Review Article

Robot-assisted minimally invasive esophagectomy (RAMIE) improves perioperative outcomes: a review

B. Feike Kingma, Michiel F. G. de Maat, Sylvia van der Horst, Pieter C. van der Sluis, Jelle P. Ruurda, Richard van Hillegersberg

Department of Surgery, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands

Contributions: (I) Conception and design: All authors; (II) Administrative support: BF Kingma, MF de Maat; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: None; (V) Data analysis and interpretation: None; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Michiel F. G. de Maat. Department of Surgery, University Medical Center Utrecht, Heidelberglaan 100, 3584 CX, Utrecht, The Netherlands. Email: m.f.g.demaat-3@umcutrecht.nl.

Abstract: Robotic assisted minimal invasive esophagectomy (RAMIE) is increasingly applied as a clinically and oncologically safe technique in the surgical treatment of esophageal cancer. This review focuses on the advantages and potential opportunities of RAMIE to improve the perioperative and oncological outcomes based on the evidence from current literature. In addition, critical notes on aspects such as procedure duration and costs are addressed in this paper.

Keywords: Robotic surgery; esophagectomy; enhanced recovery after surgery (ERAS)

Submitted Nov 08, 2018. Accepted for publication Nov 21, 2018.
doi: 10.21037/jtd.2018.11.104
View this article at: http://dx.doi.org/10.21037/jtd.2018.11.104

Introduction

For patients with locally advanced esophageal cancer, neoadjuvant chemoradiotherapy followed by esophagectomy can achieve a 5-year survival rate of approximately 40–50% (1-3). However, esophagectomy is traditionally associated with considerable postoperative morbidity and mortality (4).

Over the last decades, advancements such as centralization of care, development of enhanced recovery protocols, and application of minimally invasive techniques have improved the perioperative outcomes for surgically treated esophageal cancer patients (5-7). Nonetheless, a recent international benchmarking study concluded that a complication rate of around 60% is likely a realistic representation of the current practice for esophagectomy in high-volume centers (8). To improve the outcome for patients undergoing esophagectomy for cancer, each perioperative facet needs to be optimized. One of the most recent developments is the introduction of robot-assisted minimally invasive esophagectomy (RAMIE) (9,10). The aim of this review was to describe how RAMIE could contribute to improving perioperative care and outcomes for esophageal cancer patients.

Conventional minimally invasive esophagectomy (MIE)—benefits and limitations

MIE was first described in the 1992 and has since then been increasingly applied for the treatment of patients with esophageal cancer, aiming to improve patient outcome by reducing surgical trauma and its sequelae in terms of immunosuppression (7,11). In the only randomized controlled trial so far (i.e., the TIME trial), MIE was found to be superior to open esophagectomy in terms of intraoperative blood loss, acute immunological response, postoperative pulmonary infections, length of hospital stay, postoperative pain scores, and quality of life (12,13). Furthermore, in contrast to initial concerns regarding the oncological quality of MIE, lymph node yield and 3-year survival were equivalent when compared to open esophagectomy (12,14). These findings were in line with meta-analyses, indicating that MIE provides short-term

advantages and preserves oncological quality (15).

