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## Gastric Cancer or Esophageal Cancer or Else?

Should esophagogastric junction (EGJ) cancer be classified or managed as gastric cancer or esophageal cancer or else? The debate focused on the issue has still remained [1], though EGJ cancer is increasing worldwide, in Asia [2–5] as well as western countries [6–8]. Squamous cell carcinoma developed in EGJ region is unanimously treated as esophageal cancer. For EGJ adenocarcinoma, Siewert classification has been widely applied: type I (adenocarcinoma of the distal esophagus), tumors with an epicenter located more than 1 cm above the EGJ; type II (true cardia cancer), tumors with an epicenter located within 1 cm oral and 2 cm aboral from the EGJ; and type III (subcardial cancer), tumors with an epicenter located below 2 cm from the EGJ [9, 10]. Among Siewert classifications, Siewert type I and III tumors are usually managed like esophageal and gastric cancers, respectively. However,

in 7th AJCC TNM classification, both Siewert type II and III tumors had been classified as esophageal cancer. After some discussions [11–13], in 8th version, type III was changed to gastric cancer classification, while type II still stays in esophageal classification [14–15]. There have been many papers regarding the clinicopathologic features of Siewert type II tumors to identify the pathogenesis and appropriate treatment strategy. Some papers showed that the characteristics of Siewert type II were quite similar with gastric cancers [11, 12]. However, some papers reported that there were two distinct pathways of tumorigenesis of EGJ adenocarcinoma, related or unrelated to intestinal metaplasia, gastric atrophy, and gastric acid secretion [16–17]. The etiology as well as the treatment strategy has still remained controversy, especially for Siewert type II tumors.

In the EGJ region, the different tissues to be potentially cancerous lesion are known to exist: esophageal gland, Barrett epithelium, cardiac gland, fundic glands, etc. Therefore, some Siewert type II tumors might have different biological features from the esophageal and gastric cancers and, if so, should be regarded as the independent disease. Investigation by cancer genetics, etc. will be undoubtedly needed in the future.

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## Surgical Procedures

There have been various surgical approaches for EGJ cancers: Ivor Lewis (right thoracic and abdominal), left thoracoabdominal, transhiatal, and abdominal ones. Among them, Ivor Lewis or transhiatal approaches are mainly applied to Siewert type II tumor [18]. In the former, esophagectomy through right thoracotomy with reconstruction by gastric conduit and intrathoracic anastomosis is usually performed like esophageal cancer, while in the latter, extended total gastrectomy is done like gastric cancer. Why are those quite different procedures performed to Siewert type II EGJ cancer? Recent paper described that the choice of approach has been still based on surgeon's discretion [19]. A recent web-based worldwide questionnaire demonstrated that the majority of surgeons favor an extended gastrectomy for Siewert type II tumors (66% vs 27%) [20], while the big data based on 4996 NSQIP/SEER patients showed that esophagectomy was more frequently performed than gastrectomy (71% vs 29%) in the USA [21]. When the patients with Siewert type II tumor refer to thoracic surgeons, Ivor Lewis is likely to be indicated. Conversely, the abdominal surgeons prefer the transhiatal approach for Siewert type II tumors. The potential differences between the east and west in EGJ tumor biology were recently pointed out, and the optimal surgical approach in western countries was concluded to be Ivor Lewis [22]. That is why there have been two quite different approaches.

Several papers compared the short- and long-term outcomes between the esophagectomy and gastrectomy. No significant differences of post-operative morbidity and mortality were observed between those procedures [21, 23, 24]. As for the survival after surgery, two papers showed the better results in the esophagectomy than the gastrectomy groups [21, 23], while no difference between them was found in one report [24]. The comparison of long-term quality of life (QOL) between the two groups demonstrated the better QOL after the gastrectomy than the esophagectomy [25]. This should be considered at the decision of surgical procedures. Recently, a strong

worldwide trend toward minimally invasive surgery is observed [20], and it is increasing gaining popularity over open surgery [19]. Intent to perform the minimally invasive surgery for EGJ cancers is, also, absolutely important. Laparoscopic resection of Siewert type II tumors was reported to be feasible and oncologically equivalent as compared to open procedures [26].

