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Original Article

Comparative study between minimally invasive and open esophagectomy for the treatment of esophageal cancer

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Abstract

Background: Complete resection of the esophageal tumor is the gold standard therapy. The optimal surgical approach for esophagectomy is still controversial. This study compared the short-term outcomes of minimally invasive (MIE) and open esophagectomy for treating esophageal cancer.

Methods: A prospective study was conducted on 70 consecutive patients who received esophagectomy for esophageal carcinoma between 2017 and 2019 at Henan Cancer Hospital, Zhengzhou, China. Fifty patients received MIE (Group A), and 20 received open esophagectomy (Group B). Among Group B, 17 patients had left thoracotomy, and three had three incision esophagectomy.

Results: The mean age in Group A was 61.48 ± 8.06 years, and 61.3 ± 7.52 years in Group B (p= 0.932). In Group A, most of the tumors were located in the middle thoracic area (56%), while in the open esophagectomy group, most of the tumors were located in the lower thoracic-esophagogastric junction area (50%) (p<0.001). The most common stage in Group A was (T3N0M0) and (T3N0M0) in Group B (p= 0.044). Neoadjuvant therapy was used in 48% of patients in Group A and 15% in Group B (p=0.08). The mean number of resected lymph nodes in Group A was 28.8 ± 7.8 lymph nodes versus 22.4 ± 7.7 in the open esophagectomy group (p=0.003). The mean operative bleeding amount was 80±34.6 ml and 185± 46.2 ml for groups A and B, respectively (p=0.001). The mean ICU stay for Group A was 0.5± 0.7 days versus 0.4± 0.6 days for Group B (p=0.4). The mean postoperative hospital stay for Group A was 8± 3 days, while in Group B, the mean postoperative hospital stay was 14± 3 days (p=0.001). Postoperative complications occurred in 2 patients (4%) in Group A and seven in Group B (p= 0.001). No tumor recurrence was detected radiologically among the two groups in the three months follow-up period.

Conclusion: Minimally invasive esophagectomy may be a feasible and safe procedure for patients with early-stage esophageal cancer or locally advanced neoplasms who have received neoadjuvant therapy.

KEYWORDS

Esophagectomy; Minimally invasive; Esophageal cancer; Esophagus; Thoracoscopic; Laparoscopic

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Introduction

Esophageal cancer is the eighth most prevalent malignant tumor and the sixth leading cause of cancer-related death worldwide. Around 80% of esophageal cancer patients and deaths occur in developing countries, with squamous cell carcinomas accounting for nearly 90% of cases in high-incidence areas [1-3]. Complete resection of the esophageal tumor remains the gold standard therapy, and surgery almost offers the best chance for a cure [4]. Despite the recent improvement in anesthetic techniques and postoperative care, esophagectomy still carries high morbidity and mortality, mainly because of postoperative pulmonary complications.

Many factors can affect postoperative pulmonary functions, including age, co-comorbidities, atelectasis, aspiration, pain, and the need for postoperative mechanical ventilation [5].

Most studies comparing open and minimally invasive esophagectomy (MIE) have reported that MIE was associated with better perioperative morbidity and short-term outcomes with no difference regarding tumor recurrence or survival among patients [6-9].

Most centers that perform esophagectomy start oral feeding for the patients on 6th or 7th postoperative day. The patients remain on nil by mouth and depend mainly on intravenous nutrition or nutrition by jejunostomy or naso-intestinal tubes. The delay in the start of oral feeding adds to the morbidity and slow recovery of the patients after surgery [10]. According to a recent study, many patients who underwent minimally invasive esophagectomy began oral feeding on the first postoperative day to achieve an enhanced recovery after surgery (ERAS) and shorten the hospital stay [14].

Starting oral feeding soon after surgery helps the patients regain their normal activities faster and improve their quality of life by affecting their sense of well-being after surgery [11,12].

