


REVIEW

Selection of minimally invasive surgical approaches for treating esophageal cancer

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Funding information

This study was supported by the Ministry of Science and Technology (MOST 107-2314-B-002-248- MY3 and MOST 109-2314-B-002-273) and Esophageal Disease Education Foundation.

Abstract

Minimally invasive esophagectomy has gradually been accepted as an active treatment option for surgery of esophageal cancer. However, there is no consensus about how to perform the procedures in the thoracic and abdominal phase including anastomosis in the neck (McKeown) or chest (Ivor Lewis), VATS, robotic-assisted or reduced port approaches or various endoscopic abrasion techniques. Further studies to investigate the roles of these novel techniques are required to treat the various patient populations.

KEYWORDS

esophageal submucosal dissection, minimally invasive esophagectomy, photodynamic therapy (PDT), robotic surgery, VATS

INTRODUCTION

Esophageal cancer is one of the most important cancers threatening public health worldwide, with most cases occurring in Asian countries. According to the National Comprehensive Cancer Network (NCCN) Guidelines, esophagectomy remains the standard treatment for all stages of esophageal cancer (NCCN, version 2. 2021). However, esophagectomy remains a challenging surgery for surgeons with a high mortality rate ranging from 5%–10%¹ and surgery-related complications occurring in up to 50% of cases.² Because of the extensive surgical trauma sustained along the abdomen, chest, and neck, patients undergoing esophagectomy may experience systemic inflammatory response syndrome (SIRS), leading to complications such as infections, anastomotic leakage, and multiorgan failure.

During the last decade, important progress in esophagectomy was made in the form of introduction of minimally invasive esophagectomy (MIE). MIE utilizes thoracoscopy and laparoscopy for the thoracic and

abdominal phases of surgery, respectively, which minimizes the length of surgical incision when compared to that required in open surgery. The first large MIE case series conducted by Luketich et al. showed impressive low mortality and 30-day pneumonia rate in patients with MIE (mortality rate 1.4%, pneumonia rate 7.6%).³ Later in 2012, the first randomized control trial by Biere et al. demonstrated a decrease in pulmonary complications from 29% to 6% two weeks after MIE.⁴ The study became the cornerstone of the perioperative benefits of MIE. Several studies also showed advantages of MIE over open operation, including lower hospital stay,^{5,6} intraoperative blood loss,^{5,7,8} vocal cord palsy,⁹ and pulmonary complications.^{4,9,10} With regard to survival, MIE has an equivalent short- and long-term survival rate according to population-based studies and meta-analysis.^{5,11} In our experience in Taiwan, the application of MIE increased from around 50% in 2011 to more than 80% in 2016 in clinical practice for all stages of esophageal cancer (Figure 1). However, there are still several questions regarding MIE that need to be answered, which are related to the ideal location for anastomosis, robotic

Yu-Kwang Lee and Ke-Cheng Chen contributed equally to the manuscript.

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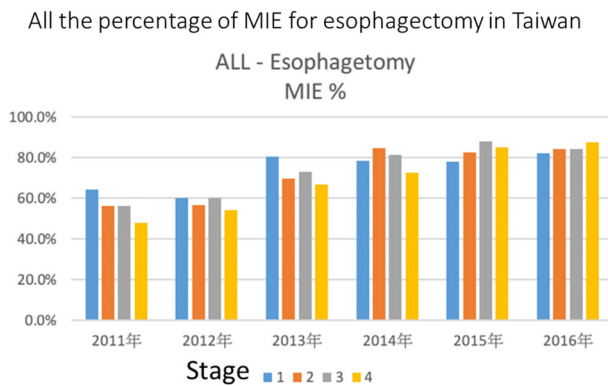


FIGURE 1 Data regarding the use of minimally invasive esophagectomy (MIE) in Taiwan from 2011 to 2016 obtained from the Taiwan National Cancer Registry

versus laparoscopic approach, and single-port versus multiport access selection.