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## Lymphadenectomy

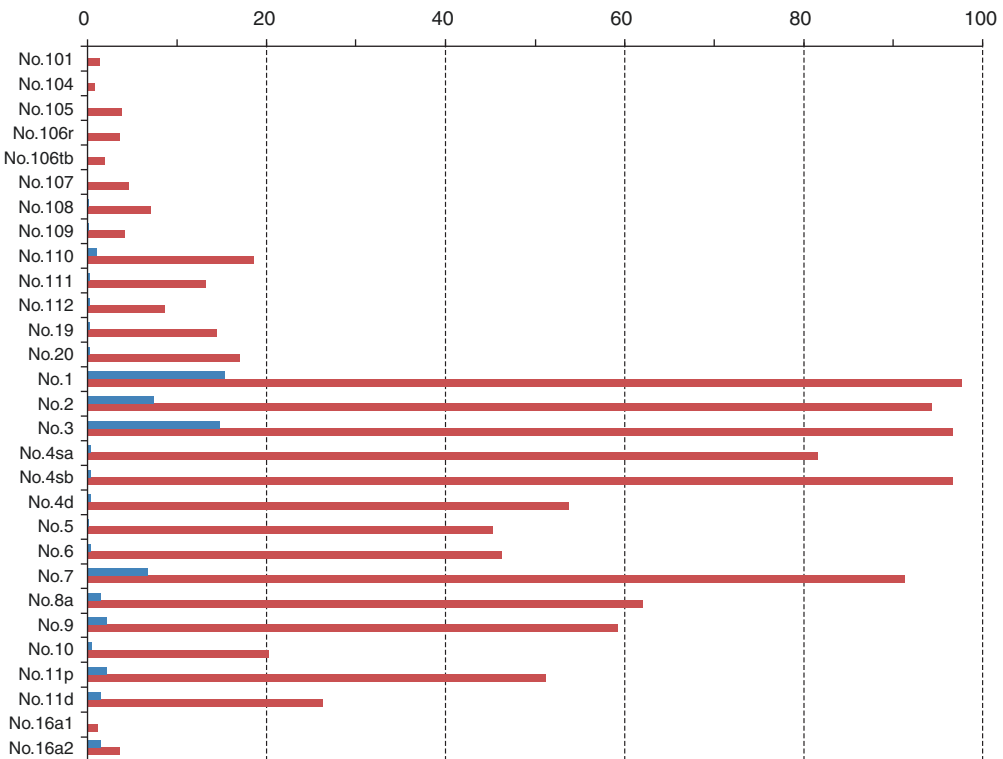
There have been many papers focusing the lymphadenectomy for EGJ cancers, to date. However, the strategy of lymphadenectomy, especially for Siewert type II tumors, has still remained controversial. The standard lymph node (LN) dissection for type II tumors has not been established, to date. However, most papers showed the significance of lymphadenectomy in the pericardial, lesser curvature and at the foot of the left gastric artery nodes (no.1, 2, 3, 7 LNs) [27–29]. Therefore, those LNs should be routinely dissected in all surgical cases with EGJ cancers, regardless of advanced or early stages. Optimal extent of lymph node dissection in the mediastinum for Siewert type II tumors has not been established. However, many papers showed the survival impact of lymphadenectomy in the lower mediastinum [27–30], while one paper described that mediastinal LN dissection was not essential in early Siewert type II tumors [31]. And, based on the analysis of recurrence pattern and lymph node metastasis, the complete mediastinal LN dissection was reported to be not mandatory for type II tumors arising within the stomach [32]. One paper showed that left renal vein nodal involvement (no.16a2; para-aortic LN) had a similar survival impact with the lower mediastinal and celiac axis LNs [29]. Now, multi-institutional prospective clinical trial to evaluate the significance of the lower mediastinal and no. 16a2 LN dissections for Siewert type II tumors is ongoing under the collaboration of the Japanese Gastric Cancer Association (JGCA) and the Japanese Esophageal Society (JES).