Although the minimally invasive techniques did not show a benefit over the open techniques in the long-term outcomes, including tumor recurrence and overall survival, the MIE procedure was accompanied by reduced surgical access trauma which resulted in less tissue injury, reduced blood loss, reduced postoperative pain, lesser analgesic requirements and reduced pulmonary complications after surgery. [13] It was reported that tubeless, non-fasting, minimally invasive esophagectomy could be a feasible and safe procedure for esophageal resection in esophageal cancer patients [14-16]. Thus, our study aimed to compare minimally invasive to open esophagectomy to treat esophageal neoplasms.

Patients and Methods

Design and patients

We have conducted a prospective study on 70 consecutive patients who received esophagectomy as a curative treatment for esophageal cancer from September 2017 to September 2019. The study was held in Henan Cancer Hospital, Zhengzhou, China.

The 70 patients were assigned into two groups according to the surgical technique. Group A (n=50) included patients who underwent minimally invasive esophagectomy, and Group B (n=20) included patients who underwent open esophagectomy.

After explaining the details and potential drawbacks of the surgical intervention, all cases provided informed written consent. The Institutional Review Board and the Ethics Committees of Henan Cancer Hospital, Zhengzhou, China, approved the study. All patients signed written consent for the publication of medical data without revealing their identities.

Preoperative workup

All patients enrolled in our study were subjected to careful clinical evaluation and laboratory investigations, including complete blood count and renal and liver function tests. Imaging techniques were performed to evaluate the tumor stage, including endoscopy for the

upper gastrointestinal tract, endoscopic ultrasound, and CT scan of the chest and abdomen.

Operative techniques

1. The minimally invasive esophagectomy procedure (MIE):

All patients had a right thoracoscopic and laparoscopic esophagectomy and at least two-field lymph node dissections. A cervical lymphadenectomy was performed when a color ultrasound revealed suspicious lymph node metastasis.

The thoracic phase of the procedure: Single lumen endotracheal tube was used for ventilating the patient; then, a left lateral decubitus position with a 30° tilt in the semi-prone position was established to start the thoracic phase. Four ports were introduced for thoracoscopy. The camera port (10mm) was placed in the seventh (7th) intercostal space posterior axillary line. Another 10mm port was introduced in the ninth (9th) intercostal space in the scapular line for the assistant. The remaining two ports were for the main surgeon; a 10 mm port in the fourth intercostal space just anterior to the posterior axillary line and another 5 mm port just below the tip of the scapula in the 6th intercostal space. (Figure 1)

Figure 1: Left lateral decubitus patient position and port positions for the thoracoscopic phase of the minimally invasive esophagectomy

Opening of the mediastinal pleura overlying the esophagus was performed from the apex of the thoracic cavity down to the level of the azygous vein using an electrical coagulation hook. The azygous vein was divided using an energy-sealing device after double clipping. (Figure 2)

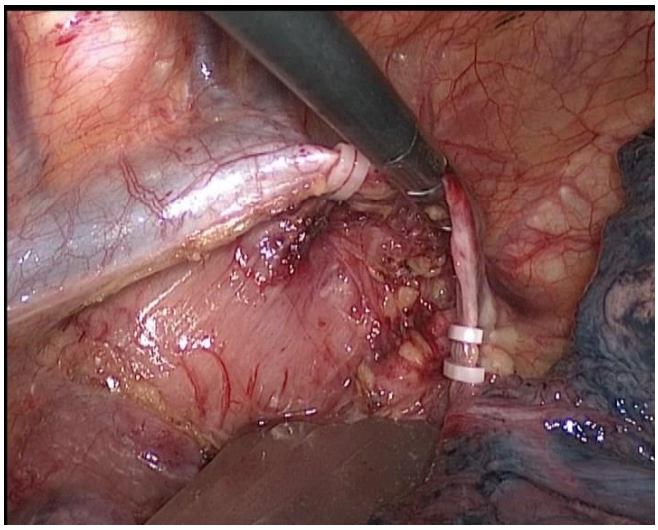

Figure 2: Ligation and division of the arch of the azygous vein

Mobilization of the entire esophagus was performed circumferentially, beginning from the top of the chest cavity down to the diaphragm. The posterior esophageal surface was mobilized from the descending thoracic aorta first. Then the anterior surface was dissected. (Figure 3)

