Review Article on Current Management of Upper Gastrointestinal Malignancies

Controversies in the surgical management of esophageal adenocarcinoma

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Abstract: The incidence of esophageal adenocarcinoma (EAC) has risen dramatically over the last decade. Over this same period, our understanding and treatments have been revolutionized. Just over a decade ago, the majority of patients with locally advanced esophageal cancer went directly to surgery and our overall survival was bleak. Our current strategy for locally advanced esophageal adenocarcinoma is a multi-disciplinary approach. This approach consists of chemotherapy plus or minus radiation followed by surgical resection followed by adjuvant immunotherapy with the presence of any residual disease. Therefore, now more than ever, the goals of surgery are to minimize morbidity, provide aggressive local control and allow patients to receive to quickly recover so they can receive adjuvant systemic therapy. Surgery continues to play a crucial role in the multi-disciplinary approach to EAC. This review will highlight the on-going areas of controversy in surgical treatment. These controversies are around surgical selection, perioperative decision making and the role of surgery. Specifically, there are controversies in the type of surgical approach offered. This review will discuss the benefits of minimally invasive versus open esophagectomy. The indications for gastrectomy versus esophagectomy in patients with gastroesophageal junction EAC. Further, at the time of operation, there is still debate and on-going trials addressing the addition of a pyloric intervention. Lastly, as we push the limits of systemic therapy, there are those who may not even need a surgical resection. This review will cover the most recent data on selective esophageal resection and the concerns regarding this approach.

Keywords: Esophagectomy; minimally invasive esophagectomy; robotic esophagectomy; extended gastrectomy

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Introduction

Background

Esophageal adenocarcinoma (EAC) is typically located within the lower third of the esophagus or gastroesophageal junction (GEJ) as opposed to esophageal squamous cell carcinoma (SCC) which is located in the upper and middle third of the esophagus. In the last decade, multi-modal therapy has become the standard of care for locally advanced esophageal carcinoma. The survival benefit of multi-modal therapy has been greater in squamous cell carcinoma compared with adenocarcinoma (1). Both adenocarcinoma and squamous cell carcinoma, however, have seen a significant improvement in disease free survival with the approval and use of adjuvant immunotherapy (2).

The current strategy for locally advanced esophageal cancer is multi-modality therapy with chemotherapy, plus or minus radiation, followed by surgical resection and adjuvant

immunotherapy with the presence of any residual disease. Therefore, the goals of surgery are to minimize morbidity, provide aggressive local control and allow patients to receive adjuvant systemic therapy. There continue to be controversies over the type of surgical resection, the need for surgery and post-operative treatment pathways.

Rationale and knowledge gap

The current review will address controversies in ECA that exist around the type of operation performed, perioperative decision making and the role of surgery. The key surgical controversies remain minimally invasive versus open esophagectomy, gastrectomy versus esophagectomy for gastro-esophageal junction tumors, the use of pyloric intervention and the role of surgery.

Objective

The objective of this review is to provide tools and knowledge to make important, individualized surgical decisions for patients with ECA.

Surgical strategies

Surgical approach

ECA can present in the lower third of the esophagus or GEJ. Tumors in the lower third of the esophagus and GEJ can be addressed through numerous techniques. To date, no esophagectomy technique has been proven to be superior to another for lower third esophageal cancers. The most common type of esophagectomy performed is the Ivor Lewis with an abdominal and chest dissection and intra-thoracic anastomoses (3). This technique has become increasingly popular due to the ability to perform a thorough mediastinal lymphadenectomy, the ability to obtain a greater distal gastric margin, and it allows the use of a better perfused region of the gastric conduit to create the esophagogastrostomy.

However, many surgeons perform transhiatal or three-field esophagectomy with equivalent oncologic outcomes for ECA (4).

