Clinicopathological features and surgical outcomes of esophagogastric junction adenocarcinoma single center experience: a retrospective cohort study

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Background
The esophagogastric cancers (EGCs) are rapidly increasing in Western countries. This study was conducted to elucidate the distribution and surgical outcomes of EGC.

Patients and methods
We retrospectively studied 90 patients who underwent curative surgery for esophagogastric junction cancer according to Siewert's classification during the period between January 2005 and July 2014. The collected information included preoperative, operative, and postoperative data. We also compared these data among the EGC subtypes.

Results
A total of 90 patients were eligible and were included in the study. The median follow-up period was 17.68 (0.2–130.92) months. Thirty-five patients had type I (38.9%), 32 had type II (35.6%), and 23 patients had type III tumors (25.6%). There were no significant differences in age, sex, and Borrmann macroscopic types between the three subtypes. Thoracotomy was used most often in type I tumors (74.3%) as compared with type II (28.1%) and type III (13%) tumors (P = 0.0001). Multivariate analysis confirmed that only tumor size (P = 0.023) and lymph node metastasis (P = 0.020) and presence of Borrmann macroscopic appearance of type II tumor (0.039) were significant and independent prognostic indicators for survival after curative resection for EGC.

Conclusion
The selection of the surgical approach for resection of EGC carcinoma should be tailored and achieving tumor-free safety margin. Tumor size and lymph node metastasis and presence of Borrmann macroscopic appearance of type II tumor were significant and independent prognostic indicators for survival after curative resection for EGC.

Keywords:
esophageal carcinoma, esophagogastric junction, gastric carcinoma, Siewert's classification, thoracotomy

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Introduction

Gastric carcinoma is the most common tumor arising from the upper gastrointestinal tract in Eastern countries [1–3]. Because of a vague definition of the cardia, the correct classification of esophagogastric cancers (EGCs) is still difficult even in experienced oncologic centers [3–8]. EGCs consist of the tumors arising from both the distal esophagus and proximal part of the stomach. The incidence of gastric cancer, EGCs, and esophageal cancer was determined to be 75.8, 4, and 20.2%, respectively, in Eastern countries and 40.2, 35.9, and 23.9%, respectively, in Western countries [2–4]. Although the incidence of gastric adenocarcinoma is more common in Eastern than in Western countries, EGCs are rapidly increasing in Western countries and not increasing in Eastern countries [5,7,9–11].

Siewert and Stein[6] categorized EGC into three subtypes in 1996 according to the site of the tumor center in relation to the anatomical esophagogastric junction (EGJ). This classification was approved by the International Gastric Cancer Association (IGCA) and the International Society for Diseases of the Esophagus (ISDE) and has been accepted worldwide [7–9].

The allocation of the three types of EGCs differs markedly between Eastern and Western countries. In Eastern countries, the incidence of type II and type III cancers is higher compared with type I cancers, whereas in Western countries the distribution is nearly the same between the three types [4,10,11].

Clinicopathological features vary for each type, providing the classification a useful tool for making optimal managements [12,13]. Although complete tumor resection (R0 resection) with lymphadenectomy is the goal of surgical treatment for GEJ cancers, the operative approaches still remain argumentative, especially the need for thoracotomy [9]. The surgical approaches to achieve R0 resection for GEJ carcinoma differs widely from esophagectomy transthoracic or transhiatal to total gastrectomy with transhiatal resection [1–3]. Although surgery is the most effective curative management of EGCs, the incidence of R1 and R2 resection is high and the prognosis still unsatisfactory [7–11].

These differences in the clinicopathological feature of EGC between Eastern and Western countries may be attributed to genetic factors, gastroesophageal reflux, Barrett's esophagus, smoking, obesity, and alcohol consumption [3–7]. No studies have discussed clinicopathological features of EGC in middle-east countries [12–15]. This study was planned to evaluate the incidence, clinicopathological features, and oncological outcomes of EGCs in Egypt to clarify the difference between EGCs in middle-east and in Western and Eastern countries according to the Siewert classification of EGCs. We examined databases for both esophageal and gastric cancer to elucidate the distribution and clinical outcomes of EGC at a single center in Egypt.

Patients and methods

We retrospectively studied patients who underwent curative surgery for EGJ adenocarcinoma (Siewert's types I, II, and III) at Gastroenterology Surgery Center, Mansoura University, Egypt, between January 2005 and July 2014. EGCs were defined as a tumor whose center is within 5 cm proximal and distal of the anatomical cardia [8]. Exclusion criteria included prior history of surgery for gastric cancer, squamous cell carcinoma of EGJ, or gastric stump cancer. Informed consent was obtained from all patients to undergo surgery after a careful explanation of the nature of the disease and possible treatment with its complications. This study was approved by the institutional review board.

