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Abstract

The best available surgical strategy in the treatment of resectable esophago-gastric junctional (EGJ) cancer is a controversial topic. In this review we evaluate the current literature and scientific evidence examining the surgical treatment of locally advanced EGJ cancer by comparing esophagectomy with gastrectomy, transhiatal with transthoracic esophagectomy, minimally invasive with open esophagectomy, and less extensive with more extensive lymphadenectomy. We also assess endoscopic procedures increasingly used for early EGJ cancer.

The current evidence does not favor any of the techniques over the others in terms of oncological outcomes. Health-related quality of life may be better following gastrectomy compared to esophagectomy. Minimally invasive procedures might be less prone to surgical complications. Endoscopic techniques are safe and effective alternatives for early-stage EGJ cancer in the short term, but surgical treatment is the mainstay in fit patients due to the risk of lymph node metastasis. Any benefit of lymphadenectomy extending beyond local or regional nodes is uncertain.

This review demonstrates the great need for well-designed clinical studies to improve the knowledge in how to optimize and standardize the surgical treatment of EGJ cancer.

Keywords: Esophago-gastric junctional cancer, cardia cancer, gastrectomy, esophagectomy, lymphadenectomy, surgery.

1. Introduction

Esophageal cancer is the 8th most common cancer and the 6th most common cause of cancer death worldwide, while gastric cancer is the 5th most common type of cancer and 2nd most common cause of cancer death.[1] A cancer located in the distal esophagus or proximal stomach is typically referred to as an esophago-gastric junctional (EGJ) cancer.[2] The main risk factors for adenocarcinoma of the EGJ are partly shared with those of esophageal adenocarcinoma, i.e. gastroesophageal reflux disease, obesity, and tobacco smoking,[3-7] and partly shared with those of gastric adenocarcinoma, i.e. Helicobacter pylori infection and dietary factors.[8, 9] The incidence of EGJ cancer has increased along with esophageal adenocarcinoma in Europe.[10] For gastric cancer, *Helicobacter pylori*-infection is the main risk factor and it seems to increase the risk in a subgroup of EGJ cancer,[8, 11] while weaker risk factors include tobacco smoking and dietary factors, i.e. salty, smoked, or poorly preserved foods.[12, 13] Both esophageal and gastric cancers are associated with a diet low in fruit and vegetables and low socioeconomic status.[4, 6, 12, 13] Assessment of prevalent risk factors for either esophageal or gastric cancer can help in distinguishing between the origin of EGJ cancer. [8, 9]

Surgery, often after completion of neoadjuvant therapy, is the cornerstone of curatively intended treatment of EGJ cancer. The 5-year survival following surgery for EGJ cancer is in the range of 25-40%.[14, 15] Even among patients with a localized (resectable) tumor who are fit and therefore eligible for surgery, the majority of operated patients die from recurrence of the EGJ cancer.[16, 17] The postoperative prognosis is closely related to tumor stage at the time of surgery, i.e. after neoadjuvant therapy, particularly with lymph nodal status.[18, 19] The addition of neoadjuvant chemotherapy or chemoradiotherapy, centralization of surgical treatment, improvements in perioperative care, as well as more accurate patient selection following developments in imaging techniques and involvement of a multi-disciplinary team, have all had positive effects on the EGJ cancer prognosis following surgery.[20, 21] Yet, the optimal

surgical strategy for these tumors remains controversial. The lack of consensus regarding the definition of EGJ cancer and the difficulties in assessing the exact origin of these tumors contribute to this controversy.[22] In this review, we evaluate the existing evidence and rationale for various surgical strategies in the surgical treatment of adenocarcinoma of the EGJ.

