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Current Issues in Minimally Invasive Esophagectomy

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Minimally invasive esophagectomy (MIE) was first introduced in the 1990s. Currently, it is a widely accepted surgical approach for the treatment of esophageal cancer, as it is an oncologically sound procedure; its advantages when compared to open procedures, including reduction in postoperative complications, reduction in the length of hospital stay, and improvement in quality of life, are well documented. However, debates are still ongoing about the safety and efficacy of MIE. The present review focuses on some of the current issues related to conventional MIE and robot-assisted MIE based on evidence from the current literature.

Keywords: Esophageal neoplasm, Minimally invasive surgical procedures, Thoracoscopy, Laparoscopy, Robotic surgical procedures

Introduction

Esophageal cancer presents a significant oncological burden globally. It is the seventh most common malignancy, and its incidence is rapidly increasing in the Western world [1,2]. Surgical treatment remains the mainstay of curative management of esophageal cancer, with a 5-year survival rate of approximately 40%–50% when preceded by chemoradiation therapy [3,4]. Esophagectomy is a highly complex surgical procedure that requires 2-field or 3-field access. Thus, it is associated with significant morbidity and mortality. With advances in thoracic surgery in the 1990s, the progress made in thoracic anesthesia, surgical instruments, and skills has enabled reduction in the surgical trauma and invasiveness. Of particular note, minimally invasive esophagectomy (MIE) has dramatically reduced the morbidity and mortality associated with esophageal surgery. Furthermore, this trend was supported by 3 prospective and randomized clinical trials that revealed the benefits of MIE even after neoadjuvant treatment [5-7]. Although several earlier studies have demonstrated that MIE is an oncologically sound procedure with some benefits for short-term outcomes, some controversies and issues still need to be clarified. This review presents an overview of some of the current issues related to MIE.

Various types of minimally invasive esophagectomy

As esophageal surgery requires 2-field or 3-field access, several different types of MIE have been reported. MIE was first introduced by Cuschieri et al. [8] in 1992. They reported a series of 5 patients who underwent thoracoscopic surgery combined with laparotomy. DePaula et al. [9] reported their experience of laparoscopic transhiatal esophagectomy in 1995. Luketich et al. [10] reported the first large series of a combined thoracoscopic and laparoscopic approach for esophageal cancer in 2003. Horgan et al. [11] and Kernstine et al. [12] reported the first case of robot-assisted MIE (RAMIE). Currently, most of the published literature uses similar terminology for MIE. However, there are still subtle differences in terminology among surgeons [13-15].

Total MIE via a transthoracic approach is currently the most common method of esophageal resection. It combines thoracoscopy with laparoscopy and creates an esophagogastric anastomosis at the intrathoracic level (Ivor Lewis) or at the cervical level (McKeown). Luketich et al. [10] reported the first large series of total MIE with 222 patients; they reported low mortality and morbidity rates, as well as short hospital stays. Moreover, they reported further improved outcomes in over 1,000 patients [16]. The Traditional Invasive versus Minimally Invasive (TIME) trial in 2012 was the first published randomized controlled trial comparing the outcomes of open esophagectomy (OE) and total MIE [5]. It demonstrated lower rates of pulmonary complications and shorter hospital stays in the MIE group, with comparable 30-day mortality and number of harvested lymph nodes (LNs).

Hybrid MIE is a combination of minimally invasive and open approaches, applying minimally invasive techniques at one level of the 2 stages. The previous literature, including 1 randomized controlled trial, has demonstrated the benefits of hybrid MIE involving a combination of laparoscopic surgery and thoracotomy [6,17,18]. Recently, results from the French randomized MIRO trial have demonstrated the benefits of laparoscopic hybrid MIE for short-term, mid-term, and long-term outcomes when compared with OE [6]. The overall major morbidity rates and pulmonary complication rates were lower in hybrid MIE than in OE, with similar 30-day mortality and oncologic parameters. A recent meta-analysis by Booka et al. [19] also demonstrated a significant reduction in pulmonary complication rate with laparoscopic hybrid MIE. Two recent reports based on big data regarding thoracoscopic hybrid MIE were published in Japan [20,21]. They reported superior perioperative outcomes of hybrid MIE when compared with OE in terms of in-hospital mortality, surgery-related mortality, and postoperative morbidity.

