomy were operated and completed by senior thoracic surgeon of our department (Department of Thoracic Surgery, Chinese PLA General Hospital) who were experienced and skilled in MIE operating. The various operative methods have a relatively uniform operation procedure. And the specific operation procedures of minimally invasive Ivor-Lewis esophagectomy and minimally invasive McKeown esophagectomy were described as follows:

Minimally Invasive Ivor-Lewis Esophagectomy (Dissociate the stomach in abdomen+dissociate the esophagus in right thorax +perform anastomosis in the right thoracic cavity).

A. Laparoscope part: Laparoscopic exploration staging; dissociate the stomach under the laparoscopy. Implant a 10 mm Trocar above or under the umbilicus as the observation hole and establish pneumoperitoneum, implant a 12 mm Trocar under costal margin on anterior axillary line of left upper abdomen with television monitoring, implant a 5 mm Trocar at 2 cm above the umbilicus on midclavicular line, implant 5 mm Trocars on symmetric positions of right upper abdomen, and put in ultrasonic scalpel and non-invasive grasping forceps respectively. Use the ultrasonic scalpel to open the greater omentum along 2 cm outside the gastroepiploic vessel arcades, enter the omental bursa, turn left to the spleen region, and separate towards the right to hepatocolic ligament.

B. Thoracoscope part: Implant the 12 mm, 5 mm, 10 mm, 12 mm Trocars respectively in the third or fourth intercostal anterior axillary line, the sixth intercostal anterior axillary line and posterior axillary line, the eighth intercostal through the right thorax, the four puncture holes are roughly diamond-shaped. Regulate the pressure of pneumothorax to about 8 mmHg. Open the upper mediastinal pleura, clear away the lymph nodes near the recurrent laryngeal nerves, disconnect the arch of azygos vein, fully dissociate the thoracic esophagus and clear away the lymph nodes around the esophagus. Remove the pneumothorax, extend the third or fourth intercostal incision to about 4 cm. Put in the mushroom head of

stapler with purse-string suture or with OrVil stapler nail head implantation method, and then cut off the esophagus; lift up the gastric tube to the thoracic cavity through the esophageal hiatus, resect the esophagus and remove the sample.

Minimally Invasive McKeown Esophagectomy (Dissociate the esophagus in right thorax+dissociate the stomach in abdomen +perform anastomosis through the left neck).

A. Thoracic cavity part: The patients take left lateral half prone position, with one-lung ventilation of left lung; implant a 10 mm Trocar in the seventh intercostal right anterior axillary line as the observation hole; implant a 12 mm Trocar in the third intercostal right anterior axillary line as the main operating hole; implant a 5 mm and 12 mm Trocar in the fifth intercostal right scapular line and the ninth intercostal right infrascapular line respectively as the accessory operation holes. Detect the tumors with the thoracoscope, to confirm the location and external invasion of tumors. Cut the upper mediastinal pleura, fully dissociate the upper esophageal front while cleaning the right recurrent laryngeal nerve lymph nodes, dissociate the arch of azygos vein, put 2 pieces of Hemolok in proximal end and distal end respectively and then disconnect them, stretch the esophagus to the front side, fully dissociate the esophagus and the posterior margin of the tumor, expose the trachea and subcarinal lymph nodes in the upper and middle segment, dissect to the surface of the pericardium in the lower segment; then use the electrocautery and the ultrasonic scalpel to dissociate the esophageal front, the assistant uses the bowel clamp to grasp the esophagus and push it forward, use the ultrasonic scalpel and electrocautery to dissociate the esophagus and tumors along the esophageal surgical plane, top to the plane above the thoracic subclavian artery, and down to expose the diaphragmatic esophageal hiatus.

B. Abdominal cavity part: The patients change to supine position with their heads 30° higher than their feet, with two-lung ventilation. CO_2 artificial pneumoperitoneum, 15 mmHg pressure; implant a 10 mm Trocar below the umbilicus as the observation hole; implant a 12 mm Trocar under costal margin of anterior axillary line as the main operation hole; implant a 10mm Trocar under the xiphoid as the liver traction hole, implant 5 mm Trocars in the middle point of the observation hole in the right clavicle midline and the main operation hole, and in its left symmetry position respectively as the accessory operation holes. Use the ultrasonic scalpel to cut off the gastric colon ligament along 2 cm outside the right gastroepiploic vascular arch, use the bowel clamp to grasp the posterior and fundus gastric region, cut off the gastrosplenic ligament and gastrophrenic ligament upwards, deal with the posterior gastric vessels; dissociate at the upper greater curvature until to expose the left crura diaphragmatis, dissociate at the lower greater curvature until the anterior pancreaticoduodenal artery could be seen in posterior gastric antrum.