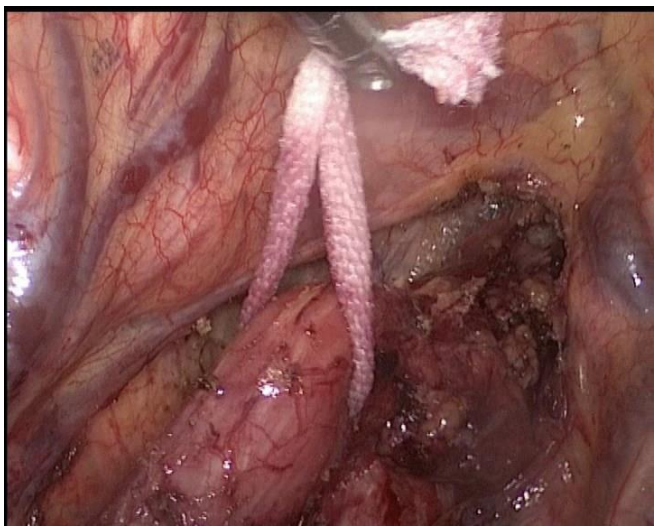

Figure 3: Thoracic esophagus mobilized with tape around it for retraction

Mediastinal lymph nodes dissection was accomplished by removing the following groups of lymph nodes (left recurrent laryngeal nerve, right recurrent laryngeal nerve, para-esophageal,

paratracheal, subcarinal, supradiaphragmatic and posterior mediastinal lymph nodes).

Exposure of the cervical esophagus: The position was modified to the supine position, and a 3 cm left cervical incision was made along the medial border of the sternomastoid muscle. Dissection of the cervical esophagus medial to the carotid sheath was accomplished, and then ligation and transection of the cervical esophagus were done using the electrical coagulation knife.

The laparoscopic phase of the operation: The patient was kept in the same supine position, and five ports were made for laparoscopic gastric mobilization with the surgeon and the cameraman standing on the right side and the assistant on the left side of the patient. A 10 mm camera port was made 2cm to the left of the umbilicus. Another 5 mm port just below the right costal margin on the midclavicular line and a 10 mm port between the umbilicus and the last port on the right paraumbilical line. The last two ports were for the main surgeon to introduce the energy-sealing device and manipulate the stomach.

Another two ports for the assistant; a 10 mm port was made just below the xiphoid process and a 5 mm port in the left anterior axillary line at the level of the umbilicus. The stomach was mobilized by dividing the gastrocolic omentum and short gastric vessels using the energy sealing device, preserving the right gastroepiploic arcade.

Gastric tube formation: The 10mm port below the xiphoid process was widened to 4 cm along the abdominal midline. A gastric tube of 4-5 cm width was constructed using linear staples along the gastric greater curvature. The esophageal specimen containing the tumor and the proximal gastric cardia were removed. Two layers of continuous Vicryl sutures were added to reinforce the stapler line of the gastric tube. (Figure 4)

Cervical anastomosis: Three-layer, hand-sewn anastomosis was constructed in the left cervical region. The gastric tube was pulled up to the cervical region with the greater curvature of the stomach facing backward and the lesser curve facing forward.

Figure 4: Gastric tube completely formed

2. The open esophagectomy procedures:

In our study, we have used two methods for open esophagectomy procedure, either three-incision esophagectomy (Mc Keown esophagectomy) [5] or the left thoracotomy approach (Sweet approach) [17].

A. Three incisions (Mc Keown) esophagectomy [5]:

Thoracic phase: A double-lumen endotracheal tube was used in all patients for right lung isolation, and the patient was put in the left lateral decubitus position. A right posterolateral thoracotomy in the 6th or 7th intercostal space was performed. Mobilization of the anterior esophageal surface was performed by dissecting the esophagus away from the pericardium and the carina and resecting all lymphatic issues together with the specimen. Then, the posterior surface of the esophagus was mobilized from the descending aorta and the spine.