Traditionally, the transthoracic approach was most frequently performed in the lateral decubitus position; however, this position requires total lung collapse, which is frequently associated with pulmonary complications. Palanivelu et al. [22] reported transthoracic MIE in the prone position in a large cohort. They reported that it was technically feasible, with a low respiratory complication rate and a shorter operative time due to the excellent exposure of the operative field and the better ergonomics. However, it is difficult to perform classical thoracotomy conversion in an urgent setting. Lately, MIE in a semi-prone position has become popular among surgeons to overcome the abovementioned problem, while retaining the benefits of the prone position [23].

Transhiatal OE was first reported by Orringer and Sloan [24]. It is regarded as less invasive and less radical than transthoracic OE. Transhiatal esophagectomy with a laparoscopic abdominal procedure is also considered to be a type of MIE. Most of the previous literature regards it as a type of total MIE [13,15], as it includes only minimally invasive abdominal procedures without a transthoracic approach. A recent systematic review by Parry et al. [25] reported that transhiatal MIE showed less blood loss and shorter hospital stays than transhiatal OE with comparable postoperative morbidity rates and LN retrieval.

Although the transhiatal approach is regarded as less invasive than the transthoracic approach, mediastinal LN dissection is insufficient for the treatment of esophageal cancer. In some institutions, a video-assisted transcervical approach for dissection of the proximal and mid-esophagus has been implemented in combination with a transhiatal approach to improve the quality of mediastinal LN dissection without transthoracic dissection and one-lung ventilation [26-28]. They reported that this approach was associated with a lower pulmonary complication rate and better postoperative quality of life, with comparable numbers of retrieved mediastinal LNs compared to transthoracic esophagectomy. Larger prospective studies should be conducted to verify these results, including long-term oncologic outcomes.

RAMIE was introduced in 2003 and was found to be a safe technique with good oncologic outcomes in the first reported series [29,30]. Based on the definition by Gottlieb-Vedi et al. [13], RAMIE is technically a form of MIE. However, most surgeons who perform RAMIE consider it to be a procedure distinct from conventional MIE, as robotic surgical systems were developed to overcome the technical limitations of conventional MIE. They believe that RAMIE has several benefits over conventional MIE. Several types of RAMIE have been reported. The ROBOT trial, which compared RAMIE with OE, included patients in whom thoracic RAMIE was combined with a laparoscopic procedure [7]. Recently, our group reported the outcomes of RAMIE [31]. We defined total RAMIE as RAMIE for thoracic as well as abdominal procedures and hybrid RAMIE as RAMIE only for thoracic procedures in combination with laparotomy. There is no consensus regarding the specific terminology for various types of RAMIE. However, we believe that they should be well defined for proper comparisons to be made in future research.

Long learning period and associated problems

Although perioperative morbidity and mortality rates have remarkably decreased with recent advances in surgical techniques and postoperative care, esophagectomy is still associated with a high mortality rate compared to other high-risk surgical procedure and has a morbidity rate up to 60%. The previous literature, including 3 randomized controlled trials, has demonstrated improved short-term outcomes of MIE. However, it is a highly complex procedure, making it difficult to achieve proficiency. In particular, thoracoscopic surgery is technically demanding due to movement of the target anatomy, mirrored intracorporeal movements of the instruments, and nearby vital structures that need to be avoided (aorta, pulmonary artery, trachea, and vagal nerve branches). Moreover, various types of MIE with different levels of complexity (transhiatal, transthoracic with cervical, or intrathoracic anastomosis) have different learning curves.