C. Cervical part: Make an incision in left anterior sternocleidomastoid muscle, dissociate and disconnect the cervical esophagus, put in the sterile drainage tube after the closure of distal incision, extend the liver traction hole below the xiphoid process to 4 cm, pull the stomach and esophagus

outside the abdominal cavity, and complete the make of gastric tube; bind the top of gastric tube with the drainage tube, pull the gastric tube to the cervical part through the esophageal hiatus with the laparoscopic monitoring (to prevent the gastric volvulus), and perform mechanical anastomosis with the esophagus. Put the gastric tube and intestinal feeding tube in place. Thoroughly stop the bleeding, place the negative pressure tube in cervical part and latex tube in abdominal part, and close the laparotomy-cervical incision.

Observation indexes

Intraoperative indexes: Intraoperative bleeding, operation time, conversion to thoracotomy or laparotomy, intraoperative complications, resection rate, number of resected lymph nodes. Postoperative indexes: incidence of severe complications, perioperative mortality, postoperative pain, number of positive lymph nodes, life quality score. Survival indexes included 1-year survival rate, 2-year survival rate, median survival time and disease free survival.

Statistical methods

SPSS 16.0 software was used for statistical analysis. The quantitative indicators were described by mean ± standard deviation, median and interquartile range, while the qualitative indicators were described by rate or constituent ratio. The number of resected lymph nodes and other quantitative indicators were compared by t test or Wilcoxon rank sum test, and the qualitative indicators were compared by χ^2 test or Fisher's exact test. The survival rate of patients was estimated by Kaplan-Meier method, the survival curves were compared by Log-rank test, and multivariate survival analysis was performed by the Cox proportional hazards regression model. Test level $\alpha=0.05$.

Results

Intraoperative data indexes

For the patients in Ivor-Lewis group and McKeown group, their intraoperative index data were shown in Table 2. The operation time of the Ivor-Lewis group (314 ± 45 min) was slightly longer than that of the McKeown group (303 ± 37 min), but the difference was not statistically significant. (P>0.05) For the index of intraoperative blood loss, the difference between the two groups (135 ± 85 ml *vs.* 143 ± 71 ml, P>0.05) was also not statistically significant. Besides, there were 5 cases of severe intraoperative complications occurred in Ivor-Lewis group (3 cases of abdominal hemorrhage, 1 case of thoracic hemorrhage, and 1 case of colon injury or necrosis); while there were 3 cases in McKeown group (2 cases of

abdominal hemorrhage and 1 case of tracheal membranous part injury), the difference between the two groups was not statistically significant (P>0.05). In Ivor-Lewis group, there were 4 cases received conversion to thoracotomy (1 cases of massive hemorrhage, 2 cases of severe adhesion, and 1 case of failure of anastomosis), 3 cases received conversion to laparotomy (2 cases of hemorrhage and 1 case of colostomy); while in McKeown group, there were 2 cases received conversion to thoracotomy (1 case of tracheal membranous part injury and 1 case of severe adhesion), 2 cases received conversion to laparotomy (both of abdominal hemorrhage), and the difference of incidence of conversion to thoracotomy or laparotomy between the two groups was not statistically significant (P>0.05).

Postoperative clinical indexes

In the aspect of postoperative complications, the total incidence of postoperative complications in Ivor-Lewis group is 19.2% (23/120), the total incidence of postoperative complications in McKeown group is 33.8% (24/65), and the difference between two groups is statistically significant (P=0.04<0.05). Among the postoperative complications, the incidence of anastomotic leakage and recurrent laryngeal nerve paralysis in McKeown group are significantly higher than that in Ivor-Lewis group (anastomotic leakage, 12.3% *vs.* 2.5%, P=0.02; recurrent laryngeal nerve paralysis, 9.2% *vs.* 1.6%, P=0.04); while in aspects of respiratory complications, cardiovascular complications, postoperative bleeding and other complications, there was no significant difference between the two groups (P>0.05, Table 3).

