Efficacy of thoracoscopically assisted en bloc esophagectomy

Ahmed M. Zidan[a], Waheed Y. Gareer[b], Mohamed Gamil[b], Sherif A. Aziz[b]

[a]Department of General Surgery, Faculty of Medicine, Benha University, Benha, [b]Department of Oncology Surgery, National Cancer Institute, Cairo, Egypt

Correspondence to: Ahmed M. Zidan, MD, Fareed Nada Street, Benha 13518, Egypt
Tel: +01227416535;
e-mail: dr.ahmedzidan@gmail.com

Received: 08 April 2022
Revised: 05 May 2022
Accepted: 12 May 2022
Published: 04 January 2023

The Egyptian Journal of Surgery 2023, 41:756–764

Background
Appropriate use of minimally invasive surgery for patients with cancer is essential. Thoracoscopically assisted en bloc esophagectomy affects early perioperative morbidity, length of hospital stay, pain management, and quality-of-life issues. The aim of this study was to evaluate the feasibility and outcomes of combined thoracoscopic, abdominal, and cervical esophagectomy for the treatment of malignant esophageal tumors.
Patients and methods
The current prospective study included 23 patients with stages I and II esophageal carcinoma who were eligible for thoracoscopically assisted en bloc esophagectomy. Intraoperative and postoperative complications were reported along with pathological safety.
Results
The mean age of the included patients was 62 ± 5.05 years. The surgical outcome showed intraoperative complications like arrhythmia in 13% of patients and bronchial injury in 4.3% and postoperative gastroesophageal fistula in 13% of patients, whereas pulmonary complications were reported in 17.2% of patients. The pathological outcome showed free longitudinal safety margin, with mean positive lymph nodes of 6.1 ± 4.48 out of 17.2 ± 5.9 lymph nodes.
Conclusion
Thoracoscopic esophagectomy is technically feasible and safe, with low morbidity and shorter hospital stay compared with open procedure. It has the potential to replace open esophagectomy in selected patients.

Keywords:
esophageal carcinoma, esophagectomy, thoracoscopic

Egyptian J Surgery 2023, 41:756–764

1110-1121

Introduction

Perhaps there is no more important issue in the care of surgical patients than the appropriate use of minimally invasive surgery (MIS) for patients with cancer. An important advancement in surgical technique has affected early perioperative morbidity, length of hospital stay, pain management, and quality of life issues, as clearly proved with MIS [1].

Beginning with the widespread introduction of laparoscopic cholecystectomy in late 1989, esophageal surgeons have increasingly incorporated MIS into their practice since the first laparoscopic fundoplication was described in 1991; as confidence with laparoscopic surgery of the esophagogastric junction grew, trials were attempted with hybrid operations combining traditional open surgery with minimally invasive approaches. Subsequently, a totally laparoscopic transhiatal approach was described; however, this approach was perceived to be very challenging and has not gained widespread acceptance and is considered as a palliative operation [2,3].

Laparoscopic transhiatal mobilization of the esophagus offers suboptimal visualization of important periesophageal structures, including the inferior pulmonary vein and the left mainstem bronchus. Moreover, decreased visibility hindered homeostatic division of periesophageal vessels and negatively impacted the completeness of the mediastinal lymph node dissection, and these problems are further exacerbated in taller patients [4].

Thoracoscopic approach provides a complete scopic excellent exposure of the mediastinal structures and lymph node dissection. The benefit of respiratory morbidity remains to be studied in a large number of patients. Minimizing the chest wall injury contributed to the reduction of constrictive pulmonary damage [5].

Moreover, sufficient experience is necessary to master the learning curve, to be of the same quality as open surgery and be performed in a feasible time period [6].

Herbella and Patti [7] stated that the available literature on minimally invasive esophagectomy is still crowded with heterogeneous studies with different techniques; no controlled or randomized trials and the few retrospective comparative cohort studies are limited by small numbers of patients and biased by historical controls of open surgery [7].

The satisfactory outcome will only be obtained in centers performing a sufficient volume of esophageal surgery that provides the surgeons with opportunities to refine their necessary skills [5].