Learning-associated morbidity is defined as morbidity during a learning curve, which could have been avoided if patients were operated on by surgeons who have completed the learning curve. It is now a recognized problem, and there is robust evidence suggesting that the implementation of MIE can have a significant effect on patients' clinical outcomes. Training in complex MIE is a long process with a reported learning curve of 50 to 119 cases [32,33]. As the reported anastomotic leakage rate dropped from 18.8% to 4.5% from the first to the fifth quintile, it is suggested that patients are exposed to an increased risk of surgical morbidity during the learning phase [32]. Moreover, early series related to MIE have reported higher rates of acute gastric conduit necrosis [33], which were attributed to a lack of proficiency in technique during the learning phase. Multiple population-based studies from several countries demonstrated higher rates of reintervention in MIE than in OE [34-37]. Some authors suggested that this finding may have reflected the learning curve of MIE experienced by surgeons and centers during the early national adaptation phase. The reported duration of the learning curve for RAMIE is 20–80 cases [38-40]. Our group analyzed the number of cases required to attain surgical proficiency for short-term postoperative outcomes [40]. We found that the rate of vocal fold palsy decreased from 36% to 17% after 60 cases, the rate of anastomotic leakage decreased from 15% to 2% after 80 cases, and the length of hospital stay decreased from 24 days to 14 days after 80 cases. Thus, it seems that the postoperative outcomes after MIE improve over time based on accumulated experience in the learning period.

According to the aforementioned results, some learning-associated morbidity is inevitable, as MIE is a surgically complex procedure. Therefore, shortening the learning curves and reducing the learning-associated morbidity remain important goals for the implementation of MIE. Gottlieb-Vedi et al. [41] reported that surgeons who performed a higher volume of cases and younger surgeons seemed to require a substantially shorter period to gain proficiency for long-term mortality and other outcomes following surgery for esophageal cancer. Moreover, some studies have demonstrated that standardized training programs were effective for surgical procedures [42]. A study by van der Sluis et al. [39] revealed that the use of a structured training pathway that involved proctoring reduced the learning curve for RAMIE from 70 to 24 cases. These findings indicate that the safe implementation of a standardized MIE training program for younger surgeons may improve patient outcomes and safety in the current surgical era.

Lymph node dissection in minimally invasive esophagectomy

The status of LNs in esophageal cancer is an important prognostic factor and has been proposed as a predictor of overall survival [43-45]. The pattern of LN metastasis of esophageal cancer relies on several factors such as tumor location, histology, depth of invasion (T-stage), and the use of neoadjuvant treatment. As many factors are associated with the pattern of LN metastasis, the optimal extent of lymphadenectomy is still under debate [46,47].

In East Asia, squamous cell carcinoma constitutes more than 90% of all resected esophageal cancers and the most frequent location of the tumor is the upper to middle esophagus. Akiyama et al. [45] investigated the distribution pattern of LN metastasis in squamous cell carcinoma and reported that the most frequent sites of LN metastasis were the upper mediastinal LNs in patients with esophageal squamous cell carcinoma in the upper thoracic esophagus, while the upper mediastinal and perigastric LNs were involved in patients with cancer in the middle thoracic esophagus. Therefore, in many centers in East Asia and especially in Japan, extensive LN dissection including abdominal, whole mediastinal, and even cervical LNs has been advocated as a standard surgical procedure with curative intent. In Western countries, a dramatic increase in the incidence of adenocarcinoma of the lower thoracic esophagus and esophagogastric junction has been reported in the past 2 decades [48,49]. Many of these cancers are associated with gastroesophageal reflux and Barrett esophagus. Some studies have indicated that only 1%–2% of Siewert type II esophagogastric adenocarcinomas showed metastasis to the LNs in the supracarinal area [50,51]. Differences in tumor characteristics (histology and the predominant location of the tumors) between Western countries and East Asian countries result in differing perspectives regarding the surgical approach for esophageal cancer, including the extent of lymphadenectomy.

Radical lymphadenectomy attempts to improve both the locoregional tumor control rate and long-term survival, though it increases postoperative morbidity. Although debates are continuing about whether the extent and the number of harvested LNs improve long-term survival, a key measurement of oncologic outcomes in esophagectomy is the extent of LN retrieval. Many researchers have reported that the number of harvested LNs was associated with good long-term survival [46,52]. Studies comparing the number of harvested LNs in MIE compared to those in OE revealed a similar extent of resection between the 2 procedures. The TIME trial and the MIRO trial showed no difference in the average number of LNs retrieved [5,6]. Some recent studies, including a meta-analysis, have confirmed these results, while others have reported a greater number of retrieved LNs in MIE [34,53,54]. The ROBOT trial reported no differences in the total number of retrieved LNs between RAMIE and OE [7]. Our group also reported that there was no difference in the number of retrieved LNs in the cervical, mediastinal, or abdominal area between the 2 groups [31].

