Review Article

Digestive Surgery

Dig Surg 2020;37:93–100
DOI: 10.1159/000497456

Received: September 5, 2018
Accepted: February 4, 2019
Published online: May 16, 2019

Minimally Invasive Esophagectomy

Pieter Christiaan van der Sluis[a] Dimitrios Schizas[b] Theodore Liakakos[b]
Richard van Hillegersberg[a]

[a]Department of Surgery, G04.228, University Medical Center Utrecht, Utrecht, The Netherlands; [b]First Department of Surgery, National and Kapodistrian University of Athens, Laikon General Hospital, Athens, Greece

Keywords
Minimally invasive esophagectomy · Robot-assisted minimally invasive esophagectomy · Esophageal cancer

Abstract
Minimally invasive esophagectomy (MIE) was introduced in the 1990s with the aim to decrease the rate of respiratory complications associated with thoracotomy, along with the benefits of reduced morbidity and a quicker return to normal activities provided by minimally invasive techniques. However, MIE is not routinely applied as a standard approach for esophageal cancer worldwide, due to the high technical complexity of this minimally invasive procedure. Therefore, the open transthoracic esophagectomy is considered to be the gold standard for resectable esophageal cancer worldwide nowadays. In this article, the current status of conventional MIE and robot-assisted minimally invasive thoraco-laparoscopic esophagectomy will be reviewed.

Minimally Invasive Esophagectomy

In 1992, Cuschieri et al. [1] were the first who reported on minimally invasive esophagectomy (MIE) in 5 patients. In this series, the esophagus was mobilized by video-assisted thoracoscopic surgery combined with laparotomy. This technique, which later was included in the category of hybrid techniques, was the first combining thoracoscopic technique and laparotomy [1, 2, 3]. The study was followed by a few reports on minimally invasive techniques in esophageal resection, with many surgeons worldwide starting to adopt techniques and combinations of thoracotomy-thoracoscopy and laparotomy-laparoscopy, in order to become competent in MIE. Collard et al. [4] and McAnena et al. [5] also reported on throracoscopic resection, while DePaula et al. [6] reported on laparoscopic transhiatal resection in 1995.

P.C.S. and D.S. contributed equally to this work.
Contribution from the EDS Visceral Medicine Course 2018, Moscow, Russia, February 27 until March 1, 2018. This Postgraduate Course was supported in part by United European Gastroenterology.

KARGER

karger@karger.com
www.karger.com/dsu

Richard van Hillegersberg
Department of Surgery
University Medical Center Utrecht
Heidelberglaan 100, NL–3584 CX Utrecht (The Netherlands)
E-Mail R.vanHillegersberg@umcutrecht.nl

It was not until 2003, when Luketich et al. [7] reported the first large series of totally MIE (thoracoscopy plus laparoscopy) and showed an impressively low morbidity and mortality in 222 patients. In this study, pneumonia rate and 30-day mortality were 7.7 and 1.4%. Until recently, MIE was performed with the patient in the left lateral decubitus position. However, this approach requires total lung collapse and is therefore often accompanied by serious pulmonary complications. In order to standardize the technique of MIE and consequently overcome the associated technical difficulties, MIE in prone position was published by Palanivelu et al. [8] in a large patient cohort. This study showed that prone position is feasible, has lower respiratory complications, and a shorter operative time because of the excellent exposure of the operative field and the better ergonomics of the surgeon's stance [9]. On the other hand, urgent conversion to a classic thoracotomy, if needed, is probably more difficult in the prone position. Esophageal resection in a modified semiprone position was later adopted by surgeons around the world, as a solution to overcome this problem, while retaining the benefits of the prone position [10].

