

Is the transthoracic approach no longer a viable option for Siewert type II esophagogastric junction carcinoma?

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Despite substantial declines in gastric cancer incidence, that of adenocarcinoma of the esophagogastric junction (AEG) has been rising remarkably worldwide and is drawing considerable attention as well as concern. AEG basically involves the anatomical border between the esophagus and the stomach, with some tumors being equally distributed between the two organs while others are predominantly in one. According to this anatomical distinction, debate persists as to whether AEG is a gastric cancer, or an independent esophageal cancer.

AEG is centered in an area ranging from 5 cm above and below the esophagogastric junction (EGJ). It is generally classified into three subtypes according to the Siewert system based on where the tumor center is located (1); type I, 1–5 cm above the EGJ; type II, 1 cm above to 2 cm below the EGJ; type III, 2–5 cm below the EGJ. Therefore, tumor burden is essentially esophageal in type I and gastric in type III, and in general the former is thus treated as an esophageal carcinoma and the latter as a gastric carcinoma (2). Type I AEG, usually arising from premalignant Barrett epithelium, is closely associated with increased body weight and gastroesophageal reflux disease (GERD). This subtype is predominant in western countries, while in Asian countries types II and III AEG are common subtypes, in marked contrast to the very rare type I tumors in these countries where the incidence of gastric carcinoma has long been very high. Therefore, AEG apparently differs geographically in regard to the prevalences of the three types, which presumably reflects differences in the *H. pylori* infection rate (3).

Type II AEG remains a highly controversial topic, with regard to its exact location relative to the esophagogastric border and being distributed equally between the two

organs, in regard to the system applied for tumor staging, surgical approaches and the extent of esophagogastric resection. AEGs, regardless of their type, have been classified using the esophageal scheme in the newly established TNM classification system, while their staging was conventionally based on the gastric scheme for the previous TNM (6th edition). Correspondingly, some researchers have supported the gastric scheme for type II AEG (4,5), while others insist that the esophageal classification system better reflects patient survival than the gastric scheme (6).

One of the most widely debated issues is the surgical approach. With uncertainty about the optimal extent of prophylactic lymph node dissection for this tumor, both subtotal esophagectomy and extended total gastrectomy have been advocated, and these two approaches have been employed even within single institutes. The former is favorable in terms of guaranteeing the proximal resection margin, while the latter focuses on the complete clearance of abdominal lymph nodes much more than mediastinal dissection. These two procedures are extremely different in terms of the surgical approach, extent of resection, and, more importantly, the type of reconstruction. Therefore, mortality, morbidity and quality of life after surgery are deemed to not be equivalent. Since the survival rate based on the extents of resection are comparable (7,8), conclusive evidence as to which procedure should be recommended is currently lacking.

Another important issue to be addressed is whether thoracotomy for securing a wide operational field should be recommended with therapeutic intent for systematic lymph node dissection. As shown conclusively in the article

by Kurokawa and colleagues (9), who presented long-term data, meticulous lymph node dissection below the left inferior pulmonary vein in the mediastinum via the left thoracoabdominal (LTA) approach offered no survival benefit over transhiatal (TH) surgery for adenocarcinoma with an oral edge within 3 cm from the EGJ. The vast majority of patients (96%) underwent total gastrectomy, and extended proximal gastrectomy was selected for the remaining cases. Their study population consisted of heterogeneous AEGs [type II (57%) and type III (38%)] and non-AEGs with esophageal infiltration, but their results apparently provide convincing evidence that the LTA approach should be abandoned as the standard procedure for AEG with limited esophageal involvement regardless of Siewert type.

Another study compared esophagectomy with versus without thoracotomy and also showed no significant overall survival benefit of either approach (10). Most notably, survival curves for these two procedures were identical in patients with type II AEG. Meanwhile, though not statistically significant, there is a non-negligible trend favoring better survival with the transthoracic esophagectomy in two subgroups; patients with type I AEG and those with a limited number of metastatic nodes [1-8]. Therefore, there is a possibility that selected patients would benefit from the transthoracic procedure based on better local control, as evidenced by longer locoregional disease free survival, as the authors described. However, treatment strategies for patients with extensive nodal disease should basically emphasize systemic therapy, rather than a local treatment such as surgical removal, since the probability of systemic recurrence after R0 esophagectomy approaches 100% when the number of involved nodes exceeds 8 in esophageal adenocarcinoma (11). Indeed, type II AEG with extensive nodal disease, even after curative resection, is associated with a dismal prognosis due to hematogenous and lymphatic recurrence (12). Taking current lines of evidence together, systematic mediastinal lymphadenectomy via thoracotomy is unlikely to improve survival, and incomplete lymph node clearance by the TH procedure in the mediastinum would apparently not adversely impact the clinical outcome at least in patients with type II AEG.

Also, we should note that the transthoracic procedure, regardless of whether right thoracotomy or left thoracophrenolaparotomy is employed, is associated an increase in the postoperative complication rate. Most importantly, the respiratory morbidity rate was found to be markedly higher (57%) with transthoracic than with

TH esophagectomy (27%) (13). The balance between the benefits (quality of local control) and disadvantages (postoperative morbidity) of each procedure is of importance on the basis of the aforementioned results. Interestingly, the minimally invasive approach using thoracoscopy was not associated with reduced pulmonary complications as compared with conventional transthoracic esophagectomy according to the Japanese nationwide database (14). Therefore, the TH approach itself appears to be beneficial in terms of reducing pulmonary complications, and minimally invasive TH esophagectomy is likely to present future challenges in managing AEG patients.

Looking again at the results obtained by Kurokawa and colleagues (9), survival was worse with the LTA than with the TH approach and this was most apparent for AEG type III; furthermore, this was confirmed by the interim analysis of their study data (15). Although type III is classified and staged using the esophageal scheme of the current TNM staging system even if the main portion of the tumor is largely gastric in location, their results highlight the possibility that these tumors should essentially be regarded as gastric cancers in terms of their responsiveness to surgical treatment. Additionally, there are studies showing the superiority of the gastric to the esophageal scheme in the current TNM staging system (4,5). Therefore, taking all features into account, it might be advisable to include type III AEG among the gastric cancers.

The definite survival advantage obtained with neoadjuvant chemoradiotherapy for cT1N1 and cT2-3N0-1 disease supports a multidisciplinary treatment policy for esophageal and EGJ cancer (16). However, surgery with or without postoperative adjuvant chemotherapy is the standard care for gastric cancer at these stages. This discrepancy underscores the need for clear criteria allowing division between esophageal and gastric tumors. In light of the study by Kurokawa and colleagues, precise delineation between type II and type III AEG would appear to provide the optimal boundary between esophageal and gastric tumors.

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Footnote

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