Cervical phase: The patient was turned supine, and the head was turned to the right. The left cervical incision along the anterior border of the left sternomastoid muscle was performed.

Exposure of the prevertebral fascia and circumferential mobilization of the cervical esophagus was performed with fingers, taking care not to injure the recurrent laryngeal nerves.

Abdominal phase:

An upper midline laparotomy was performed. Division of the short gastric vessels and mobilization of the greater omentum along the greater curvature of the stomach preserve the right gastroepiploic arcade. The opening of the phreno-esophageal membrane and

circumferential dissection of the distal esophagus was done.

The gastric tube was delivered to the cervical region by carefully pulling up the silk thread to avoid rotation of the gastric conduit.

Cervical anastomosis: A hand-sewn, three-layer embedded anastomosis was performed in the left cervical region in the same manner as the minimally invasive technique.

B. Left thoracic approach (Sweet procedure) [17]:

The patient was placed in the right lateral decubitus position after inserting a double-lumen endotracheal tube for left lung isolation. A left posterolateral thoracotomy incision was made in the 6th intercostal space. Blunt and sharp dissection of the esophagus was made using an electrocautery knife and an energy-sealing device to separate the esophagus from the descending aorta.

A 5-6 cm radial incision in the diaphragm was made, and the abdominal cavity was entered. The stomach was mobilized through the left thoracic cavity preserving the right gastroepiploic arcade. The left gastric vessels were divided using linear staplers or ligated by double clipping and cut at their base.

The preparation of the gastric tube in the left thoracic cavity was established through the left diaphragmatic incision. A mechanical end-to-end esophagogastric anastomosis was made using a circular stapling device below the aortic arch.

The following data were recorded during the surgical procedure for all patients included in the study; operative time, operative bleeding amount, and the resected lymph nodes count.

Postoperative care

The principles of treatment in the perioperative period were nearly identical for both groups. The patients were routinely transferred to the general ward after recovery from anesthesia. Admission to ICU after surgery was preferred for patients who experienced respiratory complications after recovery from anesthesia.

For the patients in Group A, oral feeding was started on the first postoperative day starting with a liquid diet. Patients who received open surgery were kept on parenteral nutrition until they began oral feeding on the 6th or 7th postoperative day.

The patients were discharged home when they could tolerate semi-liquid food without trouble and walk actively without discomfort.

Postoperative follow-up:

All patients were regularly followed up in the outpatient clinics and by phone calls. The outpatient follow-up was done one month after hospital discharge, and another visit was scheduled three months after hospital discharge.

Outcome measures

The primary outcome was a composite endpoint of postoperative complications. The secondary outcomes were operative time, lymph nodes resected, bleeding, ICU stay, feeding time, hospital stay, and postoperative complications.

Statistical analysis

The data were tabulated and analyzed using IBM SPSS software version 22.0 (IBM Inc., Chicago, IL, USA). Qualitative data were described using numbers and percentages. Continuous quantitative variables were assessed for normality; normally distributed variables were reported as mean and standard deviation (SD). Skewed variables were reported as median and interquartile range. A comparison between different groups regarding categorical variables was tested using the Chi-square test ($\chi 2$-test). When more than 20% of the cells have an expected count of less than 5, correction for the Chi-squared was conducted using Fisher's exact test or Monte Carlo correction. Confidence intervals (95%CI) were calculated. For normally distributed data, a comparison between two independent populations was done using an unpaired t-test. For abnormally distributed data, we used the Mann-Whitney U test. A p-value of 0.05 or less was considered a level of significance.

Results

Patient Characteristics and preoperative data:

No significant difference was found between Group A and group B regarding age, sex, and comorbidities. The average age of patients in Group A was 61.48 ± 8.06 years, while in Group B, it was 61.3 ± 7.52 years.