Esophagectomy versus gastrectomy

GEJ tumors are traditionally defined by their Siewert classification. However, in the most recent AJCC staging guidelines, this has been simplified to identify any tumor with any epicenter within 2 cm of the esophagus as esophageal cancer (5). Tumors with an epicenter further than 2 cm from the GEJ are considered gastric cancer (5). In clinical practice in the United States, the use of gastrectomy for GEJ tumors is prevalent for Siewert type 2 tumors has mixed results. Siewert type 2 tumors are defined as a tumor with an epicenter up to 1cm above and 2 cm below the GEJ. With the new staging system adopted in 2018, these are defined as esophageal tumors (6). A National Cancer Database study looking at Siewart type 2 compares all type 2 tumors resected from 2010 to 2016. Interestingly, 90% (8,595/9,594) received a gastrectomy (7). Yet, a propensity matched the patients and found that those who underwent an esophagectomy had a significantly better overall survival (7). In this study the reason for improved survival is largely attributable to the resection margins, with those undergoing an esophagectomy having a significantly higher rate negative-margin resection (94% *vs.* 91%, P=0.001). The second reason for improved survival with esophagectomy may be related to a more extensive mediastinal lymph node dissection as compared to gastrectomy with abdominal lymph node dissection alone. In a recent study outlining the distribution of lymph node metastases in GEJ tumors, there was an up to 13% rate of mediastinal lymph node involvement (8). Mediastinal lymph node involvement was significant regardless of histology or the use of neoadjuvant therapy, with higher rates seen in those with greater than 2 cm of esophageal tumor involvement. Therefore, they concluded that all patients with GEJ tumors with at least 2 cm of esophageal involvement undergo mediastinal lymph node dissection (8).

ECA patients who undergo neoadjuvant therapy and have an esophagectomy with R0 resection will still have nodal disease 36% of the time (9). Of the 36%, 20% will have multi-station nodal involvement. Further, increasing number of nodal stations, particularly mediastinal lymph node metastases are associated with a higher rate of recurrence (9). A single-center database found that a lower number of excised lymph nodes was independently associated with worse overall and disease-free survival following neoadjuvant therapy and esophagectomy with optimized staging and survival following removal of over 25 lymph nodes (10). Therefore, esophagectomy may provide more accurate staging and prognosis than gastrectomy for ECA.

Recent results of the Checkmate 577 study suggest, the advantage to Seiwert II patients being treated as esophageal

cancer is that they are offered effective adjuvant therapy. Immunotherapy following neoadjuvant chemotherapy with radiation followed by esophagectomy was shown to significantly improve disease free survival for all patients with residual disease following esophagectomy (2). There are no data currently available regarding the use of adjuvant immunotherapy after neoadjuvant chemotherapy.

Another potential benefit of esophagectomy is the presence of mucosal skip lesions. Aggressive GEJ adenocarcinomas can travel along the submucosal plexus of the esophagus proximal to the endoscopically identified tumor. Esophagectomy allows for a greater proximal margin. Although rare, with improved pathologic evaluation and specimen handling, this appears to be increasing in incidence.

There are potential clinical advantages and disadvantages to both gastrectomy and esophagectomy. These are highlighted in a review by Schlottmann and colleagues (11). The clinical disadvantages of a gastrectomy include vitamin B12 malabsorption and dumping while the clinical disadvantages of an esophagectomy include the necessity for post-operative acid suppression, risk of hiatal hernia and pylorospasm (11).

There is an ongoing multinational randomized clinical trial comparing transthoracic esophagectomy with extended gastrectomy in adenocarcinoma of the GEJ, type II. This trial, CARDIA, will offer the first randomized data on the differences in outcomes based on surgical approach (12). The extended gastrectomy is used to help improve the surgical margin status and therefore, these results will better highlight if resection of the entire esophagus improves recurrence free survival.

In clinical practice, the surgery should be individualized based on specific patient factors. The goal is two-fold, R0 resection and functional recovery to allow for targeted therapies. With these two factors in mind, the surgical approach should consider if the tumor extends down into the stomach too much to allow for 5 cm margins or if the tumor extends too high into the esophagus to allow for 5 cm margins. Both these margins are important to decrease the risk of recurrence both locally and systemically (13-15).