Following the initial published studies, MIE subsequently gained an increasing acceptance. Overall, total MIE via a transthoracic approach transthoracic esophagectomy (TTE) is certainly the most common modality of esophageal resection [11]. The first published randomized control trial comparing outcomes after minimally invasive TTE and open TTE was the Traditional Invasive vs. Minimally Invasive (TIME) trial in 2012. This study is still considered the cornerstone of MIE studies, assessing several perioperative outcomes, as well as oncologic outcomes, and quality of life measurements, even though the study was primarily powered to assess perioperative complications [12, 13]. To date, together with the one published RCT (TIME), there are 8 meta-analyses completed between 2009 and 2017, which have compared perioperative and oncologic outcomes of MIE and OE (Tables 1, 2) [14–21].

Several intraoperative parameters have been studied in the medical literature since the adoption of MIE techniques, such as operative time and associated blood loss. Total operative time has been shown to be consistently longer for MIE than for OE. TIME trial reported average operative time to be 329 min for MIE-TTE vs. 299 min for open TTE ($p = 0.002$) [13], which was consistent with the meta-analysis by Nagpal et al. [15] who found longer operative time during MIE when compared to OE. Kunisaki et al. [22], Shiraishi et al. [23], and Yibulayin et al. [18] have also reported longer duration, perhaps due to surgeons' learning curve of a new and complex technique. Furthermore, blood loss in MIE group was found to be lower than in OE group in studies published by Giugliano et al. [11], Nagpal et al. [15], and Guo et al. [19] The TIME trial reported an average blood loss of 200 mL for MIE patients compared to 475 mL for OE patients [13].

As far as total complication rates are concerned, a meta-analysis published by Yibulayin et al. [18], including 5,991 cases of esophageal resections, reported 41.5% for the MIE group, whereas 48.2% were allocated to OE group ($p < 0.05$). This finding was similar to that reported by Guo et al. [19] who showed significant differences in total complications between the open group and MIE group (risk ratio [RR] 1.20; 95% CI 1.08–1.34; $p = 0.0009$).

In the same studies, several perioperative complications have been studied in detail. First of all, the TIME trial [13] initially reported a significant decrease in pulmonary infection rates in MIE group of patients when compared with OE group (29 vs. 57%, $p = 0.005$), a finding similar to that reported in meta-analyses by Napgal et al. [15] and Guo et al. [19]. Similarly, Lv et al. [20] showed that patients had less respiratory complications (RR 0.74, 95% CI 0.58–0.94, $p = 0.01$) with MIE, as Xiong et al. [21]. Another potentially lethal complication following esophageal surgery is anastomotic leak. The rate of this complication ranges from 0 to 12% and has proved to be similar between MIE and OE groups [11]. Yibulayin et al. [18] in their meta-analysis, which included 50 studies that reported anastomotic leak rates, indicated that there is no evidence of reduced anastomotic leak in MIE group (OR 1.023, 95% CI 0.870–1.202, p value = 0.785) in accordance with Zhou et al. [24] conclusion [21].

Cardiovascular complications such as arrhythmia, heart failure, acute myocardial infarction, deep vein thrombosis, and pulmonary embolism were less apparent in MIE group of patients (OR 0.770, 95% CI 0.681–0.872, p value <0.05) as Zhou et al. [24] have also found in their study [18]. On the other hand, gastrointestinal complications, including gastric tube necrosis, anastomotic stricturen and delayed gastric emptying were the same between MIE and OE groups [18]. Surgical technique-related complications such as splenic laceration, tracheal laceration, pneumothorax, chylothorax, and hemorrhage were fewer in MIE patients (OR 0.770, 95% CI 0.681–0.872, p value <0.05) as opposed to Rizk et al. [25] study.

Recurrent laryngeal nerve palsy incidence has been reported in previous studies to range between 3.6 and 7%

