

Operative Complications of Minimally Invasive Esophagectomy in Patients with Esophageal Cancer: Analysis of 80 Cases

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ARTICLEINFO	A B S T R A C T	
Article type: Original Article	 Introduction: Esophageal cancer (EC) is a common cancer of the digestive system which is one of the most common cancers in our country The primary treatment of EC is surgery. Due to the development of minimally invasive techniques (MIE), in the current study, we have assessed the results of these techniques in patients with EC surgery. Methods: A total of 80 patients with middle and lower third ECs who had good 	
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Keywords: Esophageal Neoplasms Esophagectomy Gastrointestinal Neoplasms McKeown	 conditions and were operated with MIE technique (McKeown) from 2014 to 2021, were enrolled in this study. Patients were evaluated based on the following criteria: age, sex, tumor location, pathology, peri-operative complications leading the minimally invasive esophagectomy technique to being converted to an open surgery, and early post-operative complications after surgery and mortality . Results: A total of 80 patients with EC were enrolled in the study. 85% (n=68) of our patients were male and 15% (n=12) were female with an average age of 58.21±11.39 years old. 43.75% of the patients had a history of neo-adjuvant chemotherapy. Surgery was performed with McKeown technique without complications in 91.25% of the patients. In 8.75% of the patients tracheal injury (n=1), uncontrolled bleeding (n=1), and severe pleural adhesions (n=5) led the surgery plan changing into open surgery. Post-operative complications were observed in 13.75% of patients. Conclusions: This study suggests using McKeown technique in patients with EC in highly experienced medical centers in order to obtain proper results with low rate of peri- and post-operative complications. 	

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Introduction

Esophageal cancer (EC), as one of the most fatal and common cancers which causes a huge burden (1). In the past two decades, the global incidence of EC has increased around 50%. More than 482300 new cases are diagnosed with EC each year and the mortality rate is reported to be 84.3% (2, 3). EC has poor prognosis with a 5-year survival of 18% in developed countries and only half of the patients have loco-regional tumors at the time of diagnosis (4).

Although the only method for treating EC patients has been surgical resection with or without chemotherapy, the traditional open esophagectomy accompanies a high rate of complications and significant mortality and morbidity rates (5). Previous studies have shown open esophagectomy can potentially cause a rate of in-hospital mortality as high as 29% (6-8). Therefore, minimally invasive esophagectomy (MIE) has been used increasingly in the past decade (9).

MIE consists of several surgical approaches laparoscopic-thoracoscopic including McKeown or the laparoscopic-thoracoscopic Ivor Lewis procedures. Previous studies have shown lesser morbidity and mortality in EC patients who have underwent MIE. Moreover, cardiovascular and respiratory complications in patients who underwent MIE were lower than open esophagectomy, while the operation time was significantly higher in patients who underwent MIE (10, 11). Additionally, it has been reported that patients who were treated with MIE have a higher quality of life, lesser pain and constipation in 2 years after surgery (12). The goal of MIE is to maintain the effectiveness of traditional esophagectomy and reduce perioperative complications (13). Nonetheless. there are still some controversies about MIE benefits. Example given, recent studies have discovered both lower and higher odd ratios of anastomosis leakage after MIE surgery, although none of them were significant (14, 15). While most of the recent studies have been focusing on post-operation complications, the present study aims to assess the MIE technique and evaluate the peri- and post-operative complications of MIE in patients with EC.

Materials and Methods

Study Design

This prospective observational study was conducted in Ghaem Hospital, Mashhad, Iran and included patients who were candidates for MIE surgery at the Department of thoracic surgery. A total of 80 patients were enrolled in this study between 2014 and 2021 after obtaining informed consent. All patients have carried out a complete staging workup before the surgery containing barium swallow, endoscopic ultrasound, esophagoscopy, bronchoscopy, and computed tomography of the chest, abdomen, and pelvis. Patients' medical records were reviewed to obtain the following data: age, sex, tumor location, and tumor pathology. Intraoperative complications changed surgery procedure from minimally invasive esophagectomy technique to surgery. These open complications include tracheal injury, uncontrolled bleeding, severe pleural adhesions, as well as, early post-operative complications, and mortality. All esophagectomy candidates had resectable EC located in the lower or middle part of the esophagus. All the surgical procedures were operated by a single thoracic surgeon. This study was approved by the Ethics committee of Mashhad University of Medical Sciences according to the declaration of Helsinki.