EGC was divided according to the Siewert classification into three types. Type I is defined as tumors in which the center is located 1–5 cm above the EGJ, regardless of invasion to the EGJ; type II is defined as tumors invading the EGJ, in which the center is located between 1 cm above and 2 cm below the EGJ; and type III is defined as tumors invading the EGJ, in which the center is located 2–5 cm below the EGJ.

Preoperative assessment

All patients were evaluated preoperatively by means of clinical presentation, routine blood tests, upper gastrointestinal endoscopy with biopsy, barium study, abdominal computed tomography, and cardiopulmonary assessment. Cancer of the EGJ was classified on the basis of the findings of endoscopy determining the relationship between EGJ and the center of the tumor, intraoperative findings, and postoperative histopathological findings.

Operative procedure

The choice of operative approach depended on the radicality of the tumor and achieving complete macroscopic and microscopic removal of the lesion with proper lymph node dissection. The surgical approach and extent of lymphadenectomy depend on tumor location, preoperative staging, nodal status, and patient comorbidity. In general, abdominal gastrectomy with resection of the distal esophagus with at least 6 cm of macroscopic surgical margin of the tumor was performed [6,9,12]. To ensure clear resection margins in the distal esophagus, intraoperative frozen sections were prepared. The transhiatal approach was applied in selected patients when abdominal approach alone could not achieve complete resection. Thoracotomy was conducted to achieve adequate tumor-free safety margin above the tumor. Thoracotomy was needed if abdominal and transhiatal approaches failed to achieve tumor-free safety margin.

Reconstruction was performed with a narrow gastric tube in proximal gastrectomy with distal esophagectomy. An end-to-side esophagojejunostomy performed with a circular stapler or manual and Roux-en-Y bile diversion was the reconstruction of choice after total gastrectomy with distal esophagectomy.

Postoperative assessment

Postoperative complications were graded using the Clavien–Dindo classification [16]. Procedure-related mortality was defined as death in hospital or death within 30 days of operation.

All tumors were pathologically staged using the AJCC/UICC TNM Cancer Staging Manual (7th ed.) [17]. The macroscopic appearances of the tumors were divided according to Borrmann's classification [18].

Patients were followed up with computed tomography scan of the chest and abdomen, as well as an endoscopy during the first year. Follow-up visits were carried out at 3-month intervals during the first year, and then at 6-month intervals in the second and third year, and afterwards at 12-month intervals.

The collected data included demographic parameters, clinical data, preoperative radiological and endoscopic findings, operative data, histomorphologic tumor characteristics, and short-term and long-term outcomes. We also compared these data among the EGC subtypes.

Statistical analysis

Continuous variables were expressed as mean (SD) and compared using the one way analysis of variance test or expressed as median (range) and compared using the Kruskal–Wallis test depending on whether or not they were normally distributed. Categorical variables were expressed as percentages and compared using the X^2-test. The groups' overall and disease-free survival times were calculated using the Kaplan–Meier method and compared using a log-rank test. Univariate and multivariate analysis were performed using the Cox regression models to identify the prognostic factors. A P value less than 0.05 was considered significant. All statistical calculations were carried out using computer program SPSS (Statistical Package for the Social Sciences; SPSS Inc., Chicago, Illinois, USA) version 20 for Microsoft Windows.

Results

Between January 2005 and July 2014, 287 patients underwent gastrectomy for gastric carcinoma and 107 patients underwent esophagectomy for esophageal carcinoma at Gastroenterology Surgery Center, Mansoura University, Egypt. Of these 394 patients, 90 patients fulfilled the definition of the Siewert classification and were eligible to be included in the study. The ratios of true esophageal cancer, EGCs, and true gastric cancer were 46 (11.7%), 90 (22.8%), and 258 (65.5%). Thirty-five (38.9%) patients had type I, 32 (35.6%) patients had type II, and 23 (25.6%) patients had type III tumor.

Demographic and clinical characteristics of the patients are presented in Table 1. The mean age was 52.49 ± 10.53 years. Sixty-two (68.9%) patients were men. There were no significant differences in age, sex, and Borrmann macroscopic types between the three subtypes.

Initial symptoms were dysphagia (91.1%) (grade I: 15.6%, II: 25.6%, III: 38.9%, IV: 11.1%), weight loss (66.7%), nausea and vomiting (43.3%), abdominal pain (33.3%), reflux and heart burn (20%), and bleeding (10%). Dysphagia was significantly more apparent in type I and II as compared with type III. However, weight loss was significantly more apparent in type III than in type I.