Targeted therapies are beyond the scope of this surgical review, but both PDL-1 status and HER2/neu should be considered. Patients with either of this marker will have a strong benefit from additional therapies and recovery are very important (2,16). These factors strongly drive me in my practice to pursue minimally invasive esophagectomy. The next section will highlight the advantages to a minimally invasive approach over open.

There should not be a standard answer for a GEJ tumor, but an individualized decision based on patient and tumor factors.

Minimally invasive versus open esophagectomy

As we move the field of esophageal cancer surgery forward, we must improve the outcomes of surgical resection. One important way to do this is to move to a minimally invasive approach without compromising oncologic outcomes. Historically, esophagectomy has been associated with significant morbidity and mortality. Much of this morbidity and mortality is attributable to a thoracotomy and respiratory failure. In the most recent review of esophagectomies in the Society of Thoracic Surgeons database, 78% were performed open with only 22% performed by either a minimally invasive or hybrid approach (17).

There have been two randomized trials comparing minimally invasive (MIE) versus open esophagectomy. The first trial looked at 115 patients from five European hospitals with resectable intrathoracic esophageal or GEJ tumors and randomized between open (n=56) and MIE (n=59) with curative intent. There were no differences in immediate post-operative complications with fewer respiratory complications in those who underwent MIE compared to open and no difference in overall survival (18,19). In a second trial of 207 patients with resectable cancer of the middle or lower third of the esophagus were randomly assigned to undergo transthoracic open esophagectomy or hybrid MI esophagectomy. The hybrid surgery comprised a two-field abdominal-thoracic operation with laparoscopic gastric mobilization and open right thoracotomy. In this study, MIE resulted in a significantly lower incidence of intraoperative and postoperative major complications and at 3 years, there was no difference in overall survival (20). Beyond randomized trials there is a plethora of retrospective studies showing less blood loss, improved respiratory complications, and equivalent if not better survival for MIE compared to open esophagectomy (21). This holds true for MIE performed robotically or laparoscopic/thoracoscopically. In a meta-analysis comparing robotic to open esophagectomy, robotic esophagectomy among 10 studies was associated with lower rates of respiratory complications, blood loss, atrial fibrillation, wound infections, and hospital length of stay (22).

Robotic esophagectomy has gained popularity over the last decade. This is in part due to the ease from transitioning

from open to robot rather than open to laparoscopic/thoracoscopic. This transition has brought on many studies comparing the two approaches (robotic esophagectomy versus thoracoscopic/laparoscopic esophagectomy). Overall, there appear to be no differences in outcomes when comparing the two techniques. There are some single institution studies that suggest improvement in outcomes with the robotic approach. In a single institution study of 139 patients, the robotic approach had a lower rate of overall complications and a shorter hospital length of stay (23). In a separate study of the National Surgery Quality Improvement Program database, minimally invasive and robotic esophagectomy had similar rates of anastomotic leaks. However, the robotic approach anastomotic leaks required fewer operative interventions compared to MIE or open approach (24).

The challenge for surgeons adopting laparoscopic/thoracoscopic or robotic MIE is the variable learning curve. Given the prevalence of open esophagectomy and the technical nuances of MIE, many are trained in an open approach alone. The learning curve for MIE is reported to be between 20 to 175 cases and between 50 to 119 cases when the robot is used (22,25). This learning curve may be able to be shortened with the use of expert courses like those provided by the Society of Thoracic Surgeons at the Annual meeting or by direct proctorship. There are also good clinical "how to" videos to aid in the acquisition of the new skill, such as the video by Dr. Molena with the "10 steps" of a MIE (26). Addressing the learning curve is an important step in improving peri-operative outcomes. Becoming proficient in MIE is critical given the increasing need to recover quickly and get patients to adjuvant immunotherapy.