2. Tumor classification

There are several challenges to the classification of cancers in the EGJ. The EGJ itself is often difficult to define. The squamocolumnar junction, also called the Z-line, is one potential anatomical basis for the definition,[23] but in the presence of a columnar-lined esophagus (Barrett's esophagus), the Z-line shifts proximally, which is misleading.[24] Therefore, the location of the junction is better defined by the proximal margin of the gastric folds, where the tubular esophagus shifts to the sac-shaped stomach, although gastric folds can be obscured by hiatal hernias. Gastric inflation during endoscopy, however, can cause normal gastric folds to temporarily disappear, making this landmark less clear.[25] Large tumors are often difficult to evaluate in relation to any adjacent anatomical landmarks. There is no way to macroscopically assess the distal border of the gastric cardia, as the parietal cells cannot be visualized endoscopically.[26] Examination of biopsy specimens can also be problematic, because cardiac mucosa can also be found in the distal esophagus and are not necessarily found more than 3mm below the squamocolumnar junction in the anatomical gastric cardia.[27] If the mucosa below the tumor is sampled, the biopsy specimen showing healthy gastric mucosa suggests esophageal etiology of the tumor, while an inflamed mucosa indicates a gastric origin. [28-30]

The adenocarcinomas of the EGJ are often classified according to the Siewert classification, which is based on the macroscopic location of the epicenter of the tumor in relation to the EGJ.[2] Cancers occurring 1-5cm above the EGJ represent Siewert type I, cancers within 1cm above and 2cm below the EGJ are type II, and cancers 2-5cm below the EGJ are type III cancers. Cancers more proximal than 5cm above the EGJ are classified as esophageal cancers and those more distal than 5cm below the EGJ are labelled distal (or non-cardia) gastric cancers.[2] In the current (7^{th}) edition of the tumor staging manual (TNM), EGJ cancers are staged as esophageal cancer when the tumor extends to the esophagus and as gastric cancer when no esophageal extension is visible. Thus, EGJ cancers of Siewert type I and II are

staged using the TNM system for esophageal cancer, while Siewert type III cancers are staged together with gastric cancer (Figure 1).[31] However, the optimal surgical treatment of each of the Siewert type I, II and III cancers remains controversial, and the differentiation between these types is often difficult and arbitrary in clinical practice.

The distribution of the premalignant metaplasia Barrett's esophagus indicates differences in the etiology of Siewert type I-III tumors and when detected it can facilitate the Siewert categorization. Barrett's esophagus is typically present in Siewert type I tumors, while this prevalence is only 5.6% in type II and <1% in type III tumors.[7] The male predominance is also higher (10.7:1) in type I tumors compared to type II (4.9:1) and type III tumors (2.2:1).[7] These data indicate that type I tumors are esophageal adenocarcinomas, type III tumors are gastric adenocarcinomas, while type II tumors represent a mixture of these. If this is the case, the EGJ does not constitute a separate anatomic entity.