In both groups, most patients were males representing 68% in Group A and 85% in Group B. (Table 1)

Regarding the location of the tumor, there was a statistically significant difference between both groups (p= < 0.0001) as for Group A patients, most of the tumors were located in the middle thoracic area (56%), upper-middle thoracic area (10%) and middle-lower thoracic area (20%). While in the open esophagectomy group, most of the tumors were located in the lower thoracic-esophagogastric junction area (50%) and esophagogastric junction alone (25%).

Regarding the tumor histopathology, all patients in Group A were squamous cell carcinoma, while in group B, 70% of the patients were adenocarcinoma (p= <0.001). (Table 1)

The clinical tumor stage for patients in Group A was (T3N0M0) in 50% of the patients, (T2N0M0) in 32%, and (T1bN0M0) in 16%. On the other hand, 80% of the patients in the open esophagectomy group were diagnosed as (T3N0M0), 15% were (T2N0M0), and 5% were (T4N0M0) (p= 0.044). (Table 1) Neoadjuvant therapy was used in 48% of patients in Group A and 15% in Group B (p=0.08).

Table 1: Preoperative characteristics of patients with esophageal cancer who had minimally invasive (Group A) vs. open esophagectomy (Group B). Continuous data were presented as mean and standard deviation, and categorical data as numbers and percentages

	Total (n= 70)	Group A (n= 50)	Group B (n= 20)	p-value
Age, years	61.43± 7.86	61.48± 8.06	61.3± 7.52	0.932
Male	51 (72.9%)	34 (68%)	17 (85%)	0.234
Hypertension	17 (24.3%)	10 (20%)	7 (35%)	0.186
Diabetes	1 (1.4%)	1 (2%)	0	>0.99
Tumor location				
Cervical	0	0	0	<0.001
Upper thoracic	4 (5.7%)	4 (8%)	0	
Upper and mid thoracic	5 (7.1%)	5 (10%)	0	
Mid thoracic	30 (42.9%)	28 (56%)	2 (10%)	
Mid and lower thoracic	12 (17.1%)	10 (20%)	2 (10%)	
Lower thoracic	2 (2.9%)	1 (2%)	1 (5%)	
Lower thoracic and GEJ	11 (15.7%)	1 (2%)	10 (50%)	
GEJ	6 (8.6%)	1 (2%)	5 (25%)	
Pathology				
Squamous Cell Carcinoma	56 (80%)	50(100%)	6 (30%)	<0.001
Adenocarcinoma	14 (20%)	0	14 (70%)	
TNM stage				
T1bN0M0	8 (11.4%)	8 (16%)	0	0.044
T2N0M0	19 (27.1%)	16 (32%)	3 (15%)	
T2N1M0	1 (14%)	1 (2%)	0	
T3N0M0	41 (58.6%)	25 (50%)	16 (80%)	
T4N0M0	1 (1.4%)	0	1 (5%)	
Neoadjuvant treatment				
None	43 (61.4%)	26 (52%)	17 (85%)	0.08
NAC 1 cycle	2 (2.9%)	2 (4%)	0	
NAC 2 cycles	24 (34.3%)	21 (42%)	3 (15%)	
NACR 2 cycles	1 (1.4%)	1 (2%)	0	

GEJ: gastro-esophageal junction, NAC: neoadjuvant chemotherapy; NACR: neoadjuvant chemoradiotherapy

Table 2: Operative and postoperative data of patients with esophageal cancer who had minimally invasive (Group A) vs. open esophagectomy (Group B). Continuous data were presented as mean and standard deviation, and categorical data as numbers and percentages