Choosing anastomosis site: McKeown (cervical) versus Ivor Lewis (thoracic)

After esophagectomy, there is no consensus regarding the optimal method for esophagogastronomy, since anastomosis can be created in the cervical (McKeown) or intrathoracic region (Ivor Lewis). Most patients receive McKeown MIE,¹² in which the tumor is first removed via thoracoscopy, then gastric mobilization through laparoscopy, and finally left cervical esophagogastronomy through an incision at neck. For patients with lower third esophageal cancer, some surgeons perform Ivor Lewis esophagectomy in which the gastric conduit creation and abdominal lymphadenectomy is first performed through laparoscopy, and then thoracoscopic esophagogastronomy is performed. It is believed that McKeown MIE has potential advantages of less local recurrence compared to Ivor Lewis MIE, since it can achieve en bloc resection of lymph nodes from the abdomen, the chest, to the cervical area.^{12,13} Additionally, a previous study by D'Amico indicated that Ivor Lewis esophagectomy should not be applied to tumors at, or above, the level of the carina due to the risk of a positive esophageal surgical margin.¹³

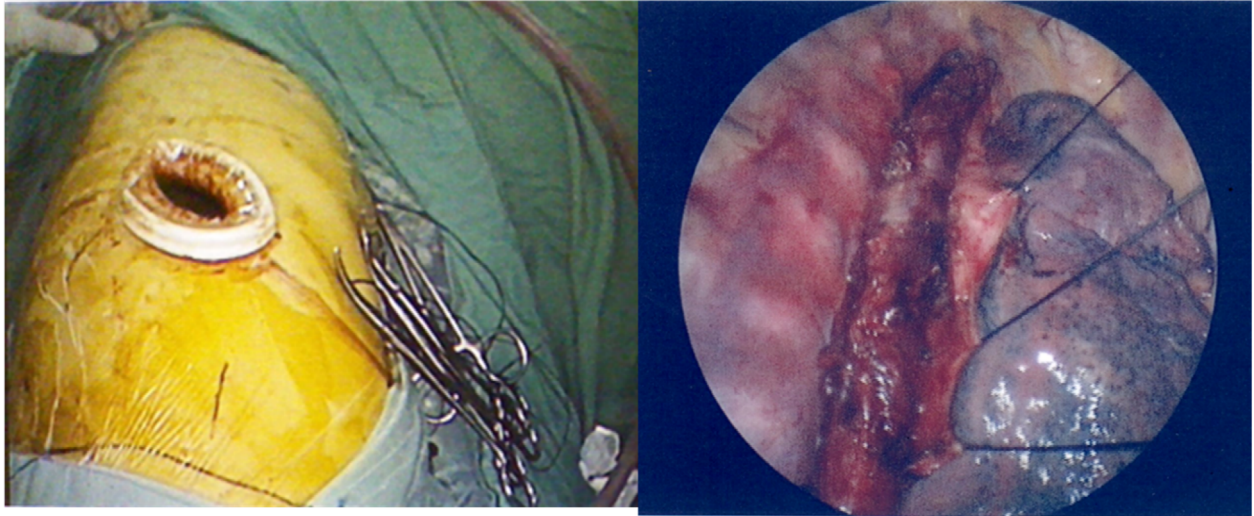
Luketich reported a series of 1011 cases of MIE comparing the benefits of McKeown MIE and Ivor Lewis MIE.¹⁴ The study showed a similar and acceptable perioperative outcome in both surgical approaches, but less incidence of recurrent laryngeal nerve injury in the Ivor Lewis MIE group. A meta-analysis by Deng et al. further showed higher vocal cord palsy, pulmonary complication, and anastomosis leakage or stricture in McKeown MIE.¹⁵ Reasons for the above results may be (i) since the neck incision was not required for Ivor Lewis MIE, exposure of cervical recurrent laryngeal nerve may be avoided; (ii) an anastomosis stoma has less tension eventually providing better blood supply in

Ivor Lewis MIE due to the lower esophagogastronomy site compared with McKeown MIE. Other systematic reviews and meta-analysis all showed similar findings comparing the two approaches.^{15–19} van Workum et al. conducted a propensity score-matched analysis comparing both surgical approaches in 787 patients, and the authors found no difference in R0 resection among two approaches.¹⁷ Even though Ivor Lewis MIE showed lower anastomosis leakage incidence than McKeown MIE, leakage in McKeown is still considered easier to manage since the anastomosis is located in the cervical area instead of the thoracic cage. In a Dutch population-based cohort study published in 2021, even though the anastomotic leakage rate was 16.9% after Ivor Lewis esophagectomy and 22.2% after McKeown esophagectomy, reoperation rate and pulmonary complication were higher in leakage after Ivor Lewis esophagectomy than McKeown esophagectomy (41.3% vs. 40.6%; 55.2% vs. 37.3%).²⁰ The learning curve for Ivor Lewis MIE is also thought to be longer compared to McKeown MIE. The choice of operative approach should be based on tumor location and surgeon experience. Until now, studies have lacked a comparison of long-term disease-free survival comparing the two surgical approaches.