For the perioperative mortality rate, there was 1 death case in minimally invasive Ivor-Lewis group (0.7%), and 1 death case in minimally invasive McKeown group (1.5%), with no statistically significant difference between the two groups. For the postoperative hospital stay, it was 10.4 ± 7.7 d and 10.8 ± 8.1 d respectively in minimally invasive Ivor-Lewis group and minimally invasive McKeown group, and the difference between the two groups was not statistically significant (P=0.74).

Follow-up indexes

Among the two groups, 180 cases of patients (97.3%) were followed up, for 1 to 18 months (mean, 8.4 ± 6.8 months). During the recent follow-up, the differences between the minimally Ivor-Lewis group and minimally invasive McKeown group of patients in aspects of acid reflux, dysphagia, emptying disorders, and chest discomfort were not statistically significant.

Table 1. *Comparison of the patients' basic data between the Ivor-Lewis group and the McKeown group.*

		Ivor-Lewis group (n=120)	McKeown group (n=65)	P value
Gender	Male	82	41	0.58

Female		38	24	
Age		57.2 ± 13.0	56.7 ± 11.6	0.8
BMI (kg/m^2)		21.1 ± 4.7	21.5 ± 5.0	0.59
Primary tumor location	Upper thoracic region	12	30	<0.001[*]
	Middle thoracic region	54	28	
	Lower thoracic region	44	7	
TNM stage	I	25	14	0.91
	II	63	32	
	III	32	19	

[*]The difference is statistically significant.

Table 2. Comparison of the patients' intraoperative indexes between the Ivor-Lewis group and the McKeown group.

	Ivor-Lewis group (n=120)	McKeown group (n=120)	P value
Total operation time (min)	314 ± 45	303 ± 37	0.09
Intraoperative blood loss (ml)	135 ± 85	143 ± 71	0.52
Incidence of severe complications (%)	5 (4.16%)	3 (4.62%)	0.82
Incidence of conversion to thoracotomy or laparotomy (%)	7 (5.83%)	4 (6.15%)	0.81

Table 3. Comparison of patients' postoperative severe complications between the Ivor-Lewis group and the McKeown group.

	Ivor-Lewis group (n=120)	McKeown group (n=120)	P value
Anastomotic leakage	3 (2.5%)	8 (12.3%)	0.02[*]
Respiratory complications	7 (5.8%)	4 (6.2%)	0.83
Cardiovascular complications	5 (4.2%)	2 (3.1%)	0.98
Recurrent laryngeal nerve paralysis	2 (1.6%)	6 (9.2%)	0.04[*]
Postoperative bleeding	2 (1.7%)	2 (3.1%)	0.92
Other severe complications	4 (6.2%)	2 (3.1%)	0.57

[*]The difference is statistically significant.

Discussion

With the development of minimally invasive surgical techniques represented by thoracoscope and surgical robots, the Minimally Invasive Esophagectomy (MIE) has become more and more mature for clinical use. It is reported that, compared with the traditional open surgery, MIE has the advantages of less trauma, less postoperative complications, rapid recovery, and high life quality postoperatively [8]. It is also reported that MIE has significantly reduced the perioperative mortality of patients with esophageal cancer [9,10]. Based on these advantages, it becomes an inevitable trend of esophageal surgery for MIE in continuous clinical spreading and in-depth development [1]. The current popular MIE operative methods mainly include the transhiatal esophagectomy, Ivor-Lewis esophagectomy and minimally invasive McKeown esophagectomy [9,11], the latter two are

commonly used in domestic China. Through the retrospective analysis, this paper initially discussed the clinical efficacy of two different MIE operative methods (minimally invasive Ivor-Lewis esophagectomy and minimally invasive McKeown esophagectomy) in the treatment of esophageal cancer.

The procedures of the two operative methods are slightly different. The main procedure of Ivor-Lewis esophagectomy includes dissociating of the stomach in abdominal cavity, lymph nodes dissection and gastric tube making; dissociating of the esophagus in thoracic cavity (right thorax), lymph nodes dissection and the esophageal stomach thoracic anastomosis. Some surgeons add a step of jejunostomy in the abdominal part to provide timely enteral nutrition postoperatively. The main procedure of McKeown esophagectomy changes the anastomotic position to the cervical part (left neck) on the basis of the Ivor-Lewis operative method. The McKeown operative procedure changes accordingly, that the patients were usually

posed at lateral position for thoracic operation, then operation in abdominal part and cervical part. Due to the change in the location of the anastomosis, the excision extension of the esophagus is naturally increased [11].