Pyloric management

There are currently no specific recommendations on the role of a gastric emptying procedure at the time of esophagectomy due to insufficient evidence (27). Despite this, many surgeons perform a prophylactic intervention during esophagectomy. The pylorus can be addressed in numerous ways, with botox injection, pyloromyotomy, pyloroplasty or simple dilation. The reason many surgeons address the pylorus is due to the bilateral vagotomy and denervation of the stomach at the time of esophagectomy. In practice, delayed gastric emptying following esophagectomy only occurs in 10–20% of patients (28,29). Therefore, the surgeon must decide to provide a gastric emptying procedure at the time of esophagectomy or to wait and provide an intervention if clinically significant delayed gastric emptying occurs.

A meta-analysis comparing pyloric drainage procedure to no intervention at the pylorus found less delayed gastric emptying with the procedure on the post-operative esophagram with no differences in post-operative complications, specifically anastomotic leak or pulmonary complications (28). In a retrospective study, patients who underwent pyloric intervention had a higher incidence of esophagitis and bile reflux on the 1-year follow-up endoscopy (30). In the era of MIE, there are now fewer surgeons performing pyloric interventions. In a study of almost 300 MIEs, approximately half underwent a pyloric drainage procedure either surgical or botox with no difference in post-operative outcomes (31). The patients that underwent a pyloric intervention had a higher rate of long-term symptoms, most significantly poor po intake and dysphagia (31).

There are newer data to suggest that a per-oral pyloromyotomy (POP) can be performed at late follow-up if and when patients have symptoms of delayed gastric emptying. There are few case series describing POP post esophagectomy, but they all report the safety and efficacy with some patients having complete return of normal gastric emptying (32,33). It is an easier technique than a per oral esophageal myotomy, because it is only a short myotomy in the distal stomach (*Figure 1*). The anatomy can be difficult post esophagectomy because the pylorus can be within the chest. Many advanced endoscopists feel that a POP is more technically demanding than a per-oral endoscopic myotomy (POEM) for achalasia because of the difficulty of creating a submucosal tunnel. However, it may be a better alternative than a pyloric intervention on all patients at the time of esophagectomy.

Surgery following clinical complete response

Surgery was the cornerstone treatment for ECA until the CROSS randomized control trial showed a significant benefit with neoadjuvant chemotherapy and radiation (1). Since this time, esophagectomy has consistently been included in the multi-modality approach to esophageal cancer. The pendulum has now swung in the other direction and the question is whether all patients who undergo neoadjuvant therapy require surgery to achieve optimal oncologic and quality of life outcomes. The argument to omit surgery is more convincing with squamous

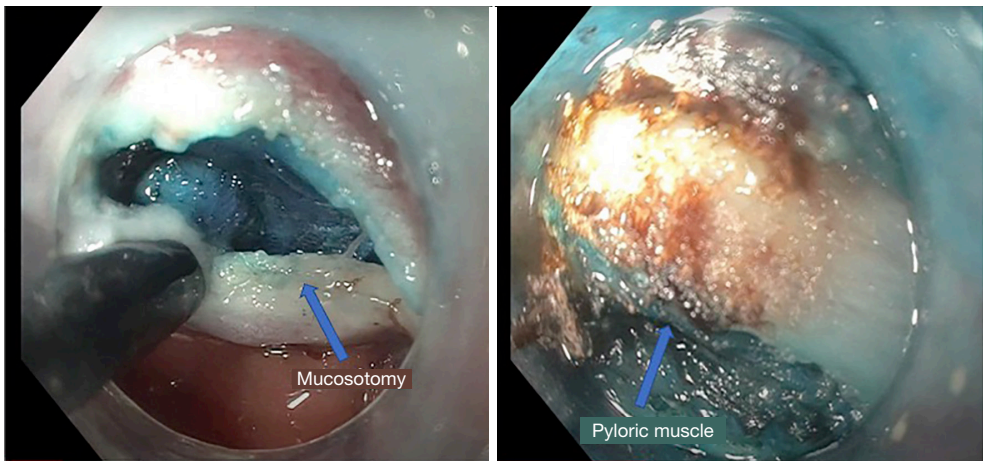

Figure 1 Gastric per oral pyloromyotomy.