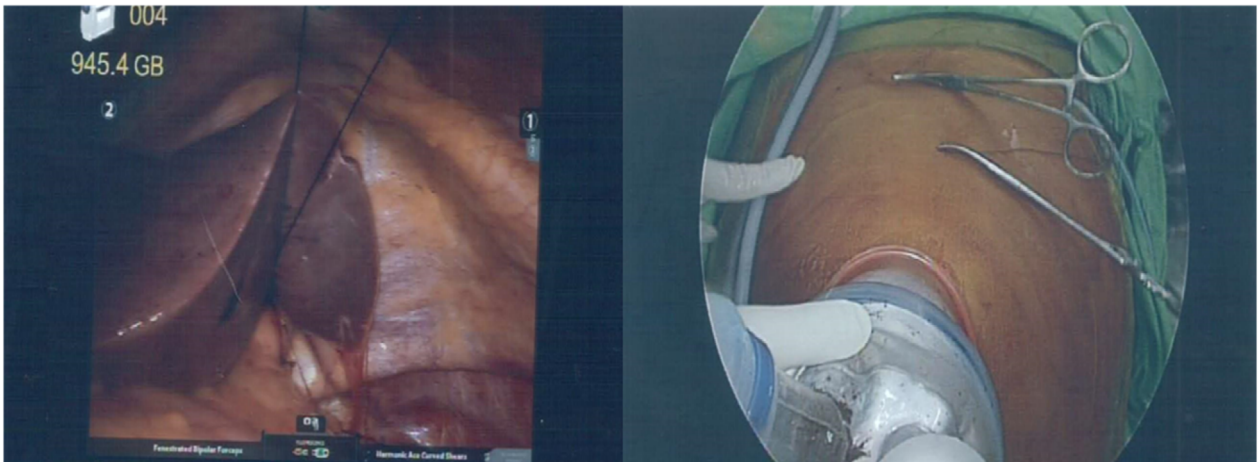
Robotic-assisted MIE versus thoracoscopic MIE

MIE performed with either a thoracoscopic approach or robotic-assisted thoracoscopic surgery (RATS) has demonstrated advantages in reducing postoperative pulmonary complications compared to that after open esophagectomy.^{4,11,21} Since robot-assisted minimally invasive esophagectomy (RAMIE) was first introduced in 2003 by Kernstine et al.,²² studies have been comparing the advantages between video-assisted thoracoscopic surgery (VATS) MIE and RAMIE. Most studies showed that, as compared to open surgery, RAMIE has a lower postoperative pneumonia rate,²³ lower postoperative vocal cord palsy,^{23,24} and more harvested lymph nodes than VATS MIE.^{23–29} As for the anastomosis leakage rate, there was mixed opinions in previous studies. Some studies showed no significance in the two groups,^{24,26} while Zheng et al. found a higher anastomosis leakage rate in RAMIE in their systematic review.²³ They suggested the reason for this may be too much exposure of the cranial end of the divided esophagus. Compared to the VATS MIE, RAMIE provides better visualization and finer dissection of the mediastinal area. The potential reasons are: (i) The 3-dimensional visualization with increased magnification of RAMIE. (ii) The flexible endowrist which enables surgeons to move more freely and accurately. However, long-term oncological outcomes remained similar to those of VATS MIE.²⁴ A previous national study from the United States using a propensity-matched method compared the long-term survival outcomes of patients who had undergone open esophagectomy, VATS MIE, or RATS MIE. The results showed similar oncological outcomes for the three approaches.

a



b



c



FIGURE 2 The method of (a) pleural tenting and (b) liver traction during single-port MIE and (c) the wound following surgery



FIGURE 3 The port placement during single-port robotic-assisted laparoscopic gastric mobilization in MIE