Moreover, the survival of patients with stages I and II disease is satisfactory, but further investigation is necessary [8].

The aforementioned gray areas have motivated the authors to conduct this study to evaluate the efficacy of thoracoscopically assisted en bloc esophagectomy.

Patients and methods

Study design and patients

The current prospective study was conducted following the ethical prospective of the World Medical Association Declaration of Helsinki where ethical approval was obtained from ethical and research committees, National Cancer Institute.

The current study was conducted at the Surgery Department, National Cancer Institute, throughout the period from January 2013 till May 2017.

The present study included 23 patients with stages I and II esophageal carcinoma who were eligible for thoracoscopically assisted en bloc esophagectomy.

Exclusion criteria included patients with preexisting lung disease (COPD and asthma); patients with cardiac, hepatic, or renal insufficiency; patients with advanced tumors; and patients who underwent neoadjuvant chemotherapy or previous thoracic or esophageal surgery.

A written informed consent was obtained from all included patients in the study after complete information.

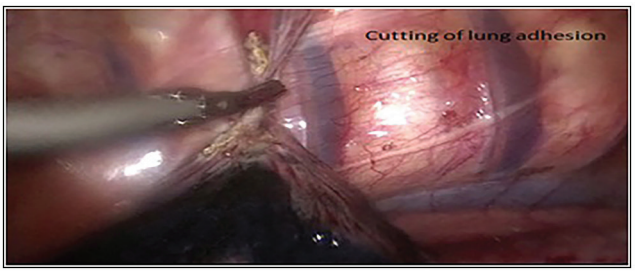
Eligible patients in this study underwent a detailed medical history and clinical examination, preoperative laboratory tests (e.g. liver, kidney, ECG, ECHO, and pulmonary function tests when needed), and were clinically staged by endoscopy, biopsy and pathology, computed tomography abdomen and pelvis, and computed tomography pulmonary angiography.

Preoperatively, improvement of the patients' nutritional status and good hydration were mandatory. The procedure was done under general anesthesia, which was induced with propofol and rocuronium and maintained with sevoflurane inhalation and intermittent injection of rocuronium or cisatracurium.

Procedure

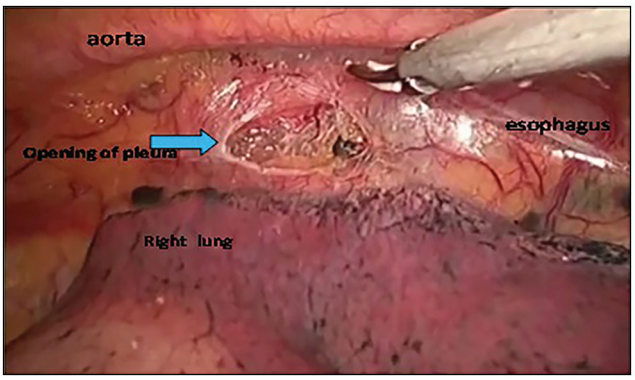
Using a (30°) telescope and HD camera (Storz), exploration of the chest cavity was done (Fig 1), followed by the release of any adhesions present, delineation of the anatomy inside the chest, and localization of the tumor site. Dissection was started by freeing the inferior pulmonary ligament then incision of the parietal pleura overlying the aorta (Fig 2) (between the aorta and azygos vein) and exposure the aorta as maximum as possible and sweeping all the lymphovascular and fatty tissue from the aortic side to the esophageal side starting from downward to upward till reaching the arch of the azygos vein. Individual small esophageal branches from the front of the aorta were secured and divided using a Harmonic scalpel or diathermy. Dissection was continued smoothly following the tissue planes with traction and

Figure 1



Exploration of the chest cavity.