cell carcinoma as it is more than twice as likely than adenocarcinoma to achieve a complete pathologic response to neoadjuvant therapy (1). As such, many of the trials that have compared definitive therapy to multi-modality therapy with esophagectomy are comprised of mostly patients with squamous cell carcinoma. There have been two randomized trials with only 10% of patients with adenocarcinoma enrolled and both showed that esophagectomy after chemoradiation improved local control but not overall survival (34). There is some controversy on the quality of these trials as the surgical group had an excessive mortality compared to the standard reported outcomes. In a single institution study of 232 patients with SCC that underwent definitive chemoradiation versus chemoradiation with surgery, the addition of surgery improved disease free and overall survival (35).

The recommendations on the value of surgery after neoadjuvant therapy are based on the ability to accurately identify patients with a complete pathologic response. A complete pathologic response can be difficult to determine based on our current imaging modalities. The current recommendations by the NCCN are for post-treatment FDG-PET/CT, chest/abdominal CT scan with contrast, and endoscopy with biopsy. These modalities all have limitations making close follow-up and a critical discussion with the patient paramount. Even when these imaging show no disease, residual disease can exist. In a retrospective study looking at outcomes of patients who had a complete clinical response by extensive imaging, 35% of patients had tumor or nodal positive disease at the time of esophagectomy (36). The consequences of inaccurately defining a complete pathologic response are missing these 35% and if disease is found at a time further out from completion of neoadjuvant therapy, then the patient will require a delayed or salvage esophagectomy if feasible.

Salvage esophagectomies historically have been associated with an increased risk of morbidity and mortality. Data from recent literature are mixed with some suggesting similar outcomes and others still reporting higher rates of morbidity and mortality (37,38). Until better tools to select patients with pathological complete response are available, surgery should remain an integral component of the treatment of locally advanced esophageal cancer. These factors make a thoughtful discussion with the patient important prior to following non-operative recommendations for patients with a clinical complete response.

There is an on-going clinical trial, the SANO trial, that is comparing the outcomes of omitting an esophagectomy in patients who have a clinical complete response. Those with a clinical complete response are randomized to surgery or close surveillance. Close surveillance in the SANO trial consists of endoscopic evaluation every three months for the first year, every four months in the second year, every six months in the third year and annual until the fifth year (39). The big problem with this trial is that pre-SANO data already showed that patients with some evidence of tumor regression but not a complete response (tumor regression grade 2) were only found to have positive biopsies with the bite-on-bite biopsy approach in 59% of cases, which mean that almost half of the patients with residual disease were not detectable with this technique.

Conclusions

The current strategy for locally advanced ECA is multimodality therapy with chemotherapy plus or minus radiation followed by surgical resection and adjuvant immunotherapy with the presence of any residual disease. There continue to be controversies over the type of surgical resection, the need for surgery and post-operative treatment pathways. Lower third ECAs may benefit from an esophagectomy over gastrectomy, balancing the clinical advantages and disadvantages. Minimally invasive approaches appear to improve short term outcomes and there continue to be no definitive recommendations for pyloric interventional at the time of surgery. Until better tools are available to select patients with pathological complete response, surgery should remain an integral component of the treatment of locally advanced esophageal cancer.