LN along the distal portion of the stomach (no. 4, 5, 6) are located far from EGJ, though

those LNs are simultaneously dissected when the total gastrectomy is performed. Many papers reported the poor prognosis and marginal therapeutic value of the Siewert type II cases with the nodal involvement in those LNs [27–29, 33]. The extended abdominal lymphadenectomy was suggested to improve survival because the poorer survival after D1 lymphadenectomy was shown in comparison with D1+/D2 lymphadenectomy [24]. Consistently, the nodal involvement around celiac axis (no. 9) was shown to impact the survival [29, 34].

To evaluate the optimal extent of LN dissection during EGJ cancer surgery, the JGCA and the JES conducted a nationwide survey to characterize the LN spread pattern of EGJ cancer in a large cohort. That was a questionnaire-based national retrospective study, in which clinical records of 3177 patients underwent R0 resection between 2001 and 2010 at the member hospitals of the JGCA and/or the JES were collected. And, the tumors of 40 mm or less in dimension were selected since large tumors were

apparently associated with poor macroscopic recognition of the anatomical EGJ. In Japan, EGJ cancers are defined as its epicenter within 2 cm proximal or distal to the EGJ according to the Japanese classification system (Nishi' classification), regardless of histological type. Among those 3177 patients, 2601 cases were proven to be histologically adenocarcinoma. The results were summarized in the previous paper [35]. The annual number of surgical cases was observed to increase steadily since 2001, especially for adenocarcinoma, in Japan. Figures 20.1, 20.2, 20.3, and 20.4 show the rates of the dissection (red bar) and LN metastasis (blue bar) according to each LN stations of all 2418 adenocarcinoma cases, 1430 early cases, 988 advanced cases, and 234 advanced cases with its epicenter within esophagus, respectively. The numbers of LN stationed are based on the Japanese classification. The cases with neoadjuvant therapy were excluded from the analysis. No. 100–112 and 107–109 LNs are located in the lower and middle mediastinum, respectively. All figures



**Fig. 20.1** Rate of dissection (red) and LN metastasis (blue) in all 2418 adenocarcinomas

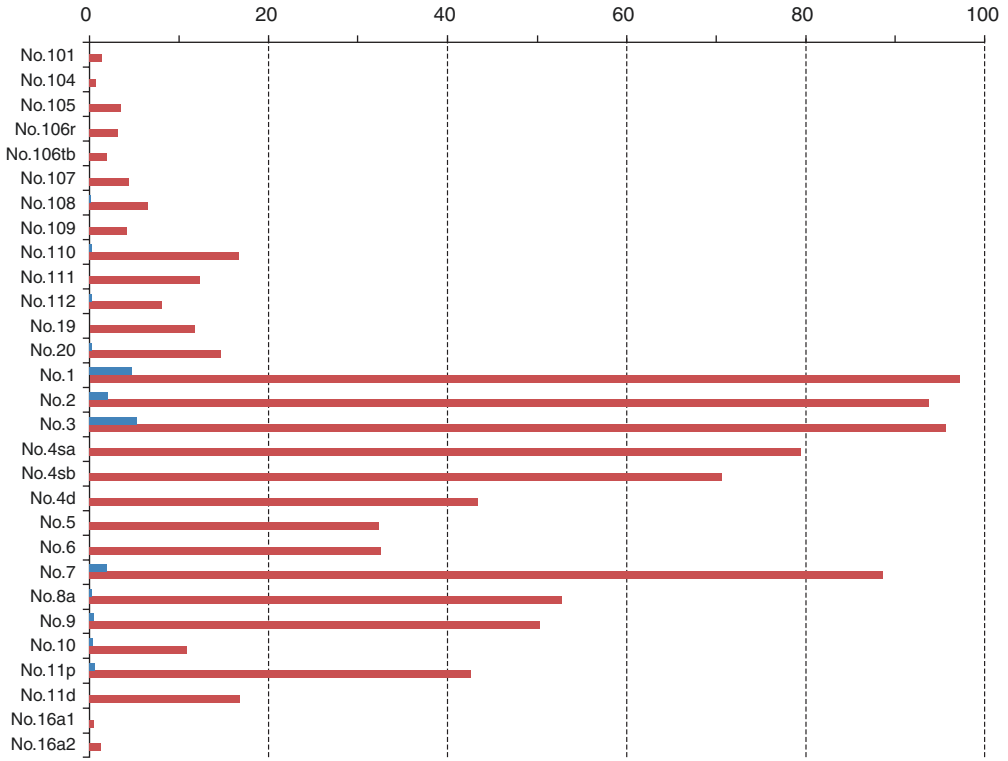


Fig. 20.2 Rate of dissection (red) and LN metastasis (blue) in 1430 early adenocarcinomas