Table 1. Meta-analyses comparing short-term results of MIE and OE

	Year of publication	Number of patients included, *n*	Intraoperative blood loss	Total operative time	Hospital stay	Total complications	Pulmonary complications	Anastomotic leak
Xiong et al. [21]	2017	488	More in OE **$p = 0.001$**	Longer in MIE **$p < 0.001$**	Shorter in MIE **$p < 0.001$**	NR	Lower in MIE **$p < 0.001$**	NSD
Yibulayin et al. [18]	2016	15,790	More in OE **$p = 0.05$**	Longer in MIE **$p < 0.05$**	Shorter in MIE **$p < 0.05$**	Lower in MIE **$p < 0.05$**	Lower in MIE **$p < 0.05$**	NSD
Lv et al. [20]	2016	6,025	More in OE **$p = 0.0009$**	Longer in MIE **$p = 0.009$**	NR	NR	Lower in MIE **$p = 0.01$**	NSD
Guo et al. [19]	2016	1,549	More in OE **$p = 0.001$**	NR	NR	Lower in MIE **$p = 0.0009$**	Lower in MIE **$p = 0.03$**	NSD
Dantoc et al. [17]	2012	1,212	NR	NR	NR	NR	NR	NR
Nagpal et al. [15]	2010	1,284	More in OE **$p < 0.001$**	Longer in MIE **$p < 0.001$**	Shorter in MIE **$p = 0.004$**	Lower in MIE **$p = 0.007$**	Lower in MIE **$p = 0.04$**	Lower in MIE **$p = 0.02$**
Sgourakis et al. [16]	2010	1,008	NR	NR	NR	Lower in MIE **$p < 0.05$**	NSD	NSD
Biere et al. [14]	2009	1,061	More in OE (in most of the included studies) ***p* value** NR	Longer in MIE (in most of the included studies) ***p* value** NR	Shorter in MIE (in most of the included studies) ***p* value** NR	NSD (in most of the included studies) ***p* value** NR	NSD	Lower in MIE **$p = 0.03$**

MIE, minimally invasive esophagectomy; OE, open esophagectomy; NR, not reported; NSD, not statistically significant.

[7]. Despite the fact that TIME trial and Xiong et al. [21] showed a significantly lower rate of vocal cord palsies and recurrent laryngeal nerve injuries, meta-analyses contacted by Nagpal et al. [15], Guo et al. [19], and Sgourakis et al. [16] failed to show any difference.

Another concern after the implementation of MIE was the length of hospital stay. Rodham et al. [26] found that those who underwent MIE left hospital 3 days earlier on average than those in OE group, whereas Guo et al. [19] observed a mean reduction of 1.8 days.

Despite less blood loss, less pulmonary complications, and shorter hospital stays in MIE group, several studies have failed to show reduced mortality rates after minimally invasive techniques [12, 13]. On the contrary, Yibulayin et al. [18] reported strong evidence of reduced mortality (OR 0.668, 95% CI 0.539–0.827, *p* value <0.05).

Oncologic outcomes in esophagectomized patients include rate of R0 resection, lymph node retrieval, disease free, and overall survival. R0 resection rate was found to be 92% in MIE and 84% in OE [3]. Burdall et al. [27] described reduction of R1 resection in their published retrospective analysis in MIE patients. More specifically, they found R1 resections of about 6.1% in MIE and 15.6% in OE.

The studies comparing the number of lymph nodes harvested in MIE compared to OE show that the resection is at least equal in MIE patients. In their studies, Osugi et al. [28] and Smithers et al. [29] reported an equal number of lymph nodes. Similarly, Biere et al. [12]

Table 2. Meta-analyses comparing oncologic outcomes of MIE and OE

	Year of publication	Number of patients included, *n*	Harvested lymph nodes	R0 resection	30-day mortality	1-year survival	2-year survival	3-year survival	5-year survival
Xiong et al. [21]	2017	488	NSD	NR	NSD	NR	NR	NR	NR
Yibulayin et al. [18]	2016	15,790	NSD	NR	Lower in MIE **$p < 0.05$**	NR	NR	NR	NR
Lv et al. [20]	2016	6,025	NSD	NSD	NSD	NR	NR	NR	NR
Guo et al. [19]	2016	1,549	NR	NR	NSD	NSD	Better in MIE **$p = 0.045$**	NR	NSD
Dantoc et al. [17]	2012	1,212	More in MIE **$p = 0.04$**	NR	NSD	NSD	NR	NSD	NSD
Nagpal et al. [15]	2010	1,284	NSD	NR	NSD	NR	NR	NR	NR
Sgourakis et al. [16]	2010	1,008	NSD	NR	NSD	NSD	NSD	NSD	NSD
Biere et al. [14]	2009	1,061	NSD (in most of the included studies) ***p* value** NR	NR	NSD	NR	NR	NR	NR