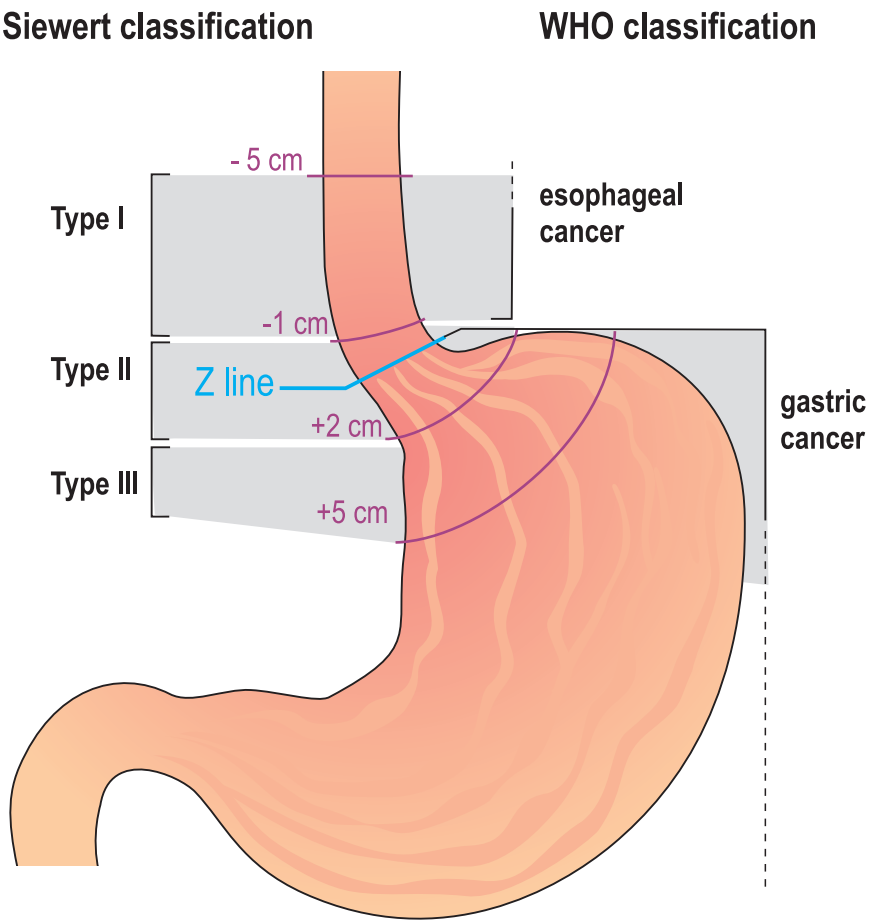

Figure 1. The Siewert classification of esophago-gastric junctional (EGJ) cancers. In the WHO classification cancers extending into the esophagus or EGJ are staged as esophageal cancer and the rest as gastric cancer. The EGJ itself can be defined by the location of the Z-line or better by the proximal margin of the gastric folds.

3. Surgical approaches for esophago-gastric junctional tumors

Regardless of the surgical approach, complete removal of the primary tumor is of highest prognostic relevance, regardless of the tumor stage.[23] Moreover, better results in both the short- and long term are achieved in high-volume centers in general, and by high-volume surgeons in particular.[32-36] Another potentially important, but controversial factor is the surgical approach, which is discussed in more detail below. Five questions addressing key aspects of the surgical approach for EJG cancer are evaluated in turn.

3.1. Esophagectomy or gastrectomy?

Esophagectomy for EGJ cancer is usually performed using a transthoracic (more common) or a transhiatal approach, and includes resection of the proximal stomach (Figure 2A). Transthoracic esophagectomy is done using laparotomy and thoracotomy, and sometimes cervical incision, allowing exposure to the entire mediastinum. Gastrointestinal continuity is preserved by an intrathoracic anastomosis (Ivor Lewis approach) or cervical anastomosis (McKeown modification includes cervical incision).[23 37 20, 38] Transhiatal esophagectomy is performed through laparotomy and cervical incision, without thoracotomy. The diaphragmatic hiatus is opened anteriorly, allowing access to the lower posterior mediastinum. A narrow gastric tube following the great curvature or colon or jejunal interposition is used to replace the resected esophagus and proximal stomach for both approaches.[7, 39, 40]

Gastrectomy for EGJ cancer includes removal of the entire stomach and the distal part of the esophagus via a laparotomy, where the diaphragm is opened (Figure 2B). The anastomosis is usually placed in the distal part of the chest. The reconstruction is typically an esophago-jejunostomy with a Roux-en-Y reconstruction.[23]

Most EGJ cancers of Siewert type I and II are surgically managed by esophagectomy, while total gastrectomy is often applied when the tumor is confined to the stomach (type III).[22] However, in clinical practice, the exact origin of EGJ tumors can sometimes be hard to define, which complicates the choice between gastrectomy and esophagectomy.[28]

A recent systematic review based on ten studies compared outcomes following esophagectomy (total n=1,780) with extended gastrectomy (total n=1,437) in EGJ cancers, and found no differences in overall survival, early postoperative mortality or morbidity, radical resection rate, or tumor recurrence.[16] The results were similar in an analysis restricted to Siewert II type tumors only (n=301). However, the studies included in the review were so

heterogeneous that statistical meta-analysis could not be reliably performed.[16] Thus, these conclusions should be interpreted with caution. A prospective study of 1,602 EGJ cancer patients found no difference in a subgroup analysis of survival between esophagectomy and gastrectomy in radically resected Siewert type II tumors (n=377).[23, 41] A register-based study from the United States found no differences in 30-day morbidity or mortality in 214 patients who underwent gastrectomy compared to 967 patients who underwent esophagectomy for EGJ cancer.[42] The Surveillance Epidemiology and End Results (SEER) program database was used to compare gastrectomy (n=1,102) with esophagectomy (n=2,714) for EGJ cancer, and found no difference in overall mortality (hazard ratio 0.95, 95% confidence interval 0.88-1.04).[42] Similar results were obtained recently in a Dutch retrospective analysis of 1,196 patients undergoing esophagectomy (n=939) or gastrectomy (n=257) for EGJ cancer.[21] The 5-year survival rates were similar regardless of surgical approach (36% and 33%, respectively).[21] However, there was a lower incidence of positive circumferential resection margins during esophagectomy compared with gastrectomy in type II tumors (n=176, 11% vs. 29%, respectively, p=0.025).[21]