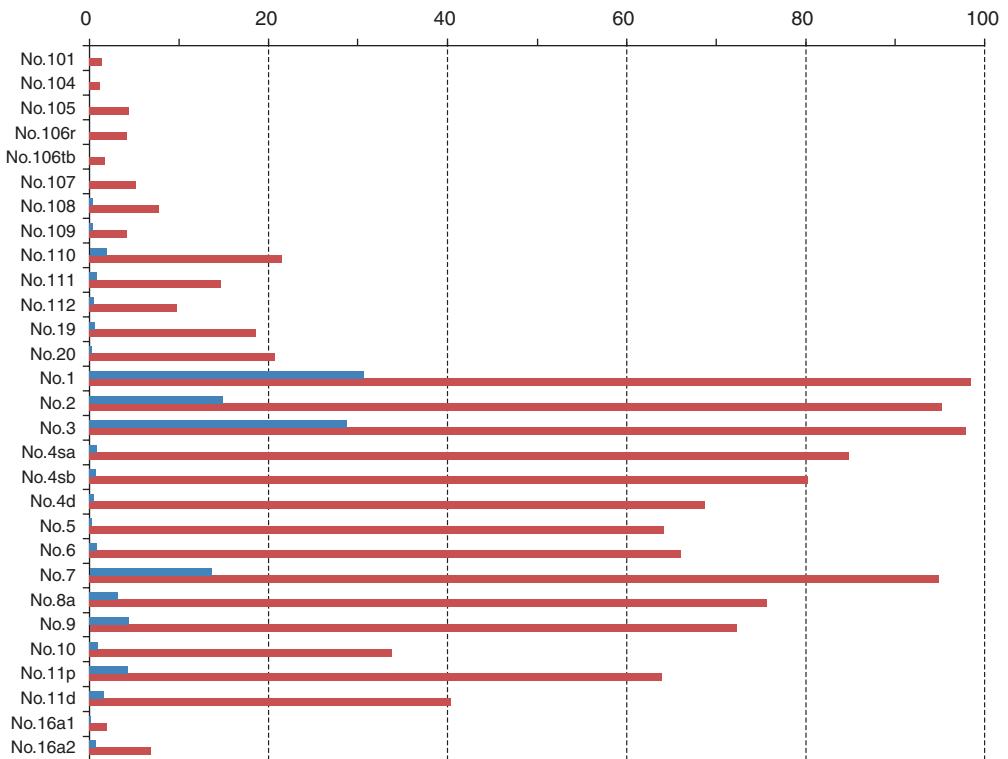
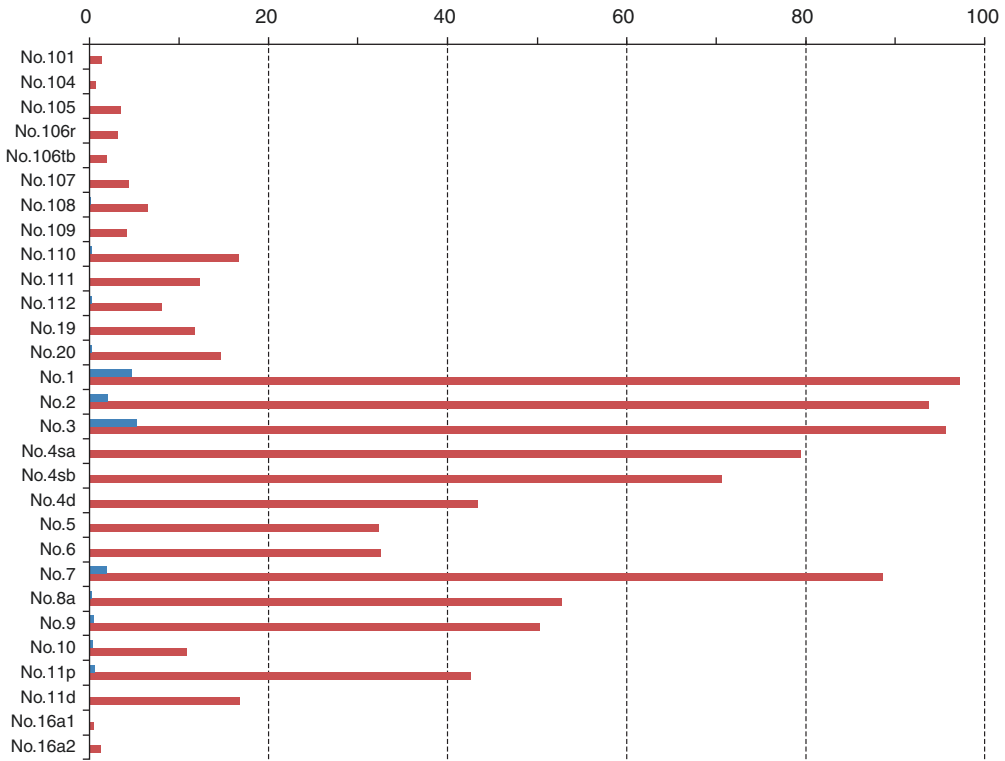