MIE, minimally invasive esophagectomy; OE, open esophagectomy; NR, not reported; NSD, not statistically significant.

confirmed these results in a randomized trial. On the other hand, Dantoc et al. [17] found an increased number of harvested lymph nodes during MIE compared to OE (16 vs. 10, $p = 0.025$). A recently published population-level study from Duke University also noted a higher number of lymph nodes (15 vs 13; $p = 0.016$) [30]. Since the adoption of MIE in prone position, the average number of harvested lymph nodes is increasing when compared to MIE in lateral decubitus position, which was used in the beginning of minimally invasive techniques [9].

In view of long-term results, Osugi et al. [28] reported comparable 3-year survival rates following hybrid MIE and OE in patients that underwent 3-field lymphadenectomy. Furthermore, Smithers et al. [29] described comparable 3-year survival rates following 2-field esophagectomies. In their systematic review, Dantoc et al. [31] described comparable 3-year survival rates but suggested an improved 1-year survival for MIE compared with OE (84.3 vs. 76.9%, $p = 0.07$). In a population-based analysis of 18,673 esophagectomies performed in England between 1996/1997 and 2007/2008, Lazzarino et al. [32] found a statistical trend toward increased 1-year survival following MIE when compared to OE. Guo et al. [19] indicated in their meta-analysis that MIE does not compromise the long-term curative effect for patients with esophageal cancer and in fact has a better 2-year survival rate.

Robot-Assisted Minimally Invasive Thoraco-Laparoscopic Esophagectomy

In 2003, robot-assisted minimally invasive thoraco-laparoscopic esophagectomy (RAMIE) was developed to overcome the technical limitations of MIE [33]. Robotic surgery benefits from a stable 3-dimensional, magnified view and articulated instruments enabling precise dissection with 7 degrees of freedom of movement [33]. For the development of RAMIE by our group, a 5-stage development process for the assessment of surgical innovation (IDEAL) was followed [34].

Our initial experience, with 21 patients with resectable esophageal cancer undergoing RAMIE (stage 1, Idea), was described in a prospective cohort study in 2006 [33]. Technical feasibility and early technical modifications were described in 2009 in a prospective cohort study including 47 patients (stage 2a, Development) [35]. In 2015, the oncological long-term follow-up was described in a prospective cohort study including 108 patients [36] (stage 2b, Exploration). Stage 1–2b focused on the development of a new technique and the description of its outcomes. Before analysis of a novel surgical technique with the current standards can be performed, the learning curve of the novel technique has to be completed. In 2012, when the trial was initiated, our center was the only center worldwide that had clearly passed the learning phase with a joint experience of >170 RAMIE procedures [37]. Stage 3 (Assessment) aims to assess effectiveness against current standards. For resectable esophageal cancer, the open TTE is considered to be the gold standard worldwide [3]. Therefore, we compared RAMIE to open TTE in a randomized controlled trial.

As no other institution worldwide had comparable surgical expertise, it was decided to perform a single center randomized controlled trial. The trial design, rationale, and the protocol were published in 2012 [38].