Although MIE seems to improve at least short-term patient outcome, it is a highly complex procedure to master. Especially the thoracoscopic part of MIE is technically demanding when using conventional minimally invasive techniques, which is mostly due to the combination of two-dimensional vision, mirrored intracorporeal movements of the instruments, moving target anatomy, and nearby vital structures that need to be avoided (e.g., aorta, pulmonary veins, trachea, main bronchi). The technical complexity of MIE is emphasized by a recent multicenter study that investigated the learning curve when transiting from MIE with a cervical anastomosis to MIE with an intrathoracic anastomosis (16). Even though all participating centers where experienced in performing MIE with a cervical anastomosis, the learning curve of a minimally invasive intrathoracic anastomosis was found to be as much as 119 cases when taking anastomotic leakage as the parameter of proficiency (16). As the anastomotic leakage rate dropped from 18.8% (first time quintile) to 4.5% (fifth time quintile), the authors concluded that patients are exposed to an increased risk of surgical morbidity during such a learning phase (16). The learning phase of MIE was also considered to be a likely explanation of the higher re-operation rates that were found when compared to open esophagectomy in multiple population-based studies in Japan, the United Kingdom, The Netherlands, and the United States (17-20). Considering these findings, it appears that the technical complexity of MIE requires a substantial learning phase, which may take several years to complete for centers with a relatively low caseload. Effective training programs and the centralization of esophageal surgical care to ensure sufficient case load are probably key to optimize the learning curve. Nonetheless, other technical limitations will remain when using conventional minimally invasive techniques in MIE, such as the fulcrum effect and the limited range of motion of the instrument tips, which might limit the global spread of this technique. This may explain the findings from a survey amongst esophageal surgeons in 2014, which indicated that only 43% of the respondents had reported MIE as their preferred approach (7). A hybrid procedure, which combines a laparoscopic abdominal phase with a conventional thoracotomy for the most challenging part, has been suggested as an alternative to MIE. A randomized controlled trial comparing hybrid versus open esophagectomy has been conducted and its full results are expected to be published soon (21).

RAMIE *vs.* open esophagectomy

Robotic surgical systems were developed to aid in overcoming the technical limitations of conventional minimally invasive surgery. Such systems create an enhanced three-dimensional vision of the surgical field and can translate the surgeon's natural hand movements into corresponding tremor-less actions of the intracorporeal instruments. RAMIE was introduced in 2003 and found to be a safe technique with good oncological outcomes in the first reported case series (9,10,22). Although these results were confirmed in a systematic review, the available evidence was limited to retrospective and prospective case series at that moment (23). Therefore, the ROBOT trial was conducted, which compared RAMIE to open esophagectomy regarding postoperative morbidity, mortality, and survival (24). A total of 112 patients were randomized in a high-volume tertiary referral center that was experienced in both techniques (24). The primary endpoint was the percentage of overall surgery-related postoperative complications, with complications being defined as those with a modified Clavien-Dindo classification (MCDC) of 2 or higher (24). The overall complication rate was significantly lower in the RAMIE group (59% *vs.* 80%), which was likely attributable to significantly lower rates of pulmonary complications (32% *vs.* 58%) and cardiac complications (47% *vs.* 22%) (25). Furthermore, RAMIE was associated with less intraoperative blood loss, lower postoperative pain scores, faster functional recovery, and better quality of life when compared to open esophagectomy (25). Radicality, lymph node yield, and overall survival did not differ between the groups, indicating that RAMIE offers short-term benefits while maintaining the high oncological standards of an open esophagectomy (25). As these results are in line with the findings from the TIME-trial, one can conclude that RAMIE is superior to open esophagectomy and a good alternative to MIE (12,25). Furthermore, it was reported that RAMIE can safely be performed with the patient in semiprone position (26), which can reduce the incidence of postoperative pulmonary complications (27). The duration of the learning curve for RAMIE has been reported to take 20–70 cases (28-30). One study found that the use of a structured training pathway that involved proctoring reduced the learning curve for RAMIE from 70 to 24 cases (30). In light of the increasing centralization of care, this seems to be a feasible number of cases in order to complete the learning curve within an acceptable time frame.

Despite the positive results from trials in favor of MIE and RAMIE, opponents of using minimally invasive techniques in esophageal surgery may emphasize the longer operating time when compared to open esophagectomy (12,25). Although the operating times are indeed longer when compared to open esophagectomy, the short term postoperative outcomes of RAMIE and MIE were found to be superior regardless (12,25). Literature is sparse and controversial regarding the relationship between the duration of surgery and outcomes after MIE (31,32). It therefore seems that limited evidence exists to support the hypothesis that the duration of surgery alone increases the risk of complications after esophagectomy. In combination with clear evidence of superiority of both RAMIE and MIE when compared to open esophagectomy (12,25), a longer duration of surgery should not be the argument to refrain from using minimally invasive techniques from patient outcome perspective.