Table 2 summarizes the intraoperative data. The median duration of surgery was 240 (120–600) min, with no difference between the subtypes. Thoracotomy was needed in type I tumors (74.3%) as compared with type II (28.1%) and type III (13%) tumors (P = 0.0001). Fifty-eight (64.4%) and 32 (35.6%) patients underwent proximal gastrectomies and total gastrectomies, respectively. Total gastrectomy was performed in 82.6% of patients with type III versus 11.4% with type I and 28.1% with type II tumors, whereas proximal gastrectomy was more common in type I (88.6%) and type II (71.9%) as compared with type III (17.4%) (P = 0.0001).

The pathological tumor characteristics are presented in Table 3. Tumor size was significantly larger in type III (6.78 ± 1.10 cm) than in types I (4.78 ± 1.85 cm) and II (4.10 ± 1.81 cm). There were no significant differences with regard to resection margin, differentiation, tumor depth, TNM stage, LN metastasis, and microvascular and perineural invasion between the subtypes.

An overall 62% of the patients had lymph node metastases and the frequency of lymph node metastases was higher in types II and III. The common nodal involvement were paracardiac (61%), lesser curvature (58%), greater curvature (18%), paraesophageal (12%), mediastinal lymph node (12%), and left gastric (2.5%) [19].

At least one postoperative complication was observed in 13 (37.1%) patients with type I, 11 (34.4%) patients with type II, and four (17.4%) patients with type III tumors (P = 0.250). No significant difference was detected in the distribution of the type of postoperative complications apart from pulmonary complications and anastomotic leakage (Table 4).

Anastomotic leakage occurred in nine cases of type I tumors, three cases of type II, and in one case of type III tumors (P = 0.035). All leakages (13 cases, 14.4%) were treated conservatively apart from one case, which needed re-exploration. Conservative treatment consisted of a nasogastric feeding tube in 11 patients and endoscopic stenting in one patient. Anastomotic stricture occurred in two cases (one was treated with

Table 1 Demographic and clinical characteristics

	Total	Type I	Type II	Type III	*P* value
Patient number (*n* (%))	90	35 (38.9)	32 (35.6)	23 (25.5)	
Age	52.49±10.53	51.31±10.88	53.13±11.10	53.39±9.42	0.702
Sex (M : F ratio)	62 : 28	25 : 10	22 : 10	15 : 8	0.882
	68.9 : 31.1%	71.4 : 28.6%	68.8 : 31.2%	65.2 : 34.8%	
BMI	26.04±5.82	24.94±4.90	26.93±4.62	26.75±8.34	0.619
Smoking	34.2%	26.9%	27.6%	52.4%	0.119
Macroscopic type (*n* (%))					0.445
Borrmann I	24 (26.7)	12 (34.3)	8 (25)	4 (17.4)	
Borrmann II	16 (17.8)	6 (17.1)	5 (15.6)	5 (21.7)	
Borrmann III	20 (22)	7 (20)	5 (15.6)	8 (34.8)	
Borrmann IV	30 (33.3)	10 (28.6)	14 (43.8)	6 (26.1)	
Abdominal pain (*n* (%))	30 (33.3)	10 (28.6)	8 (25)	12 (52.2)	0.081
Dysphagia	82 (91.1%)	35 (100%)	30 (93.8%)	17 (73.9%)	0.002
Grading					I:III=0.001 II:III=0.040
Grade I	14 (15.6%)	7 (20%)	3 (9.4%)	4 (17.4%)	0.034
Grade II	23 (25.6%)	10 (28.6%)	9 (28.1%)	4 (17.4%)	I:III=0.010 II:III=0.023
Grade III	35 (38.9%)	13 (37.1%)	13 (40.6%)	9 (39.1%)	
Grade IV	10 (11.1)	5 (14.3)	5 (15.6)	0	
Reflux symptoms (*n* (%))	18 (20)	9 (25.7)	7 (21.9)	2 (8.7)	0.270
GI bleeding (*n* (%))	9 (10)	3 (8.6)	2 (6.3)	4 (17.4)	0.372
Weight loss	60 (66.7%)	18 (51.4%)	23 (71.9%)	19 (82.6%)	0.035 I:III=0.016
Nausea, vomiting (*n* (%))	39 (43.3)	14 (40)	15 (46.9)	10 (43.5)	0.851

GI, gastrointestinal.