Between January 2012 and August 2016, 236 patients with resectable intrathoracic esophageal cancer were screened in the UMC Utrecht, of whom 138 patients were considered eligible for the ROBOT trial. Finally, 112 patients (allocation ratio 81%) were randomized in a 1:1 fashion to undergo either RAMIE or open TTE, and 109 patients were included in the intention to treat analysis. The primary endpoint of the occurrence of overall surgery-related postoperative complications (MCDC grade ≥2) occurred in 32 of 54 patients after RAMIE (59%) and in 44 of 55 patients after open TTE (80%; RR with RAMIE 0.74 [0.57–0.96; p = 0.02]). Pulmonary complications were the most frequently observed secondary endpoint and occurred in 17 of 54 patients in the RAMIE group (32%) and in 32 of 55 patients in the open TTE group (58%; RR 0.54 [0.34–0.85; p = 0.005]). Cardiac complications were observed in 17 of 45 patients in the RAMIE group (22%) and in 26 of 55 patients in the open TTE group (47%; RR 0.47 [0.27–0.83; p = 0.006]). Functional recovery at postoperative day 14 was significantly better in the RAMIE group (38 of 54 patients (70%) compared to the open TTE group (28 of 55 patients, 51%; RR 1.48 [1.03–2.13; p = 0.04]). Both at discharge as well as 6 weeks post-discharge, QoL was higher after RAMIE compared to open TTE (mean difference 13.4 (2.0–24.7, p = 0.02) and 11.1 (1.0–21.1; p = 0.03), respectively; Table 3) [39]. Mean postoperative pain (VAS) during the first 14 days was significantly lower after RAMIE compared to open TTE (1.86 vs. 2.62, p = 0.000) [39].

It was concluded that RAMIE was associated with a significant lower percentage of postoperative complications compared to open TTE. RAMIE was also associated with less blood loss, a lower percentage of pulmonary complications, and cardiac complications compared to open TTE, with lower postoperative pain and better functional recovery and short term quality of life. Oncologic outcomes, such as the percentage of radical resections (R0), the number of resected lymph nodes, and disease-free and overall survival were comparable between groups and in concordance with the highest standards worldwide nowadays [39].

Stage 4 (Long-term study) of the IDEAL recommendations is currently assessed with the extension of indications for RAMIE in upper oesophageal cancer with upper mediastinal lymph node metastases, cT4b oesophageal cancer following downstaging with neoadjuvant therapy or other types of salvage surgery, and registration of cases in the national registry database the Dutch Upper Gastrointestinal Cancer Audit [40].

The RAMIE technique is now proctored to other centers worldwide. We showed that the first 70 cases formed the initial learning phase for RAMIE and that structured proctoring program reduced the learning phase to 24 cases, which corresponded to a reduction of 66% in the number of operations and a reduction of 76% in time [37].

We started with a proctoring program for surgeons from other hospitals and designed a structured training program for RAMIE. The following conditions have to be applicable in order for the proctoring program to be successful for newly introduced surgeons: 2 motivated surgeons experienced in esophageal surgery and preferably in minimally invasive gastrointestinal surgery, a dedicated anesthesiologist, RAMIE specialized scrub nurses, a sufficient case load (>20 cases/year), and guaranteed access to a robotic system [37, 40]. The program started with 2–3 case observations in our RAMIE expert center, followed by a basic and dedicated esophageal robotic course in a cadaveric lab. The first case at the own hospital was always proctored by an expert. Hereafter, the

Dig Surg 2020;37:93–100
DOI: 10.1159/000497456

Table 3. Postoperative statistics ROBOT trial (n = 109)

	RAMIE (n = 54)	OTE (n = 55)	p value
Primary endpoint, n (%)			
Related complications (MCDC 2, 3, 4, and 5)	32 (59)	44 (80)	0.02
No related complications (MCDC 0, 1)	22 (41)	11 (20)	
Secondary endpoints, n (%)			
Pulmonary complications	17 (32)	32 (58)	0.005
Cardiac complications	12 (22)	26 (47)	0.006
Anastomotic leakage			0.57
Type I (conservative)	0 (0)	0 (0)	
Type II (nonsurgical intervention)	1 (2)	0 (0)	
Type III (surgical intervention)	12 (22)	11 (20)	
Chylothorax			0.69
Type I (dietary, low fat elemental formula gavage)	9 (17)	6 (11)	
Type II (total parenteral nutrition)	6 (11)	5 (9)	
Type III (operative)	2 (4)	1 (2)	
Recurrent laryngeal nerve injury			0.78
Type I (no therapy)	5 (9)	6 (11)	
In-hospital mortality	2 (4)	1 (2)	0.62*
30-day mortality	1 (2)	0 (0)	0.50*
Functional recovery within first 2 weeks, n (%)	38 (70)	28 (51)	0.04
Quality of life (QLQ–C30)			
Health-related quality of life (discharge)	57.9 (49.9–66.1)	44.6 (36.7–52.5)	0.02
Health-related quality of life (6 weeks)	68.7 (61.5–75.9)	57.6 (50.6–64.6)	0.03
Physical functioning (discharge)	54.5 (45.8–63.3)	41.0 (32.4–49.6)	0.03
Physical functioning (6 weeks)	69.3 (61.6–76.9)	58.6 (51.1–66.0)	0.049