Two small studies have compared health-related quality of life (HRQoL) aspects following esophagectomy and gastrectomy in EGJ cancer (including a total of 59 and 31 patients, respectively).[43, 44] Both studies suggested better HRQoL scores for global quality of life, work, leisure and social function, and fatigue, as well as fewer gastrointestinal symptoms following gastrectomy. The statistical power was insufficient for subgroup analysis for type II tumors only.[43, 44]

Taken together, extended esophagectomy and gastrectomy seem to offer similar results in terms of surgical complications or long-term oncological outcomes for EGJ cancer. Limited evidence available suggests that gastrectomy approach may increase the risk of positive

esophageal circumferential resection margins, while gastrectomy seems to be favorable regarding HRQoL outcomes. Further research is needed to examine these outcomes.

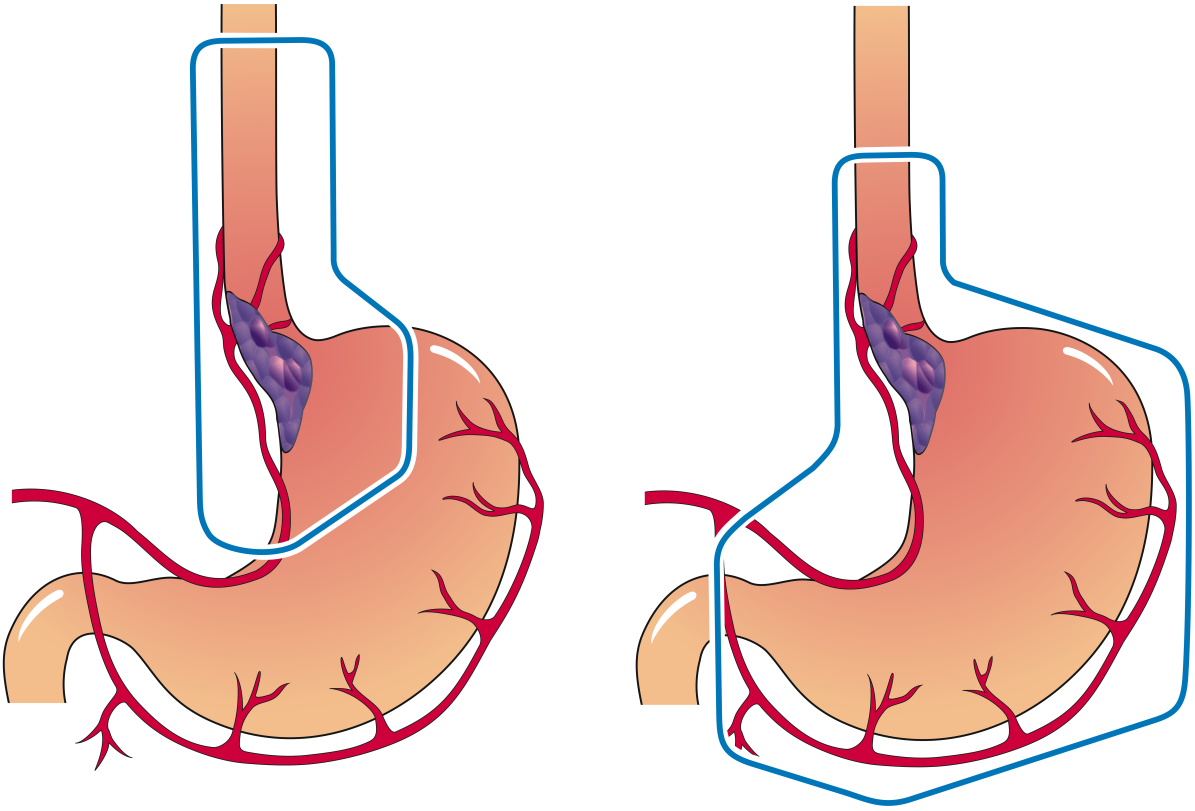

Figure 2. The difference between the resection lines in esophagectomy (left) and gastrectomy (right) for esophago-gastric junctional cancer.