For upper mediastinal lymphadenectomy, LN dissection along both the recurrent laryngeal nerves is a challenging procedure during MIE. Recurrent laryngeal LNs are among the most common metastatic sites in esophageal squamous cell carcinoma [55,56]. A proper and complete dissection of these LNs is important for locoregional control of the tumor. However, it is technically challenging due to the possibility of vocal fold palsy caused by nerve injury. Dissection of the left recurrent laryngeal nerve is especially challenging, as esophageal surgery is mostly performed through the right hemithorax. Cuesta [57] summarized 5 different surgical approaches for left laryngeal nerve LN dissection during MIE. The position of the patient, placement of the trocars, and the surgical platform (thoracoscopy or robot) might affect surgeons' preferences for the surgical approach during left recurrent laryngeal nerve LN dissection.

As robotic surgical platforms provide some technical advantages, such as articulating arms and ×10 magnification with 3-dimensional vision, some reports have suggested that RAMIE is feasible for upper mediastinal LN dissection, especially for recurrent laryngeal nerve LNs [58,59]. Our group compared outcomes between RAMIE and conventional MIE and reported that the total number of harvested LNs was significantly higher in RAMIE than in conventional MIE [60]. The number of harvested LNs in the upper mediastinum was higher in RAMIE than in MIE and specifically, the numbers of harvested LNs from the laryngeal nerve and the sub-aortic areas were significantly higher in RAMIE, while the rate of vocal fold paralysis was similar.

Quality of life after minimally invasive esophagectomy

Several previous studies demonstrated that MIE is associated with a rapid restoration of health-related quality of life. This benefit may be attributable to the reduction of postoperative complications in MIE. The TIME trial showed that MIE was associated with better short-term quality of life [5]. The physical component summary of the Short Form 36 Health Survey, European Organization for Research and Treatment of Cancer Quality of Life Questionnaires, and quality-of-life domains of talking and pain in the OES 18 questionnaire were significantly better in MIE. Moreover, the ROBOT trial demonstrated better health-related quality of life and physical functioning at discharge and at postoperative 6 weeks in the RAMIE group [7]. The MIRO trial assessed short- and long-term health-related quality of life of OE and hybrid MIE groups [61]. They reported that hybrid MIE reduced the incidence of short-term adverse events, with some degree of persistent improvements of health-related quality of life up to 2 years; however, at 3 years, there was no difference between the 2 groups.

Minimally invasive esophagectomy after neoadjuvant treatment

Neoadjuvant treatment has been proven to have survival benefits, especially for locally advanced esophageal cancers. The CROSS trial showed a better R0 resection rate, a lower node-positive rate, and longer overall survival in the neoadjuvant treatment group without significant postoperative mortality or morbidities [4]. Some previous studies have reported the efficacy of MIE in patients who underwent neoadjuvant treatment. The TIME trial examined the role of MIE in patients who had undergone neoadjuvant chemoradiotherapy for esophageal cancer [5]. The trial reported promising early postoperative outcomes. Some retrospective studies have also demonstrated that MIE was a safe procedure after neoadjuvant chemoradiation therapy [62,63]. However, MIE should be considered carefully in patients with an advanced bulky tumor before neoadjuvant treatment and in patients in whom esophagectomy was planned as salvage therapy. Moreover, possible postoperative morbidities should be carefully monitored in these patients [64].