RAMIE, robot-assisted minimally invasive esophagectomy.

proctor supervised the surgeon for the first 2–10 cases and reviewed the skills after the first 20–25 procedures [37, 40]. We have trained now 5 centers in Europe that are performing RAMIE as their preferred surgical approach with very good results. These results will be analyzed in the near future. In our opinion, it seems possible to reproduce the results for RAMIE in other centers, after passing the learning curve for RAMIE.

Discussion

Together with the previous randomized trial comparing MIE to open TTE (TIME-trial) [11], results of this randomized controlled trial provide evidence to use minimally invasive surgery for patients with resectable esophageal cancer aiming at improving postoperative outcomes and quality of life with comparable oncologic results.

The question arises whether RAMIE is superior to conventional MIE. To show the benefits of RAMIE over conventional MIE in a randomized trial would require a large number of patients as differences will be more subtle compared to the open surgical technique. Such a trial could only be performed in a worldwide multicenter fashion, where participating surgeons should be skilled in both conventional MIE and RAMIE and for both reasons, such a randomized controlled might not be feasible. A large number of patients included in national or worldwide prospective database registries, with a defined protocol for registering complications according to the definitions stated by the Esophagectomy Complications Consensus Group and reporting of patient comorbidities, could answer the question whether RAMIE or MIE is superior to open esophagectomy or to each other.

Differences between MIE and RAMIE in postoperative complications and oncologic outcomes might be marginal. Quality of life, better ergonomics for the surgeon, and cost effectiveness might be important endpoints in these prospective registry studies.

Disclosure Statement

R.H.: is a Proctor for Intuitive Surgical Inc.

References

1 Cuschieri A, Shimi S, Banting S. Endoscopic oesophagectomy through a right thoracoscopic approach. J R Coll Surg Edinb. 1992 Feb;37(1):7–11.

2 Qureshi YA, Dawas KI, Mughal M, Mohammadi B. Minimally invasive and robotic esophagectomy: evolution and evidence. J Surg Oncol. 2016 Nov;114(6):731–5.

3 Wullstein C, Ro-Papanikolaou HY, Klingebiel C, Ersahin K, Carolus R. Minimally Invasive Techniques and Hybrid Operations for Esophageal Cancer. Viszeralmedizin. 2015 Oct;31(5):331–6.

4 Collard JM, Lengele B, Otte JB, Kestens PJ. En bloc and standard esophagectomies by thoracoscopy. Ann Thorac Surg. 1993 Sep;56(3):675–9.

5 McAnena OJ, Rogers J, Williams NS. Right thoracoscopically assisted oesophagectomy for cancer. Br J Surg. 1994 Feb;81(2):236–8.

6 DePaula AL, Hashiba K, Ferreira EA, de Paula RA, Grecco E. Laparoscopic transhiatal esophagectomy with esophagogastroplasty. Surg Laparosc Endosc. 1995 Feb;5(1):1–5.

7 Luketich JD, Alvelo-Rivera M, Buenaventura PO, Christie NA, McCaughan JS, Litle VR, et al. Minimally invasive esophagectomy: outcomes in 222 patients. Ann Surg. 2003 Oct;238(4):486–94.

8 Palanivelu C, Prakash A, Senthilkumar R, Senthilnathan P, Parthasarathi R, Rajan PS, 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 Jul;203(1):7–16.