Multiport versus single-port access

As MIE evolved, researchers started examining the feasibility of single-port MIE. Four years ago, we published a study regarding the use of a single-port during both the thoracoscopic and laparoscopic phases of MIE.³⁰ In our experience, single-port laparoscopy, performed via a single port placed around the umbilicus, can provide a result similar to that of multiport laparoscopy. To facilitate single-port MIE, we also provide several tips so that the procedure can be performed more smoothly. The first tip is regarding pleural tenting and liver traction. Traditionally, in multiport laparoscopy, the liver is often kept under traction by an assistant using an additional port (Figure 2). In single-port laparoscopy, a suture is introduced through the diaphragmatic hiatus to elevate the liver, which is then stitched extracorporeally. In this way, a gentle and stable liver traction is achieved without requiring assistance provided through the extra port thus avoiding injury to the liver. The second tip is regarding the use of an augmented three-dimensional (3-D) imaging system. Since 3-D imaging provides better vision with regard to depth, more radical dissection of lymph nodes can be achieved without injuring the nerves around them. Furthermore, with the augmented 3-D imaging system, the scope can be kept at a distance, while providing a clear surgical view, to allow the operator to perform the procedures without disturbing the movement of surgical instruments. Third, the operating surgeon should stand at the patient's right side with the patient kept in the left lateral position when performing single-port

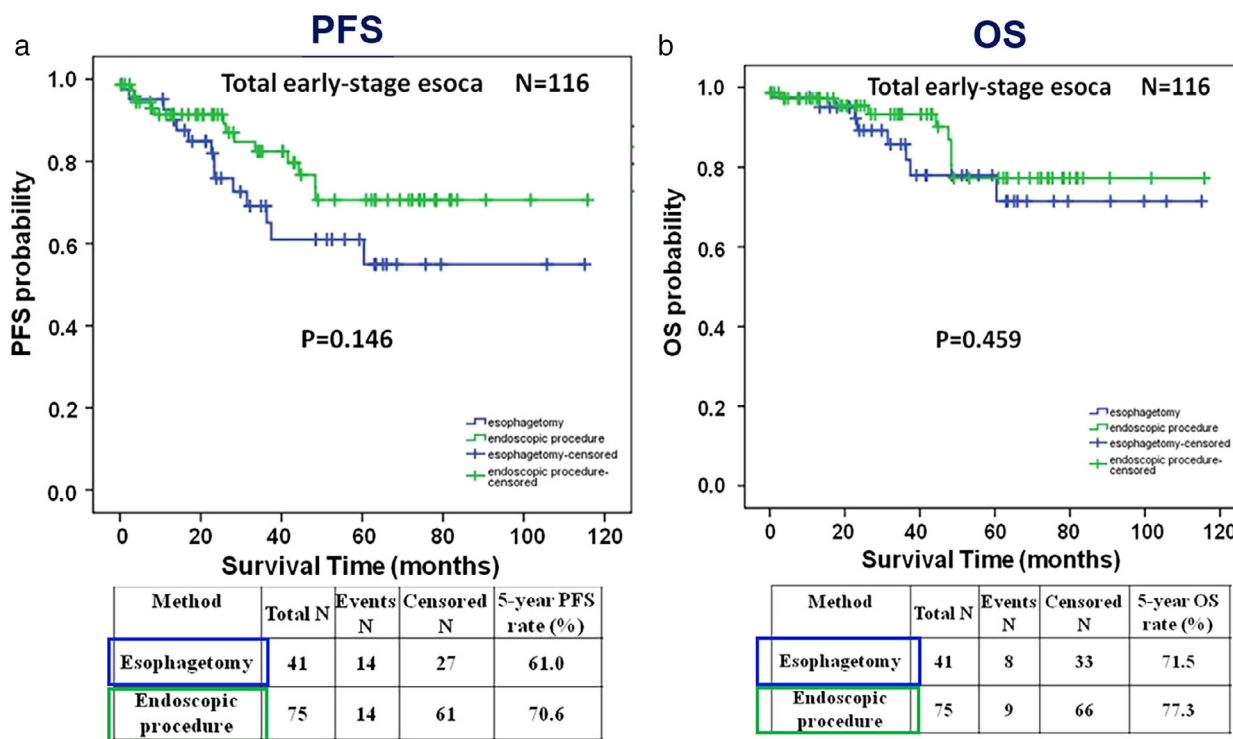


FIGURE 4 The (a) disease-free and (b) overall survival curves of patients with early esophageal cancer (stage I) treated with endoscopic submucosal dissection or esophagectomy at the National Taiwan University Hospital

VATS phase. This positioning provides more working space to the operator, especially during lymph node dissection around the bilateral recurrent laryngeal nerve regions in the deep upper mediastinum.