3.2. Transhiatal or transthoracic esophagectomy?

The two main approaches for esophagectomy for EGJ cancer are transthoracic or transhiatal resections. These procedures were described above. A randomized clinical trial (RCT) from the Netherlands compared transthoracic (n=114) with transhiatal esophagectomy (n=106) with type I or II EGJ cancers.[45, 46] Transthoracic esophagectomy entailed more perioperative morbidity, while the overall 5-year survival was similar for transhiatal and transthoracic esophagectomy (34% vs. 36%, respectively).[45, 46] A Japanese RCT compared transthoracic

(n=85) with transhiatal esophagectomy (n=82) with type II or type III EGJ cancers.[47] The study was stopped after the interim analysis because transhiatal esophagectomy did not offer survival benefit but increased postoperative morbidity.[47] In a meta-analysis including eight studies (five observational studies and three RCTs) and a total of 1,155 patients (639 operated with transthoracic and 516 with transhiatal esophagectomy), transthoracic resection was associated with increased risks of 30-day mortality, pulmonary complications, and longer hospital stay, while no differences in survival, extent of lymph node dissection, blood loss, duration of surgery, anastomotic leaks, or cardiovascular complications were observed.[17] A recent cohort study from the United Kingdom comparing transhiatal (n=263) and transthoracic (n=401) esophagectomy in patients with esophageal or EGJ cancer found no differences between these groups regarding resection margin status, complications, length of hospital stay, tumor recurrence, or survival.[48]

No studies have compared HRQoL in transhiatal esophagectomy and transthoracic esophagectomy focusing on EGJ cancers. However, an RCT from the Netherlands found no differences in HRQoL following transhiatal esophagectomy and transthoracic esophagectomy in patients with esophageal cancer.[49]

Taken together, the current evidence does not favor the transthoracic or transhiatal procedure over the other, although the transhiatal approach seems to render fewer pulmonary complications. Transhiatal esophagectomy may be preferable in type II and III tumors. There is, however, a need for large RCTs to clarify whether these approaches differ in terms of long-term overall survival.

3.3. More or less extensive lymphadenectomy?

The lymphatic tumor spread differs between the Siewert types of EGJ cancers. According to a large observational study from Germany (n=1,602) lymph node metastases occur more

frequently in type II (65.2%) and type III (77.8%) cancers, compared to type I cancers (51.9%).[23] Predominantly paracardial regions and lower posterior mediastinal lymph nodes are involved in type I tumors, whereas types II and III tumors are drained predominantly towards the coeliac axis and the greater curvature of the stomach. Metastasis in upper mediastinal lymph nodes occurs in 15% of type I tumors, but is rare in type II and III tumors.[23] In type II and III EGJ cancers the incidence of metastasis is more than 10% at the lymph node stations of the paracardial region, lesser curvature and coeliac trunk (station numbers 1 2, 3, 7, 9, 11p and 19 in the Japanese classification). Especially at lymph node stations 1 and 3, the incidence is high in both types of tumors (up to 52.5%).[50] The incidence of metastasis in the lower perigastric nodes (stations 4d - 6) seems to be especially low in type II EGJ cancers.[51] Incidence of lymph node metastasis is less than 10% at the coeliac axis, around the splenic artery, splenic hilum, and lower mediastinum in type II cancers.[52, 53]

A greater number of resected lymph nodes or splenectomy increases the probability of complete removal of macroscopic cancer, but also increases the risk of severe postoperative complications.[54, 55] Routine splenectomy does not offer any survival benefit.[53] The lymphatic drainage in type I tumors would support a surgical approach allowing both abdominal and mediastinal lymphadenectomy. Esophagectomy with proximal gastrectomy might be sufficient instead of total gastrectomy and extended lymph node dissection in type II tumors. Mediastinal lymphadenectomy may not be needed in type III tumors.