Figure 2

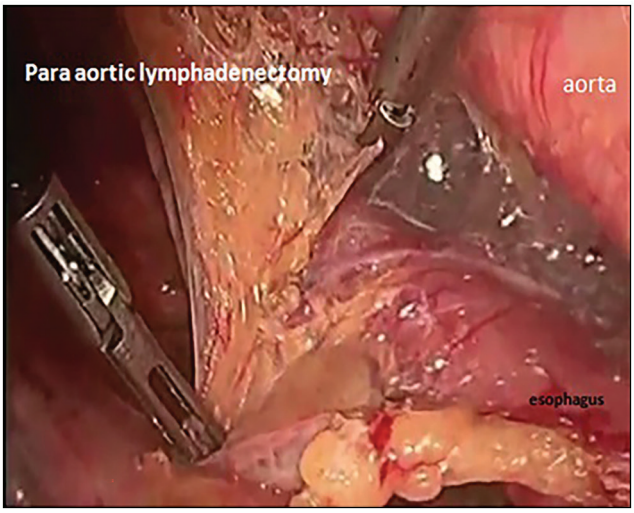


Cutting of visceral pleura.

countertraction. Any large lymphatic vessels between esophagus and aorta were clipped to avoid lymphatic leakage and subsequent chylothorax including the thoracic duct. Esophagus and all surrounding (lymphovascular and fatty tissue) para-esophageal and the covering visceral pleura, including the vessels from the aorta to the esophagus, were dissected in package till reaching the depth (plane) to the left side of the pleura and left main bronchus. Then, we started to divide the visceral pleura from the right side between esophagus and pericardium till reaching the carina, keeping the pleura attached to the esophagus, and along this side, no named vessels will be present. With an elevation of the esophagus and its related lymph nodes, carinal lymph nodes appeared and were dissected cautiously and removed in a block with the esophagus (Fig 3). The plane between the esophagus and pericardium was dissected carefully keeping in mind that inferior pulmonary vein will be encountered at a certain point. Vagus nerve trunk was cut at least 1/2 cm below the lower edge of the right main bronchus to avoid damage to the pulmonary vagal nerves and the membranous part of the right bronchus. With the forward mobilization of the esophagus and related lymphatics, membranous part of the trachea appears and it is easily separated from the esophagus till its left side (Fig 4). Mobilization of the esophagus in the left side was carried out where the arch of the azygos vein was dissected cautiously from the esophagus or it is better to be divided (Figs 5 and 6), and then division of the pleura around the esophagus from the right side between it and superior vena cava and from the left side between the esophagus and the chest wall was done. During dissection in the upper third of the esophagus, the right recurrent laryngeal nerve was identified just below the subclavian artery and we trace it to the side of the trachea and remove the lymph node around it carefully. Moreover, on the left side, we started to search for identification of the left recurrent laryngeal nerve. Before removal of its lymph node was more difficult than the right side. Lymph nodes were dissected as maximum as possible till the thoracic inlet (Figs 7 and 8).

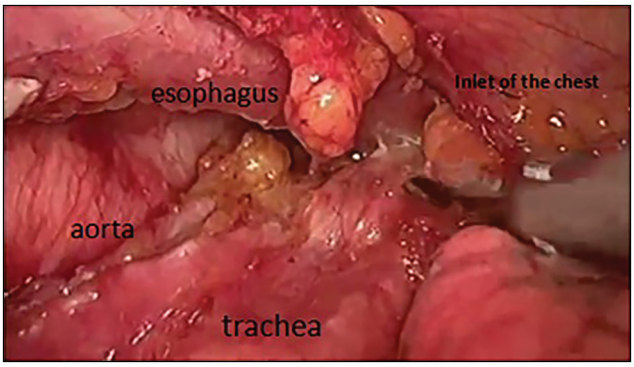
Lower part of the esophagus is the last to be dissected from the diaphragm and pleura and leave the

Figure 3



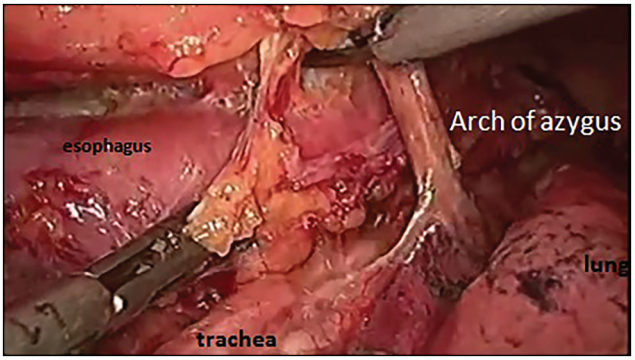
Dissection of periesophageal nodes.