	Total (n= 70)	Group A (n= 50)	Group B (n= 20)	p-value
Operative time (min)	225.9± 52	236.6± 39.2	199± 69.1	0.005
Lymph nodes resected	27± 8.2	28.8± 7.8	22.4± 7.7	0.003
Operative bleeding (ml)	110± 61	80± 34.6	185± 46.2	<0.001
Intensive care unit stay (days)	0.5± 0.7	0.5± 0.7	0.4± 0.6	0.404
Postoperative feeding time (days)	2.7± 2.6	1.2± 1	6.6± 0.5	<0.001
Postoperative hospital stay (days)	10± 4	8± 3	14± 3	<0.001
Major complications				
Pneumonia	5 (7.1%)	2 (4%)	3 (15%)	
Pleural effusion	1 (1.4%)	0	1 (5%)	
Hydropneumothorax	2 (2.9%)	0	2 (10%)	0.001
Wound infection	1 (1.4%)	0	1 (5%)	
Anastomotic leak	0	0	0	

Operative data:

The mean operative time in Group A was 236.6 minutes ± 39.2 and 199 minutes ± 69.1 minutes in Group B (p=0.005). The two groups had a significant difference in the number of resected lymph nodes. The mean number of resected lymph nodes in Group A was 28.8 ± 7.8 lymph nodes versus 22.4 ± 7.7 in the open esophagectomy group (p=0.003).

The mean operative bleeding amount in Group A was 80 ml ± 34.6 versus 185 ml ± 46.2 in Group B (p=0.001). (Table 2).

Postoperative course and complications:

There was no significant difference in the postoperative ICU stay between both groups. The mean ICU stay for Group A was 0.5± 0.7 days versus 0.4± 0.6 days for Group B (p=0.4).

As regards the postoperative complications encountered among both study groups, only two patients (4%) developed complications in Group A (postoperative pneumonia). For the open esophagectomy group, seven patients (35%) had experienced postoperative complications; three had postoperative pneumonia (15%), two had hydropneumothorax (10%), one developed pleural effusion (5%), and one patient had postoperative wound infection (5%) (p= 0.001). (Table 2)

Regarding the postoperative hospital stay, there was a statistically significant difference between both groups. The mean postoperative hospital stay for Group A patients was 8± 3 days, while in Group B, the mean postoperative hospital stay was 14± 3 days (p=0.001).

Follow-up:

No tumor recurrence was detected radiologically among the two groups in the three months follow-up period. Two patients experienced difficulty swallowing (4%) in group A; in the open esophagectomy group, one patient complained of difficulty swallowing (5%) during the three months of follow-up.

Discussion

Esophagectomy is a complex surgical procedure usually associated with high perioperative and postoperative morbidity and mortality. Respiratory complications are among the most common and annoying complications after esophageal resection. Postoperative pleural effusion, chest infection, and pulmonary atelectasis are commonly seen after esophagectomy due to painful thoracotomy incision and the morbidity of postoperative pain and reduced mobility after surgery [18,19].

Minimally invasive esophagectomy proved to be a safe and feasible way for radical excision of esophageal cancer and lymph node clearance. Moreover, MIE was safe and effective after

neoadjuvant chemotherapy or chemoradiotherapy for patients with locally advanced esophageal carcinoma [19-21].

Smita Sihag [20] and colleagues have compared minimally invasive esophagectomy and open esophagectomy regarding the early surgical outcomes using the society of thoracic surgeons national database, and they concluded that the MIE procedure was feasible and safe with mortality and morbidity rates comparable to the open technique [20].

Their results showed that MIE was associated with longer median operative time than open esophagectomy (443 versus 312 minutes; p < 0.001) and shorter median length of hospital stay (9 versus 10 days; p < 0.001). They have also reported that MIE patients experienced a higher rate of reoperation (9.9% versus 4.4%; p< 0.001) and empyema (4.1% versus 1.8%; p< 0.001).

In addition, the open technique was found to have an increased rate of wound infections (6.3% versus 2.3%; p < 0.001), postoperative transfusion (18.7% versus 14.1%; p [0.002), and ileus (4.5% versus 2.2%; p= 0.002) [20].