9 Koyanagi K, Ozawa S, Tachimori Y. Minimally invasive esophagectomy performed with the patient in a prone position: a systematic review. Surg Today. 2016 Mar;46(3):275–84.

10 Seesing MF, Goense L, Ruurda JP, Luyer MD, Nieuwenhuijzen GA, van Hillegersberg R. Minimally invasive esophagectomy: a propensity score-matched analysis of semiprone versus prone position. Surg Endosc. 2018 Jun;32(6):2758–65.

11 Giugliano DN, Berger AC, Rosato EL, Palazzo F. Total minimally invasive esophagectomy for esophageal cancer: approaches and outcomes. Langenbecks Arch Surg. 2016 Sep;401(6):747–56.

12 Biere SS, van Berge Henegouwen MI, Maas KW, Bonavina L, Rosman C, Garcia JR, et al. Minimally invasive versus open oesophagectomy for patients with oesophageal cancer: a multicentre, open-label, randomised controlled trial. Lancet. 2012 May;379(9829):1887–92.

13 Biere SS, Maas KW, Bonavina L, Garcia JR, van Berge Henegouwen MI, Rosman C, et al. Traditional invasive vs. minimally invasive esophagectomy: a multi-center, randomized trial (TIME-trial). BMC Surg. 2011 Jan;11(1):2.

14 Biere SS, Cuesta MA, van der Peet DL. Minimally invasive versus open esophagectomy for cancer: a systematic review and meta-analysis. Minerva Chir. 2009 Apr;64(2):121–33.

15 Nagpal K, Ahmed K, Vats A, Yakoub D, James D, Ashrafian H, et al. Is minimally invasive surgery beneficial in the management of esophageal cancer? A meta-analysis. Surg Endosc. 2010 Jul;24(7):1621–9.

16 Sgourakis G, Gockel I, Radtke A, Musholt TJ, Timm S, Rink A, et al. Minimally invasive versus open esophagectomy: meta-analysis of outcomes. Dig Dis Sci. 2010 Nov;55(11):3031–40.

17 Dantoc M, Cox MR, Eslick GD. Evidence to support the use of minimally invasive esophagectomy for esophageal cancer: a meta-analysis. Arch Surg. 2012 Aug;147(8):768–76.

18 Yibulayin W, Abulizi S, Lv H, Sun W. Minimally invasive oesophagectomy versus open esophagectomy for resectable esophageal cancer: a meta-analysis. World J Surg Oncol. 2016 Dec;14(1):304.

19 Guo W, Ma X, Yang S, Zhu X, Qin W, Xiang J, et al. Combined thoracoscopic-laparoscopic esophagectomy versus open esophagectomy: a meta-analysis of outcomes. Surg Endosc. 2016 Sep;30(9):3873–81.

20 Lv L, Hu W, Ren Y, Wei X. Minimally invasive esophagectomy versus open esophagectomy for esophageal cancer: a meta-analysis. OncoTargets Ther. 2016 Oct;9:6751–62.

21 Xiong WL, Li R, Lei HK, Jiang ZY. Comparison of outcomes between minimally invasive oesophagectomy and open oesophagectomy for oesophageal cancer. ANZ J Surg. 2017 Mar;87(3):165–70.

22 Kunisaki C, Hatori S, Imada T, Akiyama H, Ono H, Otsuka Y, et al. Video-assisted thoracoscopic esophagectomy with a voice-controlled robot: the AESOP system. Surg Laparosc Endosc Percutan Tech. 2004 Dec;14(6):323–7.

23 Shiraishi T, Kawahara K, Shirakusa T, Yamamoto S, Maekawa T. Risk analysis in resection of thoracic esophageal cancer in the era of endoscopic surgery. Ann Thorac Surg. 2006 Mar;81(3):1083–9.

24 Zhou C, Ma G, Li X, Li J, Yan Y, Liu P, et al. Is minimally invasive esophagectomy effective for preventing anastomotic leakages after esophagectomy for cancer? A systematic review and meta-analysis. World J Surg Oncol. 2015 Sep;13(1):269.