Figure 4



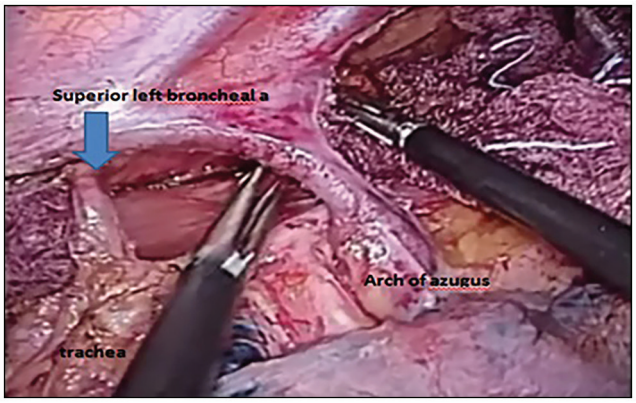
Mobilization of esophagus from trachea.

Figure 5



Mobilization of arch of azygos.

Figure 6



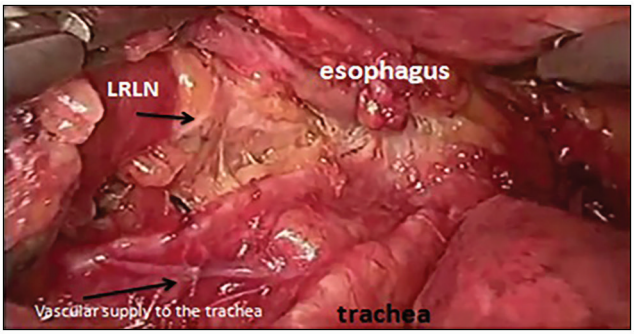
Preservation of arch of azygos and bronchial artery.

peritoneum below the diaphragm intact till the end of the dissection, which is easily and completely done from the abdominal side. After ensuring complete mobilization of the esophagus and its related lymph nodes and complete homeostasis, a chest tube was placed under direct vision in the 7th intercostals space. Port sites were closed. The patient was returned to the supine position carefully for completion of the operation.

The second stage is the formation of the gastric tube and abdominal lymph node dissection, which was done via laparoscopy or laparotomy.

The third stage is gastric pull-up and anastomosis between the esophagus and gastric tube via a cervical incision, and in some patients, deep cervical lymph node dissection was done.

Figure 7



Dissection of the left recurrent laryngeal nerve and nodes.

Evaluation and follow-up: all included patients were admitted to the ICU postoperatively and then in a few days, the patients were transferred to the ward and follow-up was planned for 6 months for postoperative complications and the pathological outcome.

Outcomes

The primary outcome was successful en block esophagectomy via thoracoscopic assisted technique with minimal intraoperative complications, operative time, and intraoperative blood loss together with free surgical margins.