Long-term survival after minimally invasive esophagectomy

Although many studies have revealed that MIE has benefits over OE in terms of short-term perioperative outcome and quality of life, the long-term outcomes of MIE remain to be established due to the heterogeneity of the procedure, small sample sizes, and the lack of long-term data. The most recent follow-up results of the TIME trial demonstrated 3-year overall survival rates of 40.4% and 50.5% in OE and in MIE, respectively, without a statistically significant difference [65]. The TIME trial also reported 3-year disease-free survival rates of 35.9% and 40.2% in OE and in MIE, respectively. In the MIRO trial, the 3-year and the 5-year overall survival rates were 55% and 39%, respectively, in OE and 67% and 60%, respectively, in hybrid MIE [6]. In the ROBOT trial, no statistically significant differences were observed in overall survival and disease-free survival between RAMIE and OE at a median follow-up of 40 months [7]. A recent meta-analysis by Gottlieb-Vedi et al. [13] including 14,592 patients from 55 relevant studies reported that MIE was associated with lower 5-year and 3-year all-cause mortality and disease-specific mortality rates than OE. The 3-year and 5-year all-cause mortality rates were lower by 18% and 15%, respectively, after MIE when compared with OE. Moreover, the 3-year and the 5-year disease-specific mortality rates were lower by 17% and 16%, respectively, after MIE when compared with OE. The authors concluded that MIE might be recommended as a standard surgical approach for esophageal cancer. Further studies are still warranted, as a greater number of high-quality cohort studies and randomized clinical trials would improve the status of the current evidence. Therefore, the results of the JCOG1409 study (Japan Clinical Oncology Group trial) planned in Japan (a randomized controlled trial comparing MIE and OE in terms of overall survival) are eagerly anticipated [66].

Conclusion

MIE is a valuable surgical option for the treatment of esophageal cancer. Many studies have suggested that MIE has advantages related to early postoperative outcomes, including reduced postoperative complications, early recovery, and improved quality of life. However, several debatable issues remain that should be clarified. The heterogeneity of the procedure, risks during the learning period, adequate extent of LN dissection, and long-term survival after MIE should be investigated in future studies.

Conflict of interest

C.H. Kang received proctor fees from Intuitive Surgical Korea. No potential conflict of interest relevant to this article was reported.

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References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. *Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries.* CA Cancer J Clin 2018;68:394-424.
2. Global Burden of Disease Cancer Collaboration, Fitzmaurice C, Akinyemiju TF, et al. *Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 29 cancer groups, 1990 to 2016: a systematic analysis for the global burden of disease study.* JAMA Oncol 2018;4:1553-68.
3. Alderson D, Cunningham D, Nankivell M, et al. *Neoadjuvant cisplatin and fluorouracil versus epirubicin, cisplatin, and capecitabine followed by resection in patients with oesophageal adenocarcinoma (UK MRC OE05): an open-label, randomised phase 3 trial.* Lancet Oncol 2017;18:1249-60.
4. Van Hagen P, Hulshof MC, van Lanschot JJ, et al. *Preoperative chemoradiotherapy for esophageal or junctional cancer.* N Engl J Med 2012;366:2074-84.
5. Biere SS, van Berge Henegouwen MI, Maas KW, et al. *Minimally invasive versus open oesophagectomy for patients with oesophageal cancer: a multicentre, open-label, randomised controlled trial.* Lancet 2012;379:1887-92.
6. Mariette C, Markar SR, Dabakuyo-Yonli TS, et al. *Hybrid minimally invasive esophagectomy for esophageal cancer.* N Engl J Med 2019; 380:152-62.
7. Van der Sluis PC, van der Horst S, May AM, et al. *Robot-assisted minimally invasive thoracolaparoscopic esophagectomy versus open*

transthoracic esophagectomy for resectable esophageal cancer: a randomized controlled trial. Ann Surg 2019;269:621-30.