In a recent systematic review of Siewert type II tumors (n=2,252, 5-year survival reported in n=812),[56] tumor involvement in para-aortal or other distant nodes indicates very poor prognosis, and seven or more metastatic lymph nodes (N3) indicate much worse survival (2.0%-17.4%) compared to no lymph node metastasis (up to 82.7%).[56] In a multi-center study of 2,303 esophageal cancer patients undergoing esophagectomy, dissection of 23 or more lymph nodes offered a slight survival benefit compared to less extensive lymphadenectomy

after adjusting for tumor stage, lymph node involvement, age, and sex ($p<0.001$), but no relative risks or confidence intervals were presented.[57] However, the potential survival benefit provided by more extensive lymphadenectomy in cancer surgery of the esophagus or EGJ has been recently challenged. A recent cohort study from Sweden (n=1,044),[58] and a study from the United Kingdom (n=606),[59] both showed similar survival between more and less extensive lymphadenectomy after controlling for surgeon volume, T stage, and other potential confounding factors. A higher number of removed lymph nodes might cause stage migration and biased results suggesting survival benefits following more extensive lymphadenectomy in observational studies. The discrepancies in scientific evidence concerning the optimal extent of lymphadenectomy are further complicated by the varying definitions for lymphadenectomy.

In summary, although EGJ cancers have a high frequency of lymph node metastasis and the presence of such metastasis indicates very poor prognosis, extensive lymphadenectomy does not gain much scientific support. Based on the available evidence, a moderately extensive lymph node removal seems to be adequate for optimizing the outcomes after EGJ cancer surgery.

3.4. Open or minimally invasive surgery?

Minimally invasive procedures have been gaining popularity in the recent years.[60] The first laparoscopic gastrectomy was performed in 1991.[61] Thereafter, laparoscopic and robot-assisted gastrectomies for gastric cancer have been examined in several studies, generally showing equal surgical and oncological outcomes compared to open techniques.[62-64]

A systematic review with 17 retrospective studies compared all minimally invasive (both abdominal and thoracic phase, n=494) or hybrid minimally invasive esophagectomy (thoracoscopy or laparoscopy, n=386) with open esophagectomy (n=718) for esophageal or

EGJ cancer.[65] Compared to open procedures, total minimally invasive and hybrid procedures had higher lymph node yield (17 nodes and 16 nodes, respectively, vs. 10 nodes in open esophagectomy), while the overall 5-year survival was similar between all resection types. However, the use of neoadjuvant treatment was greater in total minimally invasive and hybrid procedures (54.9% and 43.8% respectively vs. 34.7% in open esophagectomy), thus making comparisons regarding survival difficult. No HRQoL data were reported.[65] A population-based study from England showed that minimally invasive surgery (n=1,155) was comparable to open surgery (n=6,347) in terms of 30-day mortality and morbidity.[66] However, minimally invasive procedures required more re-interventions (21.0%) than open procedures (17.6%).[66] No long-term data were available. A recent meta-analysis evaluating 48 studies (1 RCT and 47 observational studies) compared minimally invasive procedures (thoracoscopy-assisted and all minimally invasive procedures, n=4,509) to open surgery (n=9,973) in patients undergoing esophagectomy for esophageal or EGJ cancer.[67] Results for long-term survival or the extent of lymphadenectomy were not available, but minimally invasive esophagectomy entailed lower risk of in-hospital mortality (4.6% vs. 3.0%, pooled odds ratio 0.69, 95% confidence interval 0.55-0.86) and pulmonary complications (20.4% vs. 17.8%, pooled relative risk 0.69, 95% confidence interval 0.61-0.77) compared to open esophagectomy. Following minimally invasive esophagectomy, a reduction in incidence of pulmonary embolism (pooled odds ratio 0.71, 95% confidence interval 0.51-0.99) and atrial arrhythmias (pooled odds ratio 0.79, 95% confidence interval 0.68-0.92) was observed. No differences were found regarding the risk of anastomotic leaks or gastric conduit necrosis. However, these findings must be interpreted cautiously due to selection bias, as the patients selected for minimally invasive esophagectomy were typically low-risk patients with early-stage cancers.[67]