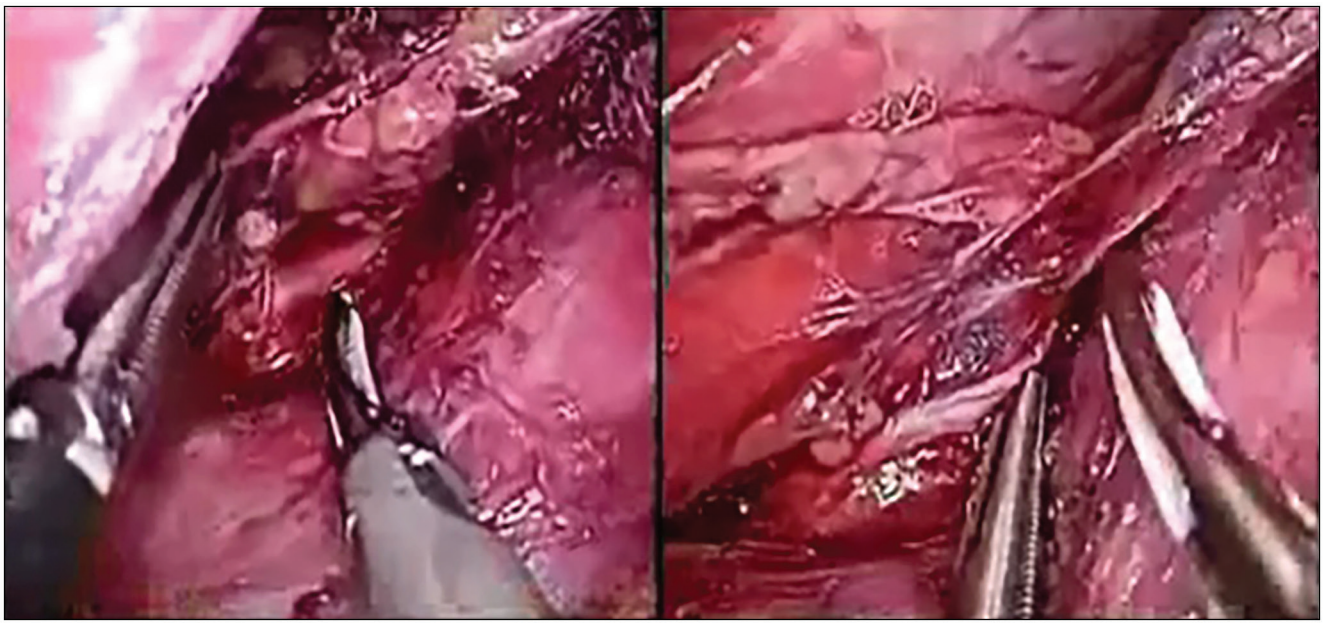
The secodary outcome was decrease in the postoperative complications.

Statistical analysis

The sample size was calculated depending on the incidence of intraoperative and postoperative complications, which were the main outcomes of this study, and 6-month follow-up, with incidence of 10% loss in follow-up.

The collected data were summarized in terms of mean±SD, median, and range for quantitative data and frequency and percentage for qualitative data. Comparisons between the different study groups were carried out using the Fisher exact test to compare proportions. The Mann–Whitney test and the Kruskal–Wallis test were used to compare two and more than two groups regarding nonparametric data. Spearman correlation coefficient (ρ) was used to test for the correlation between the estimated parameters.

Figure 8



Dissection of the right recurrent laryngeal nerve and nodes.

Statistical significance was accepted at *P* value less than 0.05. A *P* value less than 0.001 was considered highly significant, whereas a *P* value more than 0.05 was considered nonsignificant. The statistical analysis was conducted using STATA/SE version 11.2 for Windows (STATA Corporation, College Station, Texas, USA).

Results

The current study included 23 patients, comprising 18 (78.3%) males and five (21.7%) females, who were eligible for thoracoscopically assisted en bloc esophagectomy. Their mean age was 62 ± 5.05 years. Other sociodemographic data and patients' comorbidities are illustrated in Table 1.

Table 1 Sociodemographic data and patients' comorbidities

Patient characteristics	
Age	
Mean±SD	62 ± 5.05 years
Sex [*n* (%)]	
Male	18 (78.3)
Female	5 (21.7)
Smoker	
n (%)	13 (56.6)
Ex-smoker	
n (%)	2 (8.6)
Nonsmoker	
n (%)	8 (34.8)
Hypertension	
n (%)	7 (30.43)
DM	
n (%)	2 (8.6)

DM, diabetes mellitus.

Table 2 Operative data and intraoperative and postoperative complications

Operative details	
Time (min) (mean±SD)	190 ± 37.49
Blood loss (ml) (mean±SD)	74.59 ± 177.8
Amounts of blood transfusion (mean±SD)	0
Intraoperative complications	
Intraoperative arrhythmia [*n* (%)]	3 (13)
Bronchial injury [*n* (%)]	1 (4.3)
Hospital stay	
1CU(days) (mean±SD)	3.48 ± 1.68
Total hospital stay (days) (mean±SD)	11.96 ± 3.59
Postoperative complications	
Recurrent laryngeal nerve palsy [*n* (%)]	2 (8.6)
Gastroesophageal fistula [*n* (%)]	3 (13)
Delayed gastric emptying [*n* (%)]	2 (8.6)
Pleural effusion/chylothorax [*n* (%)]	2 (8.6)
Pulmonary complications [*n* (%)]	4 (17.1)
30-day mortality [*n* (%)]	1 (4.3)

The mean operative time was 190 min (range, 130–300 min). Prolonged time was observed in patient who developed intraoperative arrhythmia (three cases), where time was needed for its control. The mean amount of blood loss was 177.8 ml (Table 2). Recurrent laryngeal nerve injury was reported in 8.6% of cases, and gastroesophageal fistula was reported in 13% of cases. Other operative data and postoperative complications are shown in Table 2.