8. Cuschieri A, Shimi S, Banting S. *Endoscopic oesophagectomy through a right thoracoscopic approach.* J R Coll Surg Edinb 1992; 37:7-11.
9. DePaula AL, Hashiba K, Ferreira EA, de Paula RA, Grecco E. *Laparoscopic transhiatal esophagectomy with esophagogastroplasty.* Surg Laparosc Endosc 1995;5:1-5.
10. Luketich JD, Alvelo-Rivera M, Buenaventura PO, et al. *Minimally invasive esophagectomy: outcomes in 222 patients.* Ann Surg 2003; 238:486-94.
11. Horgan S, Berger RA, Elli EF, Espat NJ. *Robotic-assisted minimally invasive transhiatal esophagectomy.* Am Surg 2003;69:624-6.
12. Kernstine KH, DeArmond DT, Karimi M, et al. *The robotic, 2-stage, 3-field esophagolymphadenectomy.* J Thorac Cardiovasc Surg 2004; 127:1847-9.
13. Gottlieb-Vedi E, Kauppila JH, Malietzis G, Nilsson M, Markar SR, Lagergren J. *Long-term survival in esophageal cancer after minimally invasive compared to open esophagectomy: a systematic review and meta-analysis.* Ann Surg 2019;270:1005-17.
14. Watanabe M, Baba Y, Nagai Y, Baba H. *Minimally invasive esophagectomy for esophageal cancer: an updated review.* Surg Today 2013;43:237-44.
15. Giugliano DN, Berger AC, Rosato EL, Palazzo F. *Total minimally invasive esophagectomy for esophageal cancer: approaches and outcomes.* Langenbecks Arch Surg 2016;401:747-56.
16. Luketich JD, Pennathur A, Awais O, et al. *Outcomes after minimally invasive esophagectomy: review of over 1000 patients.* Ann Surg 2012;256:95-103.
17. Briez N, Piessen G, Torres F, Lebuffe G, Triboulet JP, Mariette C. *Effects of hybrid minimally invasive oesophagectomy on major postoperative pulmonary complications.* Br J Surg 2012;99:1547-53.
18. Rinieri P, Ouattara M, Brioude G, et al. *Long-term outcome of open versus hybrid minimally invasive Ivor Lewis oesophagectomy: a propensity score matched study.* Eur J Cardiothorac Surg 2017;51: 223-9.
19. Booka E, Tsubosa Y, Haneda R, Ishii K. *Ability of laparoscopic gastric mobilization to prevent pulmonary complications after open thoracotomy or thoracoscopic esophagectomy for esophageal cancer: a systematic review and meta-analysis.* World J Surg 2020;44:980-9.
20. Sakamoto T, Fujiogi M, Matsui H, Fushimi K, Yasunaga H. *Comparing perioperative mortality and morbidity of minimally invasive esophagectomy versus open esophagectomy for esophageal cancer: a nationwide retrospective analysis.* Ann Surg 2019 Jul 25 [Epub]. https://doi.org/10.1097/SLA.0000000000003500.
21. Yoshida N, Yamamoto H, Baba H, et al. *Can minimally invasive esophagectomy replace open esophagectomy for esophageal cancer?: latest analysis of 24,233 esophagectomies from the Japanese national clinical database.* Ann Surg 2020;272:118-24.
22. Palanivelu C, Prakash A, Senthilkumar R, et al. *Minimally invasive esophagectomy: thoracoscopic mobilization of the esophagus and mediastinal lymphadenectomy in prone position: experience of 130 patients.* J Am Coll Surg 2006;203:7-16.
23. Seesing MFJ, Goense L, Ruurda JP, Luyer MDP, Nieuwenhuijzen GAP, van Hillegersberg R. *Minimally invasive esophagectomy: a propensity score-matched analysis of semiprone versus prone position.* Surg Endosc 2018;32:2758-65.
24. Orringer MB, Sloan H. *Esophagectomy without thoracotomy.* J Thorac Cardiovasc Surg 1978;76:643-54.
25. Parry K, Ruurda JP, van der Sluis PC, van Hillegersberg R. *Current status of laparoscopic transhiatal esophagectomy for esophageal cancer patients: a systematic review of the literature.* Dis Esophagus 2017;30:1-7.
26. Parker M, Pfluke JM, Shaddix KK, Asbun HJ, Smith CD, Bowers SP. *Video: transcervical videoscopic esophageal dissection in minimally invasive esophagectomy.* Surg Endosc 2011;25:941-2.
27. Yoshimura S, Mori K, Yamagata Y, et al. *Quality of life after robot-assisted transmediastinal radical surgery for esophageal cancer.* Surg Endosc 2018;32:2249-54.
28. Mori K, Yamagata Y, Aikou S, et al. *Short-term outcomes of robotic radical esophagectomy for esophageal cancer by a nontransthoracic approach compared with conventional transthoracic surgery.* Dis Esophagus 2016;29:429-34.
29. Van Hillegersberg R, Boone J, Draaisma WA, Broeders IA, Giezeman MJ, Borel Rinkes IH. *First experience with robot-assisted thoracoscopic esophagolymphadenectomy for esophageal cancer.* Surg Endosc 2006;20:1435-9.
30. Ruurda JP, Draaisma WA, van Hillegersberg R, et al. *Robot-assisted endoscopic surgery: a four-year single-center experience.* Dig Surg 2005;22:313-20.
31. Na KJ, Park S, Park IK, Kim YT, Kang CH. *Outcomes after total robotic esophagectomy for esophageal cancer: a propensity-matched comparison with hybrid robotic esophagectomy.* J Thorac Dis 2019; 11:5310-20.
32. Van Workum F, Stenstra MHBC, Berkelmans GHK, et al. *Learning curve and associated morbidity of minimally invasive esophagectomy: a retrospective multicenter study.* Ann Surg 2019;269:88-94.
33. Ramage L, Deguara J, Davies A, et al. *Gastric tube necrosis following minimally invasive oesophagectomy is a learning curve issue.* Ann R Coll Surg Engl 2013;95:329-34.
34. Sihag S, Kosinski AS, Gaissert HA, Wright CD, Schipper PH. *Minimally invasive versus open esophagectomy for esophageal cancer: a comparison of early surgical outcomes from the society of thoracic surgeons national database.* Ann Thorac Surg 2016;101:1281-8.
35. Takeuchi H, Miyata H, Ozawa S, et al. *Comparison of short-term outcomes between open and minimally invasive esophagectomy for esophageal cancer using a nationwide database in Japan.* Ann Surg Oncol 2017;24:1821-7.