We have explored both two minimally invasive operative methods. Moreover, we have adopted a total endoscopic operation rather than hybrid method in thoracic cavity and laparoscopic cavity part, to minimize the incisions. After the exploration of our initial clinical practice, we have gradually formed a unified operative procedure according to our own experience; the focus of the operation should be the minimization of trauma and thorough resection (including the esophageal and proximal stomach En bolc resection and thorough lymph nodes dissection). The benefits of standardized operative procedures are revealed as shortening the learning curve of the operation, improving the smooth cooperation of the operation team (surgeons, nurses, and anesthetists), and making it easier for carrying out clinical research. In the process of MIE, both the minimally invasive Ivor-Lewis esophagectomy and Ivor-Lewis esophagectomy have about a 6% conversion rate to thoracotomy or laparotomy, most of these cases were due to intraoperative accidental complications (bleeding); While the conversion cases caused by severe thoracic-abdominal adhesions were in small numbers, suggesting that the mild thoracic-abdominal adhesions would not affect the endoscopic operation, and the previous history of thoracic or abdominal operation was not a taboo of MIE. The severe intraoperative complications were mainly accidental bleeding, especially the accidental bleeding occurred with the laparoscopic operating, with the incidence of about 4-5%. This is slightly lower than what reported in the literature. With the accumulation of operation quantity and the improvement of operative techniques, the incidence of intraoperative complications should be further reduced.

In addition, we have concluded that, the operative procedure of minimally invasive Ivor-Lewis is clear and concise, which is easy to learn and master, and could be applied to the lower-middle segment esophageal cancer, including the esophagogastric junction tumor. For several upper thoracic esophageal cancers with relatively small primary lesions, we can complete the thorough resection by changing the anastomosis position to the thoracic apex, which is fully accorded with the principle of tumor resection. While the operative method of minimally invasive McKeown is relatively complex, but makes a more thorough resection, especially in considering the potential vertical jumping shift feature of the esophageal cancer; moreover, the cervical anastomosis is more convenient than intrathoracic anastomosis; and the postoperative anastomotic leakage is easier to deal with. Through the retrospective analysis, although the operative procedure of minimally invasive McKeown is more complex, the operation time is slightly less than that of the minimally invasive Ivor-Lewis, which suggests that after familiarization with the operative procedure, the operative method of minimally invasive McKeown seems to be more advantageous in shortening the operation time. However, the difference between the two operative methods is not significant. In addition, our data suggests that, the incidence of anastomotic leakage and recurrent laryngeal nerve paralysis in the minimally invasive Ivor-Lewis esophagectomy is significantly lower than that of the minimally invasive McKeown esophagectomy. Although the cervical anastomotic leakage is easier to deal with than intrathoracic anastomotic leakage, it apparently increases the surgical risk. While the recurrent laryngeal nerve paralysis affects the patients' life quality. Moreover, the increase of cervical incisions means a relative increase in surgical trauma. Therefore, considering the surgical trauma and risk, the minimally invasive Ivor-Lewis esophagectomy seems to be more advantageous.

However, the selection of operative method should firstly consider the effectiveness of treatment (radical treatment) [12]. Since the duration of follow-up was relatively short, and the number of cases was limited, we cannot compare the difference of patients' survival with the two operative methods in this paper. Theoretically, the minimally invasive McKeown esophagectomy seems to be more advantageous in tumor resection; however, there is no definitive conclusion, which requires in-depth study and long-term follow-up observation.

In conclusion, for esophageal cancer of the upper and middle thoracic segment, the minimally invasive McKeown esophagectomy has a natural advantage in the aspect of according with the therapeutic principles of tumor surgery; for esophageal cancer of the lower and middle segment, this study showed initially that Ivor-Lewis esophagectomy has a lower incidence of anastomotic leakage and recurrent laryngeal nerve paralysis, which could also achieve the objective of thorough lymph nodes dissection and accurate staging. The differences in patients' postoperative life quality, tumor recurrence and survival rate of the two groups were not statistically significant, which suggested the feasibility, safety and good short-term efficacy of the esophagectomy. However, for esophageal cancer patients with tumors located in middle-lower thoracic region, it still need further study to confirm whether to choose the minimally invasive McKeown esophagectomy.

Conflicts of Interests

The authors declare that they have no conflicts of interest.

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