Pathological assessment of the specimen revealed 30.4% well-differentiated carcinoma, 30.4% moderately differentiated carcinoma, whereas poorly differentiated carcinoma were reported in 39.25% of cases. The mean number of positive lymph nodes was 6.1 out of a mean total of 17.2 lymph nodes. The radial safety margin was obtained in 95.7% of cases, whereas longitudinal safety margin was obtained in 100% of cases. Other tumor characteristics are reported in Table 3. There was no statistically significant correlation between the tumor site or the tumor size and the operative time, intraoperative complications, or even intraoperative complications (Tables 4 and 5).

Discussion

Multiple studies [9–11] reported that transthoracic esophagectomy is traditionally associated with thoracotomy morbidity and its complications, although it provides adequate exposure for mediastinal lymphadenectomy. Video-surgery has been employed to reduce this morbidity, to provide a suitable pathway

Table 3 Pathology results of the resected tumor

Tumor site	
Upper 1/3 [*n* (%)]	3 (13)
Middle 1/3 [*n* (%)]	10 (43.5)
Lower 1/3 [*n* (%)]	5 (21.7)
GE junction [*n* (%)]	5 (21.7)
Differentiation [*n* (%)]	
Well	7 (30.4)
Moderate	7 (30.4)
Poor	9 (39.2)
Tumor stage [*n* (%)]	
T2	7 (30.4)
T2,3	3 (13)
T3	13 (56.5)
Tumor diameter (cm) (mean±SD)	3.27 ± 0.89
Number of positive lymph nodes (mean±SD)	6.1 ± 4.48
Number of total lymph nodes (mean±SD)	17.2 ± 5.9
Safety margin	
Radial margin [*n* (%)]	
Positive	1 (4.3)
Negative	22 (95.7)
Free longitudinal margin (cm)	
Proximal (mean±SD)	18.2 ± 2.44
Distal (mean±SD)	5.9 ± 1.12

Table 4 Correlation between the site of the tumor and complications

Variable (*N*=23)	GEJ (*N*=5) [*n* (%)]	Lower third (*N*=5) [*n* (%)]	Middle third (*N*=10) [*n* (%)]	Upper third (*N*=3) [*n* (%)]	Test	*P*
Time (min)						
Mean±SD	176±48.78	189±24.08	202.22±44.38	190±17.32	KW=1.17	0.76
Blood loss (ml)						
Mean±SD	140±41.83	182.5±23.63	213±94.99	116.67±28.87	KW=5.95	0.11
Intraoperative arrhythmia						
Yes	1 (10.0)	0	2 (20.0)	0	FET	0.86
Injury/bleeding						
Yes	0	0	1[a] (10.0)	0	FET	1.00
ICU stay (days)						
Mean±SD	3±0.71	3.4±1.14	4.1±2.23	2.33±0.58	KW=4.25	0.19
Total hospital stay (days)						
Mean±SD	11.4±5.18	11.6±2.07	12.4±4.03	12±2	KW=0.94	0.81
RLN palsy (hoarseness)						
Yes	0	0	3 (30.0)	0	FET	0.36
Fistula						
Yes	0	0	3 (30.0)	0	FET	0.36
Delayed gastric emptying						
Yes	0	0	2 (20.0)	0	FET	0.60
Pleural effusion/chylothorax						
Yes	0	0	2 (20.0)	0	FET	0.60
Pulmonary complication						
Yes[b]	0	1 (20.0)	3 (30.0)	0	FET	0.64
30-day mortality						
Yes	0	0	1 (10.0)	0	FET	1.00

[a]Left bronchial injury.
[b]Two cases of bronchitis, one case of lung collapse and pneumonia, and one case of mild pulmonary infection.
[c]Death after 2 weeks from respiratory failure.
FET, Fisher exact test; KW, Kruskal–Wallis; RLN, recurrent laryngeal nerve.

