



The era of minimally invasive esophagectomy

Zhigang Li, Yifeng Sun, Yu Yang, Rong Hua, Xufeng Guo, Bin Li, Bo Ye, Haiyong Gu, Teng Mao

Department of Thoracic Surgery, Section of Esophageal Surgery, Shanghai Chest Hospital, Shanghai Jiaotong University, Shanghai 200030, China
Contributions: (I) Conception and design: Z Li; (II) Administrative support: T Mao; (III) Provision of study materials or patients: Y Sun, Y Yang; (IV) Collection and assembly of data: R Hua, X Guo; (V) Data analysis and interpretation: B Li, B Ye, H Gu; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Zhigang Li, MD, PhD. Department of Thoracic Surgery, Section of Esophageal Surgery, Shanghai Chest Hospital, Shanghai Jiaotong University, 241 Huaihai West Rd, Shanghai 200030, China. Email: dr_lizhigang@163.com.

Abstract: Minimally Invasive Esophagectomy (MIE) has become a standard surgical approach for esophageal cancer in the world. In this report, we introduce the history of MIE which is different between eastern and western countries. With the development of surgical techniques, including single-lumen endotracheal intubation, CO₂ artificial pneumothorax, and surgical positioning, the MIE has made great progress. It was approved that due to significantly reduced surgical trauma, MIE lowers postoperative morbidity and mortality while achieving a tumor resection efficacy comparable with the conventional open esophagectomy. The improvement of surgical instruments and modification of surgical approaches are the keys to gaining greater clinical advantage in the future of MIE, especially the popularity of robotic surgery.

Keywords: Minimally invasive esophagectomy (MIE); history; clinical outcome

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Since the minimally invasive surgery (MIS) was clinically introduced into biliary tract and urologic surgery in the 1990s, it has evolved with its application in gynecological, obstetric and general surgery and finally become a prevalent procedure in thoracic surgery. Interestingly, the MIS technique is now advanced in thoracic surgery rather than other disciplines. In the Asian region, where the use of minimally invasive techniques is more prevalent, the rate of minimally invasive resection for lung cancer has exceeded 80%, and the rate of minimally invasive esophagectomy (MIE) in large centers has exceeded 60%.

Below is an outlined description of MIE:

- (I) The high complication rate of conventional esophageal cancer surgery has stimulated interest in exploring minimally invasive techniques, which is expected to reduce the associated mortality;
- (II) With the development of high-definition surgical imaging systems and fine surgical instruments, MIE gained attention in more accurate tumor control, especially after the introduction of robot-assisted surgical techniques;

- (III) Given the low esophageal surgeries volume at most medical centers and long learning curve, the early benefits of MIE for surgical treatment of esophageal cancer have not been widely confirmed. This feature directly showed that the patient's long-term survival was not improved. A randomized controlled trial is needed;
- (IV) The improvement of surgical instruments and modification of surgical approaches are the keys to gaining greater clinical advantage in the future of MIE, especially the popularity of robotic surgery. However, a full understanding of esophageal cancer is the key to ultimately improve long-term survival.

History of MIE

The history of MIE in eastern and western countries are different because of the different pathological types of esophageal cancer between these two worlds, which lead to a different selection in surgical approach. In western countries, adenocarcinoma is predominant histologic type

and the gastroesophageal junction is the most common lesion site. Because the abdominal and low mediastinal lymph nodes (below the carina of the trachea) are the common metastasis sites, the Ivor Lewis esophagectomy is considered as the main option for surgical treatment of esophageal adenocarcinoma. In the early period of MIE in the West, experience in performing anti-reflux surgery played an important role to shorten the learning curve of the minimally invasive Ivor Lewis procedure. Dr. James D. Luketich is a pioneer and advocator in this field (1). In contrast, squamous cell carcinoma is the most common pathological type of esophageal cancer in Asian. Lymph node dissection is essential along the recurrent laryngeal nerve (RLN) in the upper mediastinum. Considering thorough lymph node dissection and effective tumor margin, McKeown technology is more often used in the surgical treatment of esophageal squamous cell carcinoma. Because of the stringent requirements of lymph node dissection in surgical treatment of esophageal squamous cell carcinoma surgery, early thoracoscopic image quality is not sufficient to perfectly support the above techniques. Therefore, the MIE in Asia is slightly later than that of western countries. However, when HD thoracoscopic camera appeared, their advantages in lymph node dissection were even greater than those of open surgery, which led to the rapid prosperity of MIE in Asia.

The following key techniques have played significant roles in promoting the development of MIE: (I) a single-lumen endotracheal intubation and CO₂ artificial pneumothorax greatly improves visualization of the operative details. CO₂ inflation can spontaneously separate the space around the esophagus. This allows the esophagus resection and lymph node dissection to be performed easily. The use of a single-lumen tracheal tube can favor the operation to expose the lymph nodes in the upper mediastinum very much, especially those surrounding the left RLN. The bronchial blocker is a good technical supplement for single-lumen intubation. When conversion is needed, we can easily switch to single-lung ventilation mode; (II) surgical positioning was modified for post-mediastinal approach, the patient can be placed in a prone or hemi-prone position. These positions facilitate the operation in the mediastinum, surgeons do not have to perform the operation with an uncomfortable elevation of their hands. In the case of using the prone position, a surgeon may even sit on a stool while performing the operation. Moreover, bleeding in the mediastinum does not affect visualization of the operative field since blood drains

to the lower part of the chest cavity in the prone position; (III) a high-definition monitor, 3D camera and, especially, robot-assisted techniques should be a booster for future MIE. With the assistance of a 3D camera and robotic system, surgeons can perform delicate esophagectomy and lymph node dissection in the mediastinum. It has been proven that robotic surgery can achieve more satisfactory outcomes of local lymph node dissection in the superior mediastinum.