The use of a surgical robot with multi-articulated arms and three-dimensional optics allows a more precise manipulation of the instruments compared to conventional minimally invasive techniques. This is particularly useful in narrow compartments, such as the mediastinum, and robot-assisted esophagectomy has been successfully implemented in the treatment of esophageal and EGJ cancer, with oncological and surgical outcomes comparable to conventional open and minimally invasive resection.[68, 69] An advantage is that open thoracotomy can be avoided while still enabling a precise mediastinal dissection.[68] Yet, robotic techniques, as appealing as they may seem, require further testing for all outcomes.[20] On-going RCTs on robotic surgery will hopefully provide such evidence in the future.[70]

Taken together, minimally invasive esophagectomy may have comparable oncological outcomes and superior in-hospital mortality and pulmonary complication rates compared to open procedures in esophageal and EGJ cancer, but RCTs are needed to clarify this due to selection bias in the observational studies available. Furthermore, more specific studies on outcomes in different Siewert types of EGJ cancer, as well as studies on HRQoL using minimally invasive approaches are needed.

3.5. Endoscopic or resectional procedures for early-stage EGJ cancer?

High-grade dysplasia and early cancers of the EGJ have traditionally been treated with conventional surgical resection.[71, 72] In recent years, new endoscopic procedures have emerged and these are used more and more frequently. Dysplasia and some early-stage (intra-mucosal) EGJ cancers can be more accurately staged using endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) compared to conventional biopsies, and these procedures can sometimes also be used in the treatment of such lesions (Figure 3).[73] The EMR technique is easier to learn and implement, while ESD can provide a specimen for more

accurate histopathological analysis evaluating the need for further surgery. EMR is widely used in Western countries and ESD is more common in Japan.[73]

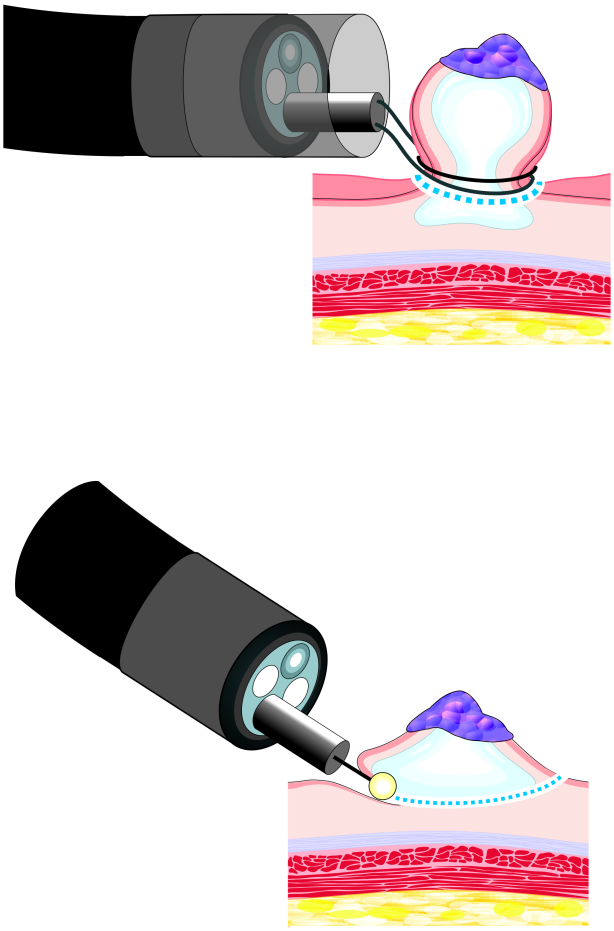

Figure 3. Ligation-assisted endoscopic mucosal resection (EMR) is performed by applying a rubber band similar to a variceal ligation band around the affected mucosa. The mucosa is then resected by a snare (A). In endoscopic submucosal dissection (ESD) the resection is instead done *en bloc* by using a special electrosurgical knife (B).