Table 5 Correlation between the stage of the tumor and complications

Variable (*N*=23)	Stage T2 (*N*=6) [*n* (%)]	Stage T2–T3 (*N*=3) [*n* (%)]	Stage T3 (*N*=14) [*n* (%)]	Test	*P*
Time (min)					
Mean±SD	191.67±13.29	201.67±12.58	189.23±49.07	KW=1.47	0.48
Blood loss (ml)					
Mean±SD)	170±83.67	166.67±28.87	182.86±83.98	KW=0.13	0.94
Intraoperative arrhythmia					
Yes	1 (16.67)	0	2 (14.29)	FET	1.00
Injury/bleeding					
Yes	0	0	1[a] (7.14)	FET	1.00
ICU stay (days)					
Mean±SD	3±0.89	3±1.73	3.78±1.93	KW=1.29	0.52
Total hospital stay (days)					
Mean±SD	10.5±2.17	11.67±1.53	12.64±4.25	KW=1.28	0.53
RLN palsy (hoarseness)					
Yes	1 (16.67)	1 (33.33)	1 (7.14)	FET	0.33
Fistula					
Yes	1 (16.67)	0	2 (14.29)	FET	1.00
Delayed gastric emptying					
Yes	1 (16.67)	0	1 (7.14)	FET	0.64
Pleural effusion/chylothorax					
Yes	0	0	2 (14.29)	FET	1.00
Pulmonary complication					
Yes	1 (16.67)	1 (33.33)	2 (14.29)	FET	0.75
30-day mortality					
Yes	0	0	1[c] (7.14)	FET	1.00
No	6 (100.0)	3 (100.0)	13 (92.86)		

[a]Left bronchial injury.
[b]Two cases of bronchitis, one case of lung collapse and pneumonia, and one case of mild pulmonary infection.
[c]Death after 2 weeks from respiratory failure.
FET, Fisher exact test; MW, KW, Kruskal–Wallis; RLN, recurrent laryngeal nerve.

for complete mediastinal lymphadenectomy, to reduce postoperative pain, and to provide a surgical specimen containing all periesophageal lymphoadiposal tissue and thoracic duct [12,13].

The operative time in the current study ranged from 130 to 300 min which matched the results of Yiabulayin *et al*. [14] and other studies [15–17], which reviewed the outcomes of the minimal invasive esophagectomy (MIE) and open approach for esophageal cancer and reported that MIE lasted longer than the open surgery.

The mean amount of blood loss reported in the current study was 177.8 ± 74.59, which is less than esophageal the amount reported by Zingg *et al*. [17], which was 320 ml, and this is assumed to the use of modern energy sources with proper hemostasis.

As reported by Yiabulayin *et al*. [14], arrhythmia is a common intraoperative complication during esophagectomy, with incidence up to 44%, especially in open esophagectomy. Arrhythmia may result from compression and anterior displacement of the heart during dissection, which will interfere with the cardiac filling. Moreover, this dissection will cause vagal stimulation, resulting in ventricular escape beats, bradycardia, or even cardiac arrest [18]. The incidence of arrhythmia was much less in the current study, as it was reported in only three (13%) cases, which were managed successfully intraoperative, and this may be owing to thoracoscopic magnification and careful manipulation and dissection in thoracoscopic esophagectomy.

Although bronchial injury was reported in only one (4.3%) case in the current study, this was higher than the results of Hulscher *et al.* [19], who reported that the rates were 1.8% during transhiatal esophagectomy and 0.8% during transthoracic esophagectomy. Moreover, the incidence was higher than Gupta *et al.* [20], who reported the incidences to be 1.3% (five patients from 382); laceration was detected intraoperatively. This higher percentage is assumed to be due to the small sample size of the current study.