Fig. 20.3 Rate of dissection (red) and LN metastasis (blue) in 988 advanced adenocarcinomas

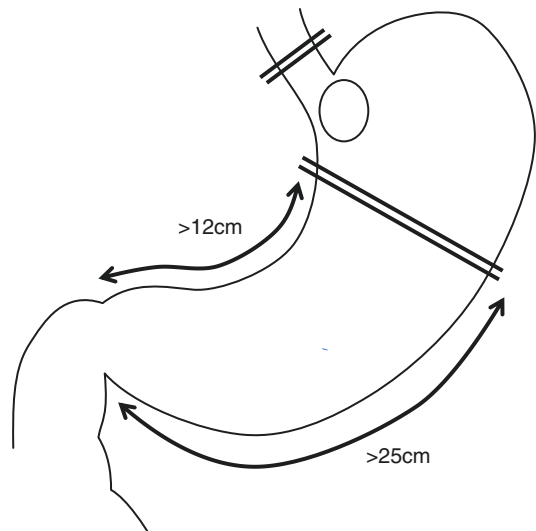


**Fig. 20.4** Rate of dissection (red) and LN metastasis (blue) in 234 advanced cases with epicenter within esophagus

were shown in the final report of the abovementioned study (not published but delivered to the participating hospitals). The results were quite consistent with previous reports. Nodes along the distal portion of the stomach (no. 4, 5, 6) were much less often metastatic in any stages, though those were dissected in most cases. And, survival analysis failed to show the benefit of those dissections. Lower mediastinal LN dissection might contribute to improve survival for the EGJ cancer with esophagus-predominance or esophageal invasion.

### Our Surgical Procedure

When more than half stomach can be preserved, the proximal gastrectomy (PG) is chosen, because the nutritional status after the PG were shown to be better than after the total gastrectomy (TG) by many studies [36–38], and no survival difference was observed between those procedures [39]. Furthermore, as the previous results showed, the dissections of no. 4, 5, and 6 LNs are not necessary for the radical resection of EGJ cancers. We