Eligibility Criteria

The criteria for inclusion were patients with middle or lower EC, resectable tumor, and patients with good tolerance for surgery. Exclusion criteria were including cervical esophageal or other cancers, severe malnutrition state (albumin < 3 g/dL), patients with distant metastasis, or unwillingness to undergo the surgery.

Operative Technique

MIE was performed in the left lateral decubitus position. The technique includes double lumen ventilation without gas insufflation; 4 Port [8 intercostal space in ASIS= Camera, 5 Intercostal space (anterior axillary & posterior axillary), 8 intercostal space in posterior axillary= Cuttery], GIA Endostapler, Esophagolysis & mediastinal lymphadenectomy with video-assisted thoracoscopic surgerv (VATS), Open abdominal approach for gastrolysis, Open

surgery approach for neck dissection, stomach used for conduit and esophagogastric anastomosis performed by hand in the neck.

Patients' care after surgery

Feeding jejunostomy was performed after the surgery was done and before admitting the patients to intensive care units (ICU). The patients were moved to the general surgical ward after one day surveillance in ICU. In order to prevent post-surgical complications, the patients were encouraged to regain early mobilization on the first day of surgery. One day after surgery, enteral feeding with jejunostomy catheter was started. The Patients were discharged after tolerating the normal diet and starting to move.

Statistical Analysis

Percentages and mean±standard deviation were used for categorical and continuous variables respectively. All analysis was performed by using SPSS software (version 26).

Results

A total of 80 patients who underwent MIE were enrolled in this study from 2014 until 2021. Table 1 shows the summary of patients' characteristics. The mean age of patients was

58.21±11.39 years and 85% (n=68) of patients were male and 15% (n=12) were female. Endoscopic investigation revealed that esophageal tumors were located in the middle part of esophagus in 65 patients while 15 patients had lower esophageal tumor (1/3)distal esophagus). of In pathologic examination. 86.25% of patients had squamous cell carcinoma and 13.75% of patients had adenocarcinoma tumors. Prior history of neo-adjuvant chemotherapy was reported in 43.75% of patients (Table 1).

MIE Surgery was successfully performed in 91.25% the patients without of complications. The MIE surgery was converted to open thoracotomy due to the following peri-operative complications in 8.75% of patients: tracheal injury (n=1), uncontrolled bleeding (n=1), and severe pleural adhesions (n=5).

Also, patients were carefully observed after surgery for early post-operative the complications. As shown in Table 2, 17.5% of post-operative patients experience complications including: Atelectasis (n=6), inferior MI (n=3), pulmonary (PTE) (n=1), thromboembolism and anastomosis leakage (n=4). Further analysis showed the mortality rate was 6.25% among patients due to respiratory insufficiency (n=3), PTE (n=1), and acute myocardial infarction (n=1).

Patients characteristics	Patients underwent MIE (n=80)			
Age (years)	58.21±11.39			
Gender				
Male	68(85%)			
Female	12(15%)			
Tumor location				
Middle esophageal	65(81.25%)			
Lower esophageal	15(18.75%)			
Pathologic finding				
SCC	69 (86.25%)			
AC	11(13.75%)			
Prior neo-adjuvant chemotherapy	35(43.75%)			

Table 1. Characteristics of patients underwent MIE .

Abbreviation : MIE: minimal invasive esophagectomy, SCC: squamous cell carcinoma, AC: adenocarcinoma.

Discussion

The primary therapy for EC is surgery. Recent studies showed traditional open esophagectomy is accompanied by high rates of morbidity and mortality (5). Hence, MIE has been introduced and implied over the past two decades which has resulted in decreased post-operative complications at referral centers (9). MIE consists of different approaches including McKeown or Ivor Lewis surgeries. The current study was designed to evaluate the peri- and post-operative complications of McKeown MIE in patients with EC.

The EC pathology may be the main factor that affects the selection of MIE approaches (16). Previous studies have shown that squamous cell carcinoma is more common in studies using McKeown surgery while adenocarcinoma is more prevalent in studies using Ivor Lewis surgery (17, 18). In the current study, 86.25% of patients had squamous cell carcinoma, therefore McKeown MIE was done in order to do adequate resection and lymph node dissection. In this study, the incidence of periand post-operative complications was 8.75% and 17.5% respectively.