Radiofrequency ablation is effective in the treatment of Barrett's esophagus-related low-grade dysplasia,[74] but has not been extensively studied in early EGJ cancer. The number needed to treat to prevent esophageal high-grade dysplasia or esophageal cancer was only 4.0 (95% CI

2.8-7.1), according to a recent multi-center RCT.[74] Radiofrequency ablation may also be used as a complementary treatment of EMR and ESD in EGJ cancer when a columnar-lined esophagus is present.[75]

Both multiband mucosectomy-EMR and ESD are effective and safe to perform in high-volume centers.[73] A recent systematic review from Japan compared 761 esophageal or EGJ lesions treated by EMR and 335 by ESD.[73] The tumor recurrence rates were 0.3% for ESD and 2.8% for EMR during a mean follow-up of 25-29 months, while EMR was faster to perform than ESD (83.3 minutes vs. 36.7 minutes).[73] Perforation occurs with both techniques in around 1% of patients. Stricture rates were similar, less than 5%, except when circumferential EMR (stepwise radical endoscopic resection) was performed (54.7%). However, all of the ESD studies in the review were from Japan, where ESD is extensively used for the common early-stage gastric cancer and the EMR studies originated from Western countries. No RCTs comparing EMR and ESD have been conducted in early EGJ cancer.[73]

A large register-based study from the United States compared EMR or ESD (n=1,427) with surgical resection (n=3,963) in T1a and T1b esophageal cancer,[76] showing a lower 30-day mortality (0.5%) in the endoscopically treated patients compared to the surgical group (3.5%). However, the 3-year survival rates were lower in the endoscopy treatment group (76.5% vs. 87.6%, respectively). The presence of lymph node metastases in the surgically treated patients was 5.0% in patients staged T1a (0.5% with mucosal lesions <2cm) and 16.6% in patients staged T1b (8.9% with mucosal lesions <2cm), which probably contributes to the lower 3-year survival in the endoscopic treatment group.[76]

Taken together, the mainstay treatment for early-stage EGJ cancers (T1) should remain resectional surgery providing the patient is deemed healthy and fit enough to undergo such surgery. In non-surgical candidates, both EMR and ESD may be used as safe and effective alternatives to surgery in intra-mucosal EGJ cancers, supported by radiofrequency ablation

when Barrett's esophagus is present. Large RCTs are needed to better define the role of endoscopic treatment for early EGJ cancer.

4. Discussion and conclusions

Studies investigating potential differences in mortality and morbidity between gastrectomy vs. esophagectomy, transhiatal vs. transthoracic approach, and minimally invasive esophagectomy vs. open surgery in adenocarcinoma of the EGJ have failed to show any clear differences between these approaches in overall survival. However, the existing literature is very limited and there is a need for well-designed RCTs. The gastrectomy approach might provide better HRQoL outcomes compared to esophagectomy, but the literature is too limited to draw firm conclusions. Transthoracic esophagectomy allows more complete lymphadenectomy of the mediastinum compared to transhiatal esophagectomy, but this does not seem to improve the survival and may rather increase pulmonary complications and prolong hospital stay. Any survival benefits of extensive lymphadenectomy remains to be proven. Current evidence would indicate a moderate lymphadenectomy. Minimally invasive surgery has emerged as a promising approach, which might potentially reduce the risk of postoperative complications and improve HRQoL compared to open techniques, but large RCTs are required to evaluate any such benefit. In early-stage cancers, resectional surgery remains the recommended therapy, but EMR and ESD are safe alternatives in patients not eligible for resection, but large RCTs are needed.

More focused research with larger patient samples is required to elucidate the differences in HRQoL between surgical approaches, as well as the optimal extent of lymphadenectomy. The available evidence does not make it possible to strongly recommend any of the well-established surgical procedures over the others in the treatment of EGJ cancer. Thus, the choice of surgical approach should be guided by the preference and experience of the

institutions and surgeons. Based on these scarce data, transthoracic or minimally invasive esophagectomy would be the treatment of choice for type I tumors, transhiatal esophagectomy or gastrectomy for type II tumors and extended gastrectomy for type III tumors to reduce the postoperative pulmonary complications and improve the quality of life after surgery. Extensive lymphadenectomy remains questionable, and we rather suggest a moderate locoregional lymphadenectomy without the harvest of distant lymph nodes or splenectomy. For T1 EGJ tumors, surgical resection remains the mainstay therapy, while endoscopic procedures should be used in patients ineligible for such surgery.

In conclusion, there is a great need for well-designed large RCTs to forward our knowledge in the surgical treatment of EGJ cancer. These trials should elucidate not only the oncological and postoperative outcomes, but also health-related quality of life perceived by the cancer patient.

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