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Footnote

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References

1. 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.
2. Kelly RJ, Ajani JA, Kuzdzal J, et al. Adjuvant Nivolumab in Resected Esophageal or Gastroesophageal Junction Cancer. N Engl J Med 2021;384:1191-203.
3. Low DE, Kuppusamy MK, Alderson D, et al. Benchmarking Complications Associated with Esophagectomy. Ann Surg 2019;269:291-8.
4. Junttila A, Helminen O, Helmiö M, et al. Long-Term Survival After Transhiatal Versus Transthoracic Esophagectomy: A Population-Based Nationwide Study in Finland. Ann Surg Oncol 2022;29:8158-67.
5. Rice TW, Kelsen DP, Blackstone EH, et al. Esophagus and esophagogastric junction. In: Amin MB, Edge SB, Greene FL, et al. editors. AJCC Cancer Staging Manual, 8th ed. New York: Springer; 2017:185-202.
6. Rice TW, Patil DT, Blackstone EH. 8th edition AJCC/UICC staging of cancers of the esophagus and esophagogastric junction: application to clinical practice. Ann Cardiothorac Surg 2017;6:119-30.
7. Kamarajah SK, Phillips AW, Griffiths EA, et al. Esophagectomy or Total Gastrectomy for Siewert 2 Gastroesophageal Junction (GEJ) Adenocarcinoma? A Registry-Based Analysis. Ann Surg Oncol 2021;28:8485-94.
8. Kurokawa Y, Takeuchi H, Doki Y, et al. Mapping of Lymph Node Metastasis From Esophagogastric Junction

Tumors: A Prospective Nationwide Multicenter Study. Ann Surg 2021;274:120-7.
9. Harrington CA, Carr RA, Hsu M, et al. Patterns and influence of nodal metastases after neoadjuvant chemoradiation and R0 resection in esophageal adenocarcinoma. J Thorac Cardiovasc Surg 2022;164:411-9.
10. Sihag S, Nobel T, Hsu M, et al. A More Extensive Lymphadenectomy Enhances Survival After Neoadjuvant Chemoradiotherapy in Locally Advanced Esophageal Adenocarcinoma. Ann Surg 2022;276:312-7.
11. Schlottmann F, Casas MA, Molena D. Evidence-based approach to the treatment of esophagogastric junction tumors. World J Clin Oncol 2022;13:159-67.
12. Leers JM, Knepper L, van der Veen A, et al. The CARDIA-trial protocol: a multinational, prospective, randomized, clinical trial comparing transthoracic esophagectomy with transhiatal extended gastrectomy in adenocarcinoma of the gastroesophageal junction (GEJ) type II. BMC Cancer 2020;20:781.
13. Casson AG, Darnton SJ, Subramanian S, et al. What is the optimal distal resection margin for esophageal carcinoma? Ann Thorac Surg 2000;69:205-9.
14. Miller C. Carcinoma of thoracic oesophagus and cardia. A review of 405 cases. Br J Surg 1962;49:507-22.
15. Alvarado CE, Luo X, Linden PA, et al. How long is long enough? A closer look at proximal margin length for esophageal adenocarcinoma. Foregut 2022;2:335-51.
16. Schokker S, Molenaar RJ, Meijer SL, et al. Feasibility study of trastuzumab (T) and pertuzumab (P) added to neoadjuvant chemoradiotherapy (nCRT) in resectable HER2+ esophageal adenocarcinoma (EAC) patients (pts): the TRAP study. J Clin Oncol 2018;36:4057.
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. Maas KW, Cuesta MA, van Berge Henegouwen MI, et al. Quality of Life and Late Complications After Minimally Invasive Compared to Open Esophagectomy: Results of a Randomized Trial. World J Surg 2015;39:1986-93.
19. 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.
20. Mariette C, Markar SR, Dabakuyo-Yonli TS, et al. Hybrid Minimally Invasive Esophagectomy for Esophageal Cancer. N Engl J Med 2019;380:152-62.
21. Lv L, Hu W, Ren Y, et al. Minimally invasive esophagectomy versus open esophagectomy for esophageal cancer: a meta-analysis. Onco Targets Ther 2016;9:6751-62.
22. Esagian SM, Ziogas IA, Skarentzos K, et al. Robot-Assisted Minimally Invasive Esophagectomy versus Open Esophagectomy for Esophageal Cancer: A Systematic Review and Meta-Analysis. Cancers (Basel) 2022;14:3177.
23. Chouliaras K, Attwood K, Brady M, et al. Robotic versus thoraco-laparoscopic minimally invasive Ivor Lewis esophagectomy, a matched-pair single-center cohort analysis. Dis Esophagus 2022;36:doac037.
24. Wu J, Putnam LR, Silva JP, et al. Impact of Robotic Approach on Post-Anastomotic Leaks After Esophagectomy for Esophageal Cancer. Am Surg 2022;88:2499-507.
25. Claassen L, van Workum F, Rosman C. Learning curve and postoperative outcomes of minimally invasive esophagectomy. J Thorac Dis 2019;11:S777-85.
26. Harrington C, Molena D. Minimally invasive Ivor Lewis esophagectomy in 10 steps. JTCVS Tech 2021;10:489-94.
27. Low DE, Allum W, De Manzoni G, et al. Guidelines for Perioperative Care in Esophagectomy: Enhanced Recovery After Surgery (ERAS(®)) Society Recommendations. World J Surg 2019;43:299-330.
28. Maus MK, Leers J, Herbold T, et al. Gastric Outlet Obstruction After Esophagectomy: Retrospective Analysis of the Effectiveness and Safety of Postoperative Endoscopic Pyloric Dilatation. World J Surg 2016;40:2405-11.
29. Urschel JD, Blewett CJ, Young JE, et al. Pyloric drainage (pyloroplasty) or no drainage in gastric reconstruction after esophagectomy: a meta-analysis of randomized controlled trials. Dig Surg 2002;19:160-4.
30. Palmes D, Weilinghoff M, Colombo-Benkmann M, et al. Effect of pyloric drainage procedures on gastric passage and bile reflux after esophagectomy with gastric conduit reconstruction. Langenbecks Arch Surg 2007;392:135-41.
31. Nobel T, Tan KS, Barbetta A, et al. Does pyloric drainage have a role in the era of minimally invasive esophagectomy? Surg Endosc 2019;33:3218-27.
32. Malik Z, Kataria R, Modayil R, et al. Gastric Per Oral Endoscopic Myotomy (G-POEM) for the Treatment of Refractory Gastroparesis: Early Experience. Dig Dis Sci 2018;63:2405-2412.
33. Anderson MJ, Sippey M, Marks J. Gastric Per Oral Pyloromyotomy for Post-Vagotomy-Induced Gastroparesis Following Esophagectomy. J Gastrointest