On the other hand, Fanyu Meng [6] et al. conducted a study comparing open and minimally invasive esophagectomy in 183 patients and concluded that the MIE procedure was superior in comparison to the open technique with more advantages regarding the intraoperative and postoperative outcomes. They have reported a statistically significant difference regarding the blood loss (182.6±78.3 versus 261.4±87.2 mL, P<0.001), hospital stay (13.9±7.5 versus 17.1±10.2 days, P=0.017), overall surgical morbidity (25.5% versus 46.1%, P=0.004), and rate of pulmonary and cardiac complication (9.6% versus 27.0%, P=0.002; 4.1% versus 12.4%, P=0.046) between MIE group and open esophagectomy; however, there was no difference observed between the groups regarding the survival period [6].

Neoadjuvant therapy has become one of the main components of managing locally advanced esophageal cancer. Tabias [22] and colleagues have conducted a study to evaluate the outcomes of open and minimally invasive Ivor Lewis esophagectomy after neoadjuvant therapy.

Their results showed that patients who received MIE procedures have significantly shorter median ICU stay (p=0.002) and shorter hospital stay (p<0.0001), which are nearly similar to our study results [22]. They have also found that respiratory complications were significantly reduced in MIE patients (8.9% versus 29.7%, p=0.004). Regarding the anastomotic leakage, there was no difference between both groups (open: 1.4% versus MIE:0%, p=1.0), which was compatible with our study results. Also, they have found no significant difference between both groups regarding mortality at 30 days and 90 days (p= 0.506 and p= 0.634, respectively).

The five years overall survival rates were similar between both groups (open: 61% versus MIE: 50%, p= 0.933) [22].

Luketich [23] and the working group also evaluated the outcome of minimally invasive esophagectomy in 222 patients in a single institution with extensive open and minimally invasive esophagectomies experience. They concluded that MIE results were comparable to the open technique or even better as they found decreased mortality rates and shorter hospital stay than most of the open esophagectomy series [23].

Luketich [13] and colleagues conducted another multicenter prospective group study to evaluate the feasibility of minimally invasive esophagectomy, and they concluded that MIE was a safe and feasible procedure with low perioperative morbidity and mortality with good oncologic results. The estimated 3-year overall survival was 58.4%, and locoregional recurrence was observed in 6.7% of the study group [13].

Sihag [20] and their group established a comparative study between open versus minimally invasive Ivor Lewis esophagectomy regarding the perioperative outcomes in a single high-volume center [20]. The results of this study were very close to our study results as they concluded that minimally invasive esophagectomy

led to a significant reduction in postoperative pulmonary complications [20].

The non-fasting tubeless MIE could be a better procedure for esophageal cancer patients in terms of reducing morbidity and a better economic procedure that could reduce the financial costs as the hospital stay and ICU stay period was significantly reduced; this could be better evaluated in future multicenter studies [15].

Most of the experienced centers worldwide have adopted the MIE as the routine approach for esophagectomy for esophageal cancer patients due to its great advantages over the open technique [8].

MIE with early oral feeding after surgery and a single mediastinal drainage tube may provide new hope for esophageal cancer patients seeking minimally invasive surgery with less postoperative morbidity, a shorter hospital stay, and improved quality of life [8,13].

Study limitations

The selection bias was one of the main limitations that could not be avoided entirely during the surgical procedure selection for the study groups. Its effect on the assignment of the study group was unavoidable.

Another important limitation was the short follow-up period for the patients after the surgical procedure (3 months). This affected the study regarding some important variables, including the tumor recurrence on a long follow-up period and overall survival.

Conclusion

Minimally invasive esophagectomy may be a safe and feasible procedure for patients with early-stage esophageal cancer or locally advanced neoplasms who have received neoadjuvant therapy. Furthermore, compared to open esophagectomy, MIE may be associated with less operative blood loss and more resected lymph nodes.

Compared to open esophagectomy, MIE significantly reduced postoperative complications, including pulmonary complications. Furthermore, the MIE group's postoperative hospital stay was significantly shorter compared to the open esophagectomy group.

Conflict of interest: Authors declare no conflict of interest.

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