Anastomotic technique in RAMIE

While the construction of a cervical anastomosis is identical for all surgical approaches to esophagectomy, many surgeons experience difficulties when creating an intrathoracic anastomosis during conventional MIE. Although some small case series have reported satisfactory results with a conventional minimally invasive hand-sewn intrathoracic esophagogastric anastomosis, this technique is exceedingly difficult and therefore MIE with a stapled intrathoracic anastomosis has become common practice (33,34). A stapled anastomosis can be made entirely mechanically in circular direction or semi-mechanically in linear direction. Currently available literature suggests that these stapling techniques are comparable regarding anastomotic leakage, while linear stapling might be associated with less benign stricture formation (35). Benign stricture formation is a troublesome long-term complication and prevention of this complication is important, since it can seriously impact the patient's ability to eat and often requires multiple endoscopic dilatations to resolve (36). Hand-sewing of the esophagogastric anastomosis has been suggested to reduce the incidence of benign stricture formation when compared to stapling, which was demonstrated by two meta-analyses (37,38). As no clear difference was found regarding anastomotic leakage and mortality in these studies (37,38), it could be justified to prefer a hand-sewn anastomosis for the restoration of gastro-intestinal continuity during esophagectomy. Robotic assistance can be of great use in this context, as it diminishes the difficulty of performing an intrathoracic hand-sewn anastomosis. By translating the surgeon's natural hand movements on the console to the surgical instruments with endo-wrists, a robotic system can achieve a large range of motion that enables manual suturing. Several case series have been published, which suggest that a robot-assisted hand-sewn intrathoracic anastomosis is safe and feasible for RAMIE (39-41). Prospective randomized studies are warranted to investigate hand-sewing versus stapling in terms of anastomotic leakage and benign stricture formation after RAMIE with an intrathoracic anastomosis.

Lymphadenectomy in RAMIE

Although the extent of nodal dissection in esophagectomy is well-studied, practice varies worldwide (42). The therapeutic value of a high nodal yield was recently demonstrated in a population-based study in the Netherlands that included 2,698 patients, which found that harvesting at least 15 lymph nodes was significantly associated with improved overall survival after esophagectomy (43). This was found across all subgroups of patients, including both squamous cell carcinoma and adenocarcinoma, both transthoracic and transhiatal approaches, both cN0 and cN+, and both ypN0 and ypN+ (43). A meta-analysis confirmed that a high lymph node yield significantly increases survival after esophagectomy in both Western and Eastern patient populations, regardless of whether neoadjuvant therapy has been administrated or not (44). The ROBOT trial showed that a mean of 27 and 25 lymph nodes were harvested in RAMIE and open esophagectomy, respectively (not significantly different), demonstrating that robotic surgery is at least comparable to open surgery in retrieving of a sufficient amount of lymph nodes (25).

The routine performance of lymphadenectomy in the paratracheal regions (levels 2, 3 and 4) is still under debate and is considered to be technically challenging in esophageal cancer surgery. Although many surgeons prefer to only perform a paratracheal dissection for proximal or mid-esophageal tumors, it should not be underestimated that upper mediastinal lymph node metastases are found in a substantial part of patients who undergo esophagectomy for more distal tumors (45). In a recent study in patients who underwent esophagectomy for mid- to distal esophageal tumors, it was found that dissection of the paratracheal

lymph nodes has a high therapeutic value in terms of long-term survival (46). However, the balance between oncological principles and the risk of iatrogenic damage is important and may have twofold consequences for the patient. Nearby vital structures such as the superior vena cava, recurrent laryngeal nerves, and the membranous part of the trachea and main bronchi all must be spared during dissection. Damage to these structures can result into severe complications such as severe bleeding with hemodynamic shock, permanent vocal cord paralysis, and fistulas between gastric conduit and major airway structures. However, the technical advantages of RAMIE enable a meticulous and safe dissection in these anatomical areas. More research is needed to investigate the benefits and risks of performing a paratracheal lymphadenectomy during esophagectomy in general and for the different surgical approaches.

The extent of nodal dissection can be further improved by near-infrared (NIR) fluorescent imaging modalities that are standardly integrated into the latest robotic platforms. This visual support can identify lymph nodes when a patient's tumor is injected preoperatively with labeled colloid or also preoperatively with indocyanine green (ICG) dye (47). Of course, it should be mentioned that conventional minimally invasive cameras are also available with NIR fluorescent imaging modes.