Surg 2020;24:715-9.
34. Vellayappan BA, Soon YY, Ku GY, et al. Chemoradiotherapy versus chemoradiotherapy plus surgery for esophageal cancer. Cochrane Database Syst Rev 2017;8:CD010511.
35. Barbetta A, Hsu M, Tan KS, et al. Definitive chemoradiotherapy versus neoadjuvant chemoradiotherapy followed by surgery for stage II to III esophageal squamous cell carcinoma. J Thorac Cardiovasc Surg 2018;155:2710-21.e3.
36. Piessen G, Messager M, Mirabel X, et al. Is there a role for surgery for patients with a complete clinical response after chemoradiation for esophageal cancer? An intention-to-treat case-control study. Ann Surg 2013;258:793-9; discussion 799-800.
37. Swisher SG, Marks J, Rice D. Salvage esophagectomy for persistent or recurrent disease after definitive chemoradiation. Ann Cardiothorac Surg 2017;6:144-51.
38. Mitchell KG, Nelson DB, Corsini EM, et al. Morbidity following salvage esophagectomy for squamous cell carcinoma: the MD Anderson experience. Dis Esophagus 2020;33:doz067.
39. Eyck BM, van der Wilk BJ, Noordman BJ, et al. Updated protocol of the SANO trial: a stepped-wedge cluster randomised trial comparing surgery with active surveillance after neoadjuvant chemoradiotherapy for oesophageal cancer. Trials 2021;22:345.

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