Successful transthoracic esophagectomy without conversion to thoracotomy was done in all cases included in this study, and this was less than Braghetto *et al.* [21], where there was 1.44% conversion to thoracotomy, and Luketich *et al.* [22], who reported that thoracotomy was required in 5.4% of patients. This is assumed to be owing to proper selectin of the patients included in this study, where locally advanced cases were not included in the current study, and also owing to uses of modern energy sources for proper control of bleeding intraoperative during the careful dissection.

As reported by Natsugoe *et al*. [23] and Dexter *et al*. [24], the incidence of recurrent laryngeal nerve (RLN) injury reported varies from 14 to 45.3% in open thoracotomy and from 2.6 to 36% in the thoracoscopic. In the current study, only two (8.6%) patients developed hoarseness. The reason for this low number could be due to routine proper exposure, skilled technique, and the use of an ultrasonic scalpel. This was similar to the reports of Yiabulayin *et al.* [14] who studied 51 patients from 2010 to 2015, and one patient developed RLN palsy.

The mean hospital stay was 11.96 days and ICU stay was 3.48 days in the current study. This matched with Nagpal *et al.* [25], who studied a total of 672 patients for MIE where the mean hospital stay was 11.34 days and Natsuko ICU stay 3.32 days.

The reported pulmonary complications in this study occurred in 17.2% ranging from pneumonia with mild pleural effusion, which was treated conservatively with repeated aspiration of the pleural effusion, to severe bilateral bronchopneumonia needing ventilatory support. Persistent partial lung collapse on the right side of the chest after removal of the chest tube was reported, which was treated conservatively without the need of chest tube, and it was resolved over 6 weeks. This matched with the results of Fabian *et al*. [12] and also Yiabulayin *et al.* [14], who conducted a meta-analysis of 50 studies that included 14 781 cases and reported pulmonary complication rate at 17.1% (813/4761). However, Pennathur *et al.* [26] reported a low incidence (8%) of perioperative pneumonia.

Anastomotic leakage is an important complication that leads to significant morbidity and adversely increases pulmonary complications. In the current study, three (13%) cases developed leakage from the cervical wound that appeared on the fifth and seventh day postoperatively, where in two patients, wound discharge pus mixed with saliva was seen, and the third patient had a neck abscess and was drained by local anesthesia. All patients were managed conservatively in the form of local wound care and clear oral fluids till discharge became minimal and then a semisolid food was allowed till fistula completely closed by the end of third week. One patient needed more supportive therapy in the form of total parenteral nutrition for 7–10 days. These results matched the results of Zhou *et al.* [27], who conducted a large systematic review and meta-analysis study including 43 studies involving 5537 patients, and the occurrence of leakage ranged from 4 to 17%. The prevention of this leakage appears quite important in clinical research. Anastomotic

technical errors and occult ischemia of the mobilized gastric fundus were regarded as the two major causes in the etiology of anastomotic leakage.

Following the updated clinical practice guidelines in treatment of esophageal carcinoma, lymph node staging is crucial for optimum oncological resection. The recommended number of lymph nodes is 12 according to the 7th edition of AJCC, Hou *et al.* [28], and other studies [29,30]. These guidelines were followed in the current study where the mean lymph node sampling was 17.2 lymph nodes. This was similar to a retrospective review of 603 patients by Wu *et al*. [31], who showed that patients with negative lymph node count more than or equal to 14 had better survival. So, we believe that via thoracoscopy, owing to its high magnification and better visualization of mediastinal structures, we can remove more lymph nodes easily and effectively.

The radial margin was positive in only one (4.3%) case, and this was much less than that reported by Gilbert *et al*. [32], who reported an incidence of 19%, and this is assumed to be owing to inclusion of locally advanced tumors in their studies. Moreover, the current results matched with Li *et al*. [33], who reported that the R0 tumor resection rate was 95.9% and positive margin was 4.1%. The longitudinal safety margin was negative in all cases following the recent clinical practice guidelines.

Conclusion

According to the current results, thoracoscopic esophagectomy is technically feasible and safe, with low morbidity and shorter hospital stay compared with open procedure. It has the potential to replace open esophagectomy in selected patients.

Recommendations

Further studies should be carried out with a large sample size to detect factors involved in anastomotic leak after esophagectomy and how to prevent them.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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