According to our previous prospective propensity score matched study, which compared multi- and single-port MIE with 50 patients in each arm, the pain score was significantly reduced in the single-port MIE group seven days after surgery (1.56 vs. 1.07, $p = 0.001$).³¹ Both multi- and single-port MIE had similar operation times, length of intensive care unit stay, blood loss volume, number of dissected lymph nodes, and rates of ventilator use, postoperative anastomotic leakage, pulmonary complications, and vocal cord palsy. These results suggest that single-port is noninferior to multiport MIE in terms of surgical complications and also provides an additional benefit of reduction in postoperative pain. Feasibility of single-port use in both thoracoscopy and laparoscopy has also been confirmed in other studies.^{32,33} However, the clinical value of this novel approach requires verification in terms of its cost/benefit, life quality and oncological outcome.

Additionally, the single-port technique used in RATS MIE has been explored. Our experience at NTUH with single-port RAMIE was published in 2020³⁴ (Figure 3). In the 11 patients included in the study, we performed esophagectomy in the chest with a four-port da Vinci robotic system and then performed gastric mobilization and conduit creation in the abdomen with a 5-cm single-incision glove port robotic surgery. No mortality was found, yet one anastomosis leakage, one postoperative pneumonia, and one hiatal hernia were found as postoperative complications. To overcome possible port collision, we adapted a triangular position of the robotic scope and the EndoWrists to create sufficient space for robotic manipulation. Egberts et al. also reported a case series of single-incision RAMIE.³⁵ Contrary to our approach, in their case series, the incision for single-port was conducted at the cervical area with multiport robotic assisted laparoscopy for gastric tube mobilization. There was no mortality in the study and no robotic arm collision. However, the authors stated that single-incision at the cervical area could be challenging due to the rather short distance between the ports within the incision site (this could only be avoided by experienced surgeons and the da Vinci Xi system). There are still limited studies on the feasibility of single-port RAMIE. More studies are required to analyze the potential benefit and an ideal solution for possible port collision which is a concern for most surgeons.

Treatment options other than esophagectomy

Although esophagectomy remains the mainstream treatment for esophageal cancer, other treatment options for early esophageal cancer are available, including endoscopic submucosal dissection (ESD), photodynamic therapy (PDT), and radiofrequency ablation. According to the NCCN guidelines, endoscopic therapy is recommended for patients with

T1a esophageal cancer (NCCN, version 2.2021). A previous study comparing esophagectomy and ESD showed that progression-free survival and overall survival were similar for the above two interventions in patients with early esophageal cancer.³⁶ Our data also showed that the survival rates of patients with stage I esophageal cancer were similar between the esophagectomy and ESD groups (Figure 4). Other studies focusing on R0 resection margin and disease-free survival also showed excellent results of ESD in early esophageal cancer patients.^{37,38} For the patients with early local recurrence PDT after a complete pathological response to concurrent chemoradiation therapy (CCRT), photodynamic therapy (PDT) has been used as an alternative endoscopic therapeutic option.^{31,39,40} The use of PDT includes injection of the photosensitizer, followed by a light irradiation 48 h after the injection. Our data show that PDT has a tumor response that is equivalent to that achieved with esophagectomy.⁴¹

In conclusion, MIE is feasible for the treatment of esophageal cancer since its perioperative and oncological outcomes are comparable to that of open esophagectomy. However, this approach is still evolving, and the solution of each problem requires more solid clinical evidence for which further comparative studies should be performed in the future.

CONFLICT OF INTEREST

The authors did not receive any financial support for this study.

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How to cite this article: Lee Y-K, Chen K-C, Huang P-M, Kuo S-W, Lin M-W, Lee J-M. Selection of minimally invasive surgical approaches for treating esophageal cancer. *Thorac Cancer*. 2022;13(15):2100–5. <https://doi.org/10.1111/1759-7714.14533>