In a study conducted by Luketich et al., on 222 patients who underwent McKeown MIE, the rate of major complications was 32% and the mortality rate was 1.4% (19). Anastomosis leakage as a common postoperative complication, is associated with high mortality and morbidity (7). It was stated that MIE and open esophagectomy have equal rates of anastomosis leakage, ranging from 0 to 12% (20). In this study, the incidence of anastomosis leakage was 5% among patients underwent McKeown surgery. Chowdappa et al, showed that the incidence of anastomosis leakage was 3.7% in the patients underwent MIE and 5.1% in the patients underwent open esophagectomy (21). A recent meta-analysis on 50 studies that reported post-operative anastomosis leakage, showed no difference between MIE and open esophagectomy (13). Also, different meta-analyses demonstrated both lower and higher odd ratios of anastomosis leakage in MIE technique in comparison with open esophagectomy but neither of them was statistically significant (14, 15, 22). As well, a study done by Walther et al. investigated the influence of anastomosis site on the anastomosis leakage rate (23). In this study, it was shown that the cervical and intrathoracic anastomosis have similar rates of anastomosis leakage. However, a metaanalysis performed by Marker et al., showed that cervical anastomosis has a higher rate of leakage in comparison to intrathoracic anastomosis (24).

Pulmonary and cardiac complications following esophagectomy can cause serious morbidity or even mortality. In the current study, the rate of pulmonary infection was 3.75% in patients who underwent MIE. In the first clinical randomized trial (TIME trial) comparing MIE and open esophagectomy, it was shown that the MIE has a significantly lower rate of pulmonary infection (25).

complications	Tatients under went Mill (n=00)			
Peri-operative complication				
Tracheal injury	1 (1.25%)			
Uncontrolled bleeding	1 (1.25%)			
Severe pleural adhesions	5 (6.25%)			
Post-operative complication				
Atelectasis	6 (7.50%)			
Inferior MI	3 (3.75%)			
PTE	1 (1.25%)			
Anastomosis leakage	4 (5%)			
Mortality	5 (6.25%)			

Table 2. Per	i- and post-operative complication i	n patients underwent MIE.
	complications	Patients underwent MIE (n=80)

Abbreviation: MIE: minimal invasive esophagectomy, MI: myocardial infraction, PTE: pulmonary thromboembolism.

Moreover, several studies stated that the incidence of pulmonary complications is significantly lower in patients underwent MIE (14, 15). The following reasons may provide possible explanations for the observed results: the lesser retraction of the lungs, lesser trauma to lung parenchyma during MIE, and the lower rate of chest wall muscles injury during MIE results in decreased post-operative and pain, improvement in the drainage of bronchial secretion (26). However, two recent studies suggested that MIE is followed by a higher rate of pulmonary infection in comparison to open esophagectomy (6, 27). This controversy may suggest the role of surgeon in selecting operation techniques on operative complications. It's notable that the learning curve of MIE is considerable in reducing operative complications. Van workum et al., designed a study to investigate the effect of learning curve in reducing operative complications. According to their results reducing the anastomosis leakage rate from 18.8% to 8% occurred in a period of 119 days (28).

Our study showed that the incidence of myocardial infarction and pulmonary thromboembolism were 3.75% and 1.25% after the MIE respectively. These results are in accordance with previous studies. Metaanalyses showed that the MIE has lesser cardiovascular complications such as heart failure, deep vein thrombosis, pulmonary thromboembolism, and arrhythmia (29,13).

Furthermore, our results showed that the incidence of peri-operative complications was 8.75% which includes severe pleural adhesions, uncontrolled blood loss, and tracheal injury. A meta-analysis done by Yibulayin et al., showed that there are less peri-operative complications in patients who underwent MIE (13).

The mortality rate of patients was 6.25% in the current study. Zhou et al., demonstrated that the patients who underwent MIE have reduced rates of in-hospital mortality in comparison to open esophagectomy (29). In this study, 43.75% of patients had neoadjuvant chemotherapy. Also, a large randomized controlled trial showed a significant 5-year survival improvement in patients with EC who experienced esophagectomy and neo-adjuvant therapy compared to esophagectomy alone (30).

The current study had several limitations including a small number of patients, an absence of control patients, and a short follow-up time. A large randomized clinical trial with a long follow-up period is needed to observe long-term complications and mortality rates.

Conclusion

This study suggests using of McKeown technique in patients with esophageal cancer, in highly experienced medical centers in order to obtain proper results with a low rate of peri- and post-operative complications.

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