36. Seesing MFJ, Gisbertz SS, Goense L, et al. *A propensity score matched analysis of open versus minimally invasive transthoracic esophagectomy in the Netherlands.* Ann Surg 2017;266:839-46.
37. Mamidanna R, Bottle A, Aylin P, Faiz O, Hanna GB. *Short-term outcomes following open versus minimally invasive esophagectomy for cancer in England: a population-based national study.* Ann Surg 2012;255:197-203.
38. Hernandez JM, Dimou F, Weber J, et al. *Defining the learning curve for robotic-assisted esophagogastrectomy.* J Gastrointest Surg 2013; 17:1346-51.
39. Van der Sluis PC, Ruurda JP, van der Horst S, Goense L, van Hillegersberg R. *Learning curve for robot-assisted minimally invasive thoracoscopic esophagectomy: results from 312 cases.* Ann Thorac Surg 2018;106:264-71.
40. Park S, Hyun K, Lee HJ, Park IK, Kim YT, Kang CH. *A study of the learning curve for robotic oesophagectomy for oesophageal cancer.* Eur J Cardiothorac Surg 2018;53:862-70.
41. Gottlieb-Vedi E, Mackenzie H, van Workum F, et al. *Surgeon volume and surgeon age in relation to proficiency gain curves for prognosis following surgery for esophageal cancer.* Ann Surg Oncol 2019;26: 497-505.
42. Van Workum F, Fransen L, Luyer MD, Rosman C. *Learning curves in minimally invasive esophagectomy.* World J Gastroenterol 2018; 24:4974-8.
43. Altorki N, Kent M, Ferrara C, Port J. *Three-field lymph node dissection for squamous cell and adenocarcinoma of the esophagus.* Ann Surg 2002;236:177-83.
44. Stein HJ, Feith M, Bruecher BL, Naehrig J, Sarbia M, Siewert JR. *Early esophageal cancer: pattern of lymphatic spread and prognostic factors for long-term survival after surgical resection.* Ann Surg 2005;242:566-73.
45. Akiyama H, Tsurumaru M, Udagawa H, Kajiyama Y. *Radical lymph node dissection for cancer of the thoracic esophagus.* Ann Surg 1994; 220:364-72.
46. Rizk NP, Ishwaran H, Rice TW, et al. *Optimum lymphadenectomy for esophageal cancer.* Ann Surg 2010;251:46-50.
47. Kutup A, Nentwich MF, Bollschweiler E, Bogoevski D, Izbicki JR, Holscher AH. *What should be the gold standard for the surgical component in the treatment of locally advanced esophageal cancer: transthoracic versus transhiatal esophagectomy.* Ann Surg 2014;260:1016-22.
48. Pera M, Cameron AJ, Trastek VF, Carpenter HA, Zinsmeister AR. *Increasing incidence of adenocarcinoma of the esophagus and esophagogastric junction.* Gastroenterology 1993;104:510-3.
49. Hesketh PJ, Clapp RW, Doos WG, Spechler SJ. *The increasing frequency of adenocarcinoma of the esophagus.* Cancer 1989;64:526-30.
50. Leers JM, DeMeester SR, Chan N, et al. *Clinical characteristics, biologic behavior, and survival after esophagectomy are similar for adenocarcinoma of the gastroesophageal junction and the distal esophagus.* J Thorac Cardiovasc Surg 2009;138:594-602.
51. Parry K, Haverkamp L, Bruijnen RC, Siersema PD, Ruurda JP, van Hillegersberg R. *Surgical treatment of adenocarcinomas of the gastro-esophageal junction.* Ann Surg Oncol 2015;22:597-603.