Extended indications and future developments in RAMIE

The use of RAMIE can be especially helpful in extended oncological indications. The thoracic aperture is notoriously difficult to access especially in open surgery, due to the scapula and transverse direction of the thoracotomy that hamper the reach of the instruments and view on this area. MIE achieves better vision and access to the upper thoracic structures by the placement of trocars in more proximal intercostal spaces. Conventional minimally invasive techniques, however, are hindered by straight instruments and a relatively great distance between the trocars and the target anatomy, which reduces the level of control. RAMIE can provide advantages in this regard, as better overview and an increased range of motion can be achieved. A recent study demonstrated that RAMIE can be applied to achieve adequate oncological results (i.e., lymph node yield and radicality rate) for patients with proximal tumors and lymph node involvement in the superior mediastinum, although an increased preoperative mortality (7–10%) and recurrent nerve injury rate (17%) were reported (48). Acute respiratory distress syndrome (ARDS) seemed to contribute to the increased mortality rate, which could possibly be explained by the combination of extended irradiation fields and the surgical trauma along the trachea and vagal nerve in the superior mediastinum. It must furthermore be noted that most cases of recurrent laryngeal nerve injury were classified as grade 1.

In addition to better access to the superior mediastinum, RAMIE can facilitate the resection of cT4b tumors that have been down-staged by chemoradiotherapy (49). The extended irradiation scheme [50 Gy, compared to 41.4 Gy for < cT4b tumors according the CROSS regimen (1)] frequently induces severe fibrosis, which can make dissection of the anatomical planes between the esophagus and the surrounding structures (i.e., main bronchus, aorta, atrium) very challenging. However, the stability of the robotic instruments and a zoomed-in three-dimensional view allow very precise exploration of the structures and could help in preventing damage with preservation of the resection margins. The first small case series shows that RAMIE can achieve a radical resection in 90% of the down-staged cT4b cases (49). Larger series and long-term results are still awaited.

The future opportunities of RAMIE probably reside in the fact that a surgical robot is a platform that can be developed further to keep up with technical developments such as artificial intelligence. Surgical literature is increasingly addressing the possibilities of machine learning in the context of surgical navigation and to enhance surgical training (50,51). Moreover, in the future it might be possible to interconnect robotic systems and thereby allow assistance from a peer surgeon in a remote center. The possibilities are expected to be explored further in the near future.

Costs perspectives of RAMIE

Cost-effectiveness is an important aspect when implementing new techniques in health care. RAMIE is frequently challenged in this context, since it requires the capital investment of a surgical robot and the relatively high costs of maintenance. However, postoperative complications are known to significantly increase the total treatment costs of esophagectomy and RAMIE is associated with less postoperative complications and shorter length of hospital stay when compared to open esophagectomy

(25,52). The necessary investments for RAMIE are therefore expected to be at least partially counterbalanced by the saving of costs that would be associated with the complications after open esophagectomy. Unfortunately, insight is lacking with regard to the cost-effectiveness of RAMIE when compared to conventional MIE, as no clear evidence is available to support clinical benefits of either technique that might be translated to a difference in treatment costs, apart from higher investment costs for RAMIE. This implies that RAMIE is probably a more expensive treatment modality when compared to conventional MIE at this moment. However, the additional possibilities that RAMIE offers over conventional MIE (e.g., hand-sewn intrathoracic anastomosis, operating on high mediastinal tumors, developments in the context of artificial intelligence) should not be overlooked in the discussion on cost-effectiveness. In addition, robotic assistance has been suggested to improve the surgeon's ergonomic conditions when operating. Musculoskeletal complaints are reported in 74% of conventional minimally invasive surgeons and a survey amongst urologists found that shoulder and neck complaints are significantly less common when performing robot-assisted surgery (53). As work-related musculoskeletal complaints can result in sick leave of surgeons and the costs attached to that (54), improving the ergonomic conditions in the operating room could positively contribute to the overall costs balance of surgical treatment. Lastly, the current situation is that only one manufacturer is producing surgical robotic systems that are permitted for use on human patients (i.e., Intuitive Surgical Inc.), which creates a monopoly position. The future arrival of competing companies on this marked will expectantly decrease the required investments for robotic surgical systems, which will likely result in altered costs perspectives for RAMIE.