25 Rizk NP, Bach PB, Schrag D, Bains MS, Turnbull AD, Karpeh M, et al. The impact of complications on outcomes after resection for esophageal and gastroesophageal junction carcinoma. J Am Coll Surg. 2004 Jan;198(1):42–50.

26 Rodham P, Batty JA, McElnay PJ, Immanuel A. Does minimally invasive oesophagectomy provide a benefit in hospital length of stay when compared with open oesophagectomy? Interact Cardiovasc Thorac Surg. 2016 Mar;22(3):360–7.

27 Burdall OC, Boddy AP, Fullick J, Blazeby J, Krysztopik R, Streets C, et al. A comparative study of survival after minimally invasive and open oesophagectomy. Surg Endosc. 2015 Feb;29(2):431–7.

28 Osugi H, Takemura M, Higashino M, Takada N, Lee S, Kinoshita H. A comparison of video-assisted thoracoscopic oesophagectomy and radical lymph node dissection for squamous cell cancer of the oesophagus with open operation. Br J Surg. 2003 Jan;90(1):108–13.

29 Smithers BM, Gotley DC, Martin I, Thomas JM. Comparison of the outcomes between open and minimally invasive esophagectomy. Ann Surg. 2007 Feb;245(2):232–40.

30 Markar SR, Wiggins T, Antonowicz S, Zacharakis E, Hanna GB. Minimally invasive esophagectomy: lateral decubitus vs. prone positioning; systematic review and pooled analysis. Surg Oncol. 2015 Sep;24(3):212–9.

31 Dantoc MM, Cox MR, Eslick GD. Does minimally invasive esophagectomy (MIE) provide for comparable oncologic outcomes to open techniques? A systematic review. J Gastrointest Surg. 2012 Mar;16(3):486–94.

32 Lazzarino AI, Nagpal K, Bottle A, Faiz O, Moorthy K, Aylin P. Open versus minimally invasive esophagectomy: trends of utilization and associated outcomes in England. Ann Surg. 2010 Aug;252(2):292–8.

33 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 Sep;20(9):1435–9.

34 McCulloch P, Altman DG, Campbell WB, Flum DR, Glasziou P, Marshall JC, et al.; Balliol Collaboration. No surgical innovation without evaluation: the IDEAL recommendations. Lancet. 2009 Sep;374(9695):1105–12.

35 Boone J, Schipper ME, Moojen WA, Borel Rinkes IH, Cromheecke GJ, van Hillegersberg R. Robot-assisted thoracoscopic oesophagectomy for cancer. Br J Surg. 2009 Aug;96(8):878–86.

36 van der Sluis PC, Ruurda JP, Verhage RJ, van der Horst S, Haverkamp L, Siersema PD, et al. Oncologic Long-Term Results of Robot-Assisted Minimally Invasive Thoraco-Laparoscopic Esophagectomy with Two-Field Lymphadenectomy for Esophageal Cancer. Ann Surg Oncol. 2015 Dec;22(S3 Suppl 3):S1350–6.

37 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 Jul;106(1):264–71.

38 van der Sluis PC, Ruurda JP, van der Horst S, Verhage RJ, Besselink MG, Prins MJ, et al. Robot-assisted minimally invasive thoraco-laparoscopic esophagectomy versus open transthoracic esophagectomy for resectable esophageal cancer, a randomized controlled trial (ROBOT trial). Trials. 2012 Nov;13(1):230.

39 van der Sluis PC, van der Horst S, May AM, Schippers C, Brosens LA, Joore HC, et al. Robot-assisted Minimally Invasive Thoracolaparoscopic Esophagectomy Versus Open Transthoracic Esophagectomy for Resectable Esophageal Cancer: A Randomized Controlled Trial. Ann Surg. 2018 Oct;1.

40 van Hillegersberg R, Seesing MF, Brenkman HJ, Ruurda JP. [Robot-assisted minimally invasive esophagectomy. German version]. Chirurg. 2016 Aug;87(8):635–42.