Short-term benefits of MIE

The original intent of MIE was to reduce the high complication rate of esophagectomy. Does MIE really improve perioperative results? The most influential clinical study was the randomized controlled trial (2) published in 2012, which showed that the incidence of pneumonia was significantly lower in the MIE group than open surgery group (9% *vs.* 29%, $P < 0.005$); the rate of RLN injury was also significantly lower in the MIE group. Lesser postoperative pain and better protection of RLN may be the main reasons for the decrease in the incidence of pneumonia. However, other perioperative parameters, including surgical mortality, showed no differences between MIE and OPEN group. We have not yet seen the long-term results of MIE, especially regarding the difference in local tumor recurrence. Although the use of MIE can achieve the same outcomes for lymph node dissection as open surgery and better protect the RLN, the outcome of local tumor control still needs to be studied with long-term follow-up. If the technical superiority of MIE in the protection of lung function was attributed to the omission of para-RLN lymph node dissection, we should be cautious to advocate the use of MIE. In addition, this study only included less than 60 patients in each group. Randomized studies with large sample sizes are needed to verify the perioperative advantage of MIE. Japanese researchers are working on this (3). A national data review in Japan (MIE 1,751 *vs.* OPEN 3,601) reported higher perioperative complications in patients undergoing MIE than in patients undergoing open surgery (44.3% *vs.* 40.8%, $P = 0.016$) (4). MIE showed longer operative time, higher anastomotic leak rate and re-operation rate in this retrospective study. Morality within 30 days after surgery showed no differences between the two groups. A multicenter, retrospective study in North America also showed only moderate improvements in perioperative recovery in patients undergoing MIE (5).

According to the current clinical data, MIE seems to

benefit early recovery after operation. However, this result is uncertain due to the following factors: First, the early studies did not eliminate the impact of the learning curve and many factors can compromise the outcomes in the early stages of performing MIE. Second, the initial thoracoscopic equipment cannot provide a high-definition, stable surgical view. This certainly has an impact on the quality of surgery. Finally, the pioneer doctors who perform MIE were mainly young surgeons with less experience. This will certainly have a great impact on the anastomotic leak rate. Therefore, we are confident that we will see better and more stable outcomes of modified MIE in the future.

Does MIE improve long-term survival?

A new surgical technique, especially for the treatment of cancer, should be assessed based on the tumor control rate and improvement in long-term survival. To date, accurate data on the long-term survival of patients with esophageal cancer undergoing MIE are not available, and most retrospective studies have shown an equivalent result. An European, multicenter clinical trial has shown there is no difference in the 3-year survival, regardless of overall survival or disease-free survival, between open surgery and MIE groups (overall survival, 40.4% *vs.* 50.5%, respectively, $P=0.207$) (6). In the past, multiple meta-analyses and a few clinical trials have failed to verify the advantage of MIE in improving long-term survival. Several retrospective studies had bias in grouping patients. More patients with early-stage tumors were assigned to the MIE group. Moreover, delicate lymph node dissection, which was performed under a high-definition surgical view, resulted in a shift in the patient's tumor staging. Therefore, the data of superior survival rate in patients undergoing MIE is not reliable.

The reasons why MIE cannot improve the long-term survival of patients with esophageal cancer are as follows. First, the surgical treatment of esophageal cancer has been evolving for decades. The principles of tumor resection and lymph node dissection were established 20 years ago and served as bible for the surgeries. MIE only changed the surgical approach but did not change the treatment strategy. Thus, the long-term survival of patients with esophageal cancer cannot be changed. Second, MIE was developed within the past 10 years and has become popular in large centers within the past five years. Therefore, the learning curve can seriously interfere with the analysis of long-term survival (7). Third, after gaining proficiency in performing

MIE, most of the excellent surgeons refuse to perform open surgery. Therefore, it is becoming more and more difficult to carry out a randomized, controlled trial.

The future

In the future, MIE can provide the following benefits to patients. First, the minimally invasive effects of MIE should be further improved to realistically reduce perioperative complications. Fully programmed surgical techniques can play a role in reducing complications, especially anastomotic leaks, and even improving overall survival with minimally invasive interventions. Assuming that the overall complication rate of esophageal cancer could be reduced to less than 20% after MIE, the patient's long-term survival shall be improved. Second, robot-assisted surgery may improve the short- and long-term efficacy of esophageal cancer treatment. The robotics can provide a high-definition view of the surgical site and perform a delicate operation and the same quality of surgery. It has been confirmed that robot-assisted surgery can significantly improve the effects of bilateral lymph node dissection in patients with esophageal squamous cell carcinoma (8). The sites near the RLN are the most common locations of lymph node metastasis of esophageal cancer. Good local tumor control will further improve long-term survival. A randomized controlled trial in Europe has confirmed the improved survival in patients with esophageal cancer undergoing robot-assisted esophagectomy (9). Third, comprehensive treatment is still the key to ultimate improvements in the treatment of esophageal cancer.

Summary

The current clinical data have shown the advantages of MIE in reducing postoperative complications and improving quality of life. However, these data need to be verified by large-sized studies, especially data from the patients operated by surgeons who have had proficiency in performing MIE after his learning curve. High-definition endoscopic instruments and a more skilled hand can improve the long-term prognosis of patients with esophageal cancer undergoing MIE. In addition, decreased postoperative complications, improved long-term quality of life and an increased success rate of retreatment will help improve overall survival. The main problem for MIE in the future is how to improve surgical outcomes after neoadjuvant and radical chemoradiotherapy.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/shc.2018.06.09>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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