Summary

Robotic systems can facilitate minimally invasive surgery by improving the view of the surgical field and increasing the range of motion of the instruments. A recent randomized controlled trial showed that RAMIE is superior to open esophagectomy in terms of postoperative complications, length of hospital stays, and quality of life. However, the clinical benefits of RAMIE over conventional MIE are not entirely clear yet and in this light the cost-effectiveness of RAMIE is frequently challenged. However, the technical advantages of robotic assistance provide opportunities that might lead to improvements in perioperative care. One potential technical advantage of RAMIE is the possibility to construct a hand-sewn instead of a stapled intrathoracic anastomosis, which might be less prone to developing benign strictures. Additionally, a meticulous dissection along the recurrent laryngeal nerves can be performed during RAMIE and the upper thoracic inlet can easily be reached to operate on tumors and involved lymph nodes located in the upper mediastinum. Furthermore, an important advantage of robotic systems is that they provide a computerized platform that can be developed further towards image guided surgery. More high-quality prospective studies are needed to provide more clarity regarding the advantages and opportunities of RAMIE in the treatment of esophageal cancer.

Acknowledgements

None.

Footnote

Conflicts of Interest: R van Hillegersberg and JP Ruurda are proctors for Intuitive Surgical Inc. (Sunnyvale, California, USA). Other authors have no conflicts of interest to declare.

References

1. Shapiro J, van Lanschot JJ, Hulshof MC, et al. Neoadjuvant chemoradiotherapy plus surgery versus surgery alone for oesophageal or junctional cancer (CROSS): long-term results of a randomised controlled trial. Lancet Oncol 2015;16:1090-8.
2. Goense L, van der Sluis PC, van Rossum PSN, et al. Perioperative chemotherapy versus neoadjuvant chemoradiotherapy for esophageal or GEJ adenocarcinoma: A propensity score-matched analysis comparing toxicity, pathologic outcome, and survival. J Surg Oncol 2017;115:812-20.
3. Visser E, Leeftink AG, van Rossum PS, et al. Waiting Time from Diagnosis to Treatment has no Impact on Survival in Patients with Esophageal Cancer. Ann Surg Oncol 2016;23:2679-89.
4. Hulscher JB, van Sandick JW, de Boer AG, et al. Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the esophagus. N Engl J Med 2002;347:1662-9.