52. Peyre CG, Hagen JA, DeMeester SR, et al. *The number of lymph nodes removed predicts survival in esophageal cancer: an international study on the impact of extent of surgical resection.* Ann Surg 2008;248:549-56.
53. Nagpal K, Ahmed K, Vats A, et al. *Is minimally invasive surgery beneficial in the management of esophageal cancer?: a meta-analysis.* Surg Endosc 2010;24:1621-9.
54. Dantoc M, Cox MR, Eslick GD. *Evidence to support the use of minimally invasive esophagectomy for esophageal cancer: a meta-analysis.* Arch Surg 2012;147:768-76.
55. Sato F, Shimada Y, Li Z, et al. *Paratracheal lymph node metastasis is associated with cervical lymph node metastasis in patients with thoracic esophageal squamous cell carcinoma.* Ann Surg Oncol 2002;9: 65-70.
56. Wu J, Chen QX, Zhou XM, Mao WM, Krasna MJ. *Does recurrent laryngeal nerve lymph node metastasis really affect the prognosis in node-positive patients with squamous cell carcinoma of the middle thoracic esophagus?* BMC Surg 2014;14:43.
57. Cuesta MA. *Review of different approaches of the left recurrent laryngeal nerve area for lymphadenectomy during minimally invasive esophagectomy.* J Thorac Dis 2019;11:S766-70.
58. Kim DJ, Park SY, Lee S, Kim HI, Hyung WJ. *Feasibility of a robot-assisted thoracoscopic lymphadenectomy along the recurrent laryngeal nerves in radical esophagectomy for esophageal squamous carcinoma.* Surg Endosc 2014;28:1866-73.
59. Motoyama S, Sato Y, Wakita A, et al. *Extensive lymph node dissection around the left laryngeal nerve achieved with robot-assisted thoracoscopic esophagectomy.* Anticancer Res 2019;39:1337-42.
60. Park S, Hwang Y, Lee HJ, Park IK, Kim YT, Kang CH. *Comparison of robot-assisted esophagectomy and thoracoscopic esophagectomy in esophageal squamous cell carcinoma.* J Thorac Dis 2016;8:2853-61.
61. Mariette C, Markar S, Dabakuyo-Yonli TS, et al. *Health-related quality of life following hybrid minimally invasive versus open esophagectomy for patients with esophageal cancer, analysis of a multicenter, open-label, randomized phase III controlled trial: the MIRO trial.* Ann Surg 2020;271:1023-9.
62. Warner S, Chang YH, Paripati H, et al. *Outcomes of minimally invasive esophagectomy in esophageal cancer after neoadjuvant chemoradiotherapy.* Ann Thorac Surg 2014;97:439-45.
63. Spector R, Zheng Y, Yeap BY, et al. *The 3-hole minimally invasive esophagectomy: a safe procedure following neoadjuvant chemotherapy and radiation.* Semin Thorac Cardiovasc Surg 2015;27:205-15.
64. Goense L, van Rossum PS, Ruurda JP, et al. *Radiation to the gastric*

fundus increases the risk of anastomotic leakage after esophagectomy. Ann Thorac Surg 2016;102:1798-804.

65. Straatman J, van der Wielen N, Cuesta MA, et al. *Minimally Invasive versus open esophageal resection: three-year follow-up of the previously reported randomized controlled trial: the TIME trial.* Ann Surg 2017;266:232-6.

66. Kataoka K, Takeuchi H, Mizusawa J, et al. *A randomized phase III trial of thoracoscopic versus open esophagectomy for thoracic esophageal cancer: Japan Clinical Oncology Group Study JCOG1409.* Jpn J Clin Oncol 2016;46:174-7.