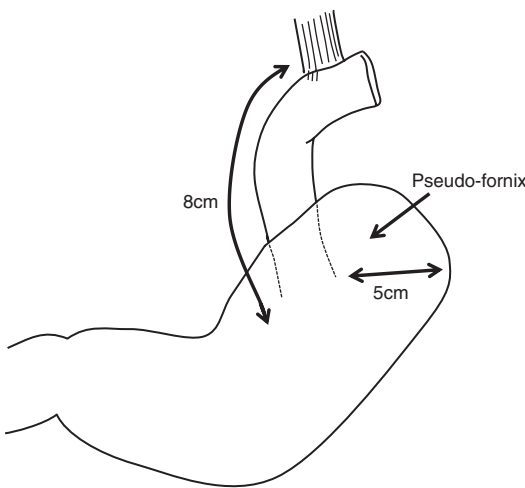


**Fig. 20.5** Shema of remnant stomach

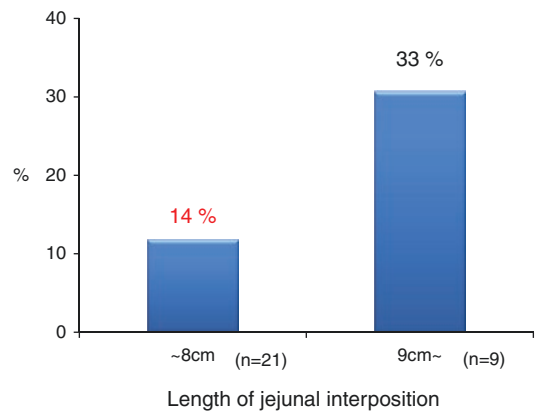
think that the TG should be avoided at the utmost. Usually, the stomach of 12 cm or more along the lesser curvature and 25 cm or more along the greater curvature from the pylorus ring is preserved (Fig. 20.5).

When the lower mediastinal LN dissection is considered to be beneficial, no. 110, 111, and 112 LNs are usually dissected (Video 20.1). Both side pleura are preserved, and the inferior pulmonary vein is a point of the upper margin of dissection. The reconstruction is usually done by jejunal interposition (JI) (Video 20.2). Frozen section analysis for the margin is usually submitted to confirm no cancer cells in the resection line. The jejunum-gastrostomy is created on the posterior wall of the remnant stomach by the circular stapler. That anastomotic site is at 5 cm distance from the resection line of the stomach (Fig. 20.6).

The length from the esophagojejunostomy to jejunum-gastrostomy is 8 cm. Some paper recommends the 15–25 cm distance between those anastomoses [40], but our data (Fig. 20.7, not published) showed that the frequency of reflux esophagitis was lower after the short than the long JIs. When the lower mediastinal LN dissection is thought to be unnecessary, laparoscopic proximal gastrectomy is done followed by esophagogastrostomy. That anastomotic site is at the anterior wall with 5 cm distance from the resection line of the stomach (Fig. 20.8). And, several stiches between the esophagus and stomach are added to

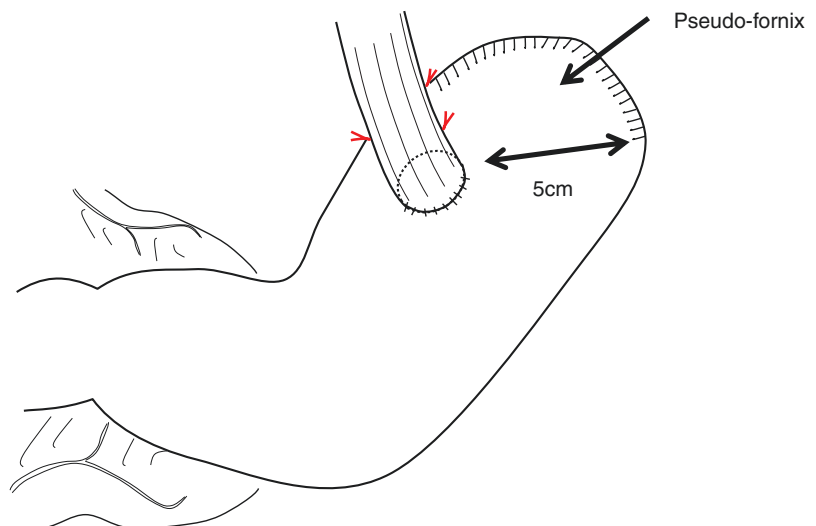


**Fig. 20.6** Shema of reconstruction of jejunal interposition



**Fig. 20.7** Frequency of reflux esophagitis according to length of interposed jejunum

**Fig. 20.8** Shema of esophagogastrostomy



fix and prevent the reflux. Severe reflux esophagitis after PG has not been developed in our recent cases, though higher frequency of reflux esophagitis after PG was previously reported to be than TG [41].

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