5. Findlay JM, Tustian E, Millo J, et al. The effect of formalizing enhanced recovery after esophagectomy with a protocol. Dis Esophagus 2015;28:567-73.
6. Low DE, Allum W, De Manzoni G, et al. Guidelines for Perioperative Care in Esophagectomy: Enhanced Recovery After Surgery (ERAS((R))) Society Recommendations. World J Surg 2019;43:299-330.
7. Haverkamp L, Seesing MF, Ruurda JP, et al. Worldwide trends in surgical techniques in the treatment of esophageal and gastroesophageal junction cancer. Dis Esophagus 2017;30:1-7.
8. Low DE, Kuppusamy MK, Alderson D, et al. Benchmarking Complications Associated with Esophagectomy. Ann Surg 2019;269:291-8.
9. van Hillegersberg R, Boone J, Draaisma WA, et al. First experience with robot-assisted thoracoscopic esophagolymphadenectomy for esophageal cancer. Surg Endosc 2006;20:1435-9.
10. 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.
11. Cuschieri A, Shimi S, Banting S. Endoscopic oesophagectomy through a right thoracoscopic approach. J R Coll Surg Edinb 1992;37:7-11.
12. 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.
13. Maas KW, Biere SS, van Hoogstraten IM, et al. Immunological changes after minimally invasive or conventional esophageal resection for cancer: a randomized trial. World J Surg 2014;38:131-7.
14. 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.
15. Yibulayin W, Abulizi S, Lv H, et al. Minimally invasive oesophagectomy versus open esophagectomy for resectable esophageal cancer: a meta-analysis. World J Surg Oncol 2016;14:304.
16. van Workum F, Stenstra MH, Berkelmans GH, et al. Learning Curve and Associated Morbidity of Minimally Invasive Esophagectomy: A Retrospective Multicenter Study. Ann Surg 2019;269:88-94.
17. Sihag S, Kosinski AS, Gaissert HA, et al. 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; discussion 1288-9.
18. 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.
19. Seesing MF, Gisbertz SS, Goense L, et al. A Propensity Score Matched Analysis of Open Versus Minimally Invasive Transthoracic Esophagectomy in the Netherlands. Ann Surg 2017. [Epub ahead of print].
20. Mamidanna R, Bottle A, Aylin P, et al. Short-term outcomes following open versus minimally invasive esophagectomy for cancer in England: a population-based national study. Ann Surg 2012;255:197-203.
21. Briez N, Piessen G, Bonnetain F, et al. Open versus laparoscopically-assisted oesophagectomy for cancer: a multicentre randomised controlled phase III trial - the MIRO trial. BMC Cancer 2011;11:310.
22. van der Sluis PC, Ruurda JP, Verhage RJ, 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;22 Suppl 3:S1350-6.
23. Ruurda JP, van der Sluis PC, van der Horst S, et al. Robot-assisted minimally invasive esophagectomy for esophageal cancer: A systematic review. J Surg Oncol 2015;112:257-65.
24. van der Sluis PC, Ruurda JP, van der Horst S, 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;13:230.
25. 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.
26. Seesing MFJ, Goense L, Ruurda JP, et al. Minimally invasive esophagectomy: a propensity score-matched analysis of semiprone versus prone position. Surg Endosc 2018;32:2758-65.
27. Markar SR, Wiggins T, Antonowicz S, et al. Minimally invasive esophagectomy: Lateral decubitus vs. prone positioning; systematic review and pooled analysis. Surg

Oncol 2015;24:212-9.
28. Hernandez JM, Dimou F, Weber J, et al. Defining the learning curve for robotic-assisted esophagogastrectomy. J Gastrointest Surg 2013;17:1346-51.
29. Sarkaria IS, Rizk NP, Grosser R, et al. Attaining Proficiency in Robotic-Assisted Minimally Invasive Esophagectomy While Maximizing Safety During Procedure Development. Innovations (Phila) 2016;11:268-73.
30. van der Sluis PC, Ruurda JP, van der Horst S, et al. Learning Curve for Robot-Assisted Minimally Invasive Thoracoscopic Esophagectomy: Results From 312 Cases. Ann Thorac Surg 2018;106:264-71.
31. Goense L, van Rossum PS, Tromp M, et al. Intraoperative and postoperative risk factors for anastomotic leakage and pneumonia after esophagectomy for cancer. Dis Esophagus 2017;30:1-10.
32. Valsangkar N, Salfity HV, Timsina L, et al. Operative time in esophagectomy: Does it affect outcomes? Surgery 2018;164:866-71.
33. Agasthian T, Shabbir A. VATS hand sewn intrathoracic esophagogastric anastomosis. J Vis Surg 2017;3:90.
34. Elshaer M, Gravante G, Tang CB, et al. Totally minimally invasive two-stage esophagectomy with intrathoracic hand-sewn anastomosis: short-term clinical and oncological outcomes. Dis Esophagus 2018;31.
35. Zhou D, Liu QX, Deng XF, et al. Comparison of two different mechanical esophagogastric anastomosis in esophageal cancer patients: a meta-analysis. J Cardiothorac Surg 2015;10:67.
36. van Heijl M, Gooszen JA, Fockens P, et al. Risk factors for development of benign cervical strictures after esophagectomy. Ann Surg 2010;251:1064-9.
37. Markar SR, Karthikesalingam A, Vyas S, et al. Hand-sewn versus stapled oesophago-gastric anastomosis: systematic review and meta-analysis. J Gastrointest Surg 2011;15:876-84.
38. Liu QX, Min JX, Deng XF, et al. Is hand sewing comparable with stapling for anastomotic leakage after esophagectomy? A meta-analysis. World J Gastroenterol 2014;20:17218-26.
39. Cerfolio RJ, Bryant AS, Hawn MT. Technical aspects and early results of robotic esophagectomy with chest anastomosis. J Thorac Cardiovasc Surg 2013;145:90-6.
40. Egberts JH, Stein H, Aselmann H, et al. Fully robotic da Vinci Ivor-Lewis esophagectomy in four-arm technique-problems and solutions. Dis Esophagus 2017;30:1-9.
41. Zhang Y, Xiang J, Han Y, et al. Initial experience of robot-assisted Ivor-Lewis esophagectomy: 61 consecutive cases from a single Chinese institution. Dis Esophagus 2018;31.
42. Hagens ERC, van Berge Henegouwen MI, Cuesta MA, et al. The extent of lymphadenectomy in esophageal resection for cancer should be standardized. J Thorac Dis 2017;9:S713-23.
43. Visser E, van Rossum PSN, Ruurda JP, et al. Impact of Lymph Node Yield on Overall Survival in Patients Treated With Neoadjuvant Chemoradiotherapy Followed by Esophagectomy for Cancer: A Population-based Cohort Study in the Netherlands. Ann Surg 2017;266:863-9.
44. Visser E, Markar SR, Ruurda JP, et al. Prognostic Value of Lymph Node Yield on Overall Survival in Esophageal Cancer Patients: A Systematic Review and Meta-analysis. Ann Surg 2019;269:261-8.
45. Boone J, Schipper ME, Moojen WA, et al. Robot-assisted thoracoscopic oesophagectomy for cancer. Br J Surg 2009;96:878-86.
46. Miyata H, Sugimura K, Yamasaki M, et al. Clinical Impact of the Location of Lymph Node Metastases After Neoadjuvant Chemotherapy for Middle and Lower Thoracic Esophageal Cancer. Ann Surg Oncol 2019;26:200-8.
47. Kunzli HT, van Berge Henegouwen MI, Gisbertz SS, et al. Pilot-study on the feasibility of sentinel node navigation surgery in combination with thoracolaparoscopic lymphadenectomy without esophagectomy in early esophageal adenocarcinoma patients. Dis Esophagus 2017;30:1-8.
48. van der Horst S, Weijs TJ, Ruurda JP, et al. Robot-assisted minimally invasive thoraco-laparoscopic esophagectomy for esophageal cancer in the upper mediastinum. J Thorac Dis 2017;9:S834-42.
49. van Hillegersberg R, Seesing MF, Brenkman HJ, et al. Robot-assisted minimally invasive esophagectomy. Chirurg 2017;88:7-11.
50. Hashimoto DA, Rosman G, Rus D, et al. Artificial Intelligence in Surgery: Promises and Perils. Ann Surg 2018;268:70-6.
51. Hung AJ, Chen J, Gill IS. Automated Performance Metrics and Machine Learning Algorithms to Measure Surgeon Performance and Anticipate Clinical Outcomes in Robotic Surgery. JAMA Surg 2018;153:770-1.
52. Goense L, van Dijk WA, Govaert JA, et al. Hospital costs of complications after esophagectomy for cancer. Eur J Surg Oncol 2017;43:696-702.

53. Alleblas CC, de Man AM, van den Haak L, et al. Prevalence of Musculoskeletal Disorders Among Surgeons Performing Minimally Invasive Surgery: A Systematic Review. Ann Surg 2017;266:905-20.
54. Janki S, Mulder EE, IJzermans JNM, et al. Ergonomics in the operating room. Surg Endosc 2017;31:2457-66.

Cite this article as: Kingma BF, de Maat MF, van der Horst S, van der Sluis PC, Ruurda JP, van Hillegersberg R. Robot-assisted minimally invasive esophagectomy (RAMIE) improves perioperative outcomes: a review. J Thorac Dis 2019;11(Suppl 5):S735-S742. doi: 10.21037/jtd.2018.11.104