Table 2 Intraoperative data

	Total	Type I	Type II	Type III	*P* value
Thoracotomy (*n* (%))	38 (42.2)	26 (74.3)	9 (28.1)	3 (13)	0.0001 I:II, I:III
Extent of resection					0.0001 I:II, II:III=0.0001
Proximal gastrectomy with distal esophagectomy	58 (64.4%)	31 (88.6%)	23 (71.9%)	4 (17.4%)	0.0001 I:III=0.0001, II:III=0.0001
Total gastrectomy with distal eosophagectomy	32 (35.6%)	4 (11.4%)	9 (28.1%)	19 (82.6%)	
Splenectomy	48 (53.3%)	15 (42.9%)	20 (62.5%)	13 (56.5%)	0.257
Reconstruction (*n* (%))					0.264
Hand sewn	79 (87.8)	33 (94.3)	26 (81.3)	20 (87)	
Stapler	11 (12.2)	2 (5.7)	6 (18.8)	3 (13)	
Drainage procedure (*n* (%))	58 (64.4)	31 (88.6)	23 (71.9)	4 (17.4)	
Pyloroplasty (*n* (%))	40 (69)	20 (64.5)	17 (73.9)	3 (75)	0.734
Pyloromyotomy (*n* (%))	18 (31)	11 (35.5)	6 (26.1)	1 (25)	
Duration of surgery (min)	240 (120-600)	240 (180-360)	240 (120-600)	240 (180-360)	0.355
Blood loss	75 (0-1500)	125 (50-1500)	50 (50-800)	200 (0-1300)	0.801
Blood transfusion	0 (0-1500)	0 (0-1500)	0 (0-1000)	0 (0-1000)	0.184
Neoadjuvant ttt (*n* (%))	2 (2.2)	0	2 (6.3)	0	0.157
Adjuvant ttt (*n* (%))					0.26
Chemotherapy	28 (31.1)	9 (25.7)	9 (28.1)	10 (43.5)	
Chemoradiotherapy	30 (33.3)	10 (28.6)	11 (34.4)	9 (39.1)	

endoscopic stenting and the other was treated with endoscopic dilatation).

There was no significant difference in the severity of complications according to the Clavien–Dindo grade among the groups. Hospital stay tended to be longer in type I patients, but with no significant difference ($P = 0.063$).

There were six hospital deaths (6.7%) (three cases in type I, two cases in type II, and one case in type III): two cases in type I due to sepsis secondary to anastomotic leakage, one case in type I due to live cell failure, two cases in type II due to cardiopulmonary causes, and one case in type III due to anastomotic leakage.

Survival outcomes

In all, 1-, 3-, and 5--year survival rates for all patients were 57, 24, and 13%, respectively. Also, 1-, 3-, and 5--year disease-free survival rates for all patients were 51, 28, and 24%, respectively.

Table 3 Pathological tumor characteristics

	Total	Type I	Type II	Type III	*P* value
Tumor size	5.49±2.13	4.78±1.85	4.10±1.81	6.78±1.10	0.0001 I:III=0.001, II:III=0.0001
Cut margin R0/R1 (*n* (%))	70/20 (77.8/22.2)	27/8 (77.1/22.9)	26/6 (81.3/18.7)	17/6 (73.9/26.1)	0.806
Grading (*n* (%))					
Grades I and II	76 (84.4)	30 (85.7)	29 (90.6)	17 (73.9)	0.23
Grades III and IV	14 (15.6)	5 (14.3)	3 (9.4)	6 (26.1)	
Number of LN removed	21 (13-33)	19 (10-30)	21 (11-29)	22 (12-33)	0.35
Number of LN infiltrated	6 (0-18)	4 (0-15)	5 (0-16)	7 (0-18)	0.45
Patients with lymph node infiltration (*n* (%))	62 (68.9)	21 (60)	23 (71.9)	18 (78.3)	0.52
Tumor depth (*n* (%))					
T1	6 (6.7)	1 (2.9)	4 (12.5)	1 (4.3)	0.14
T2	41 (45.6)	15 (42.9)	12 (37.5)	14 (60.9)	
T3	40 (44.4)	18 (51.4)	16 (50)	6 (26.1)	
T4	3 (3.3)	1 (2.9)	0	2 (8.7)	
LN metastasis (*n* (%))					0.52
N0	28 (31.1)	14 (40)	9 (28.1)	5 (21.7)	
N1	24 (26.7)	11 (31.4)	7 (21.9)	6 (26.1)	
N2	23 (25.6)	7 (20)	9 (28.1)	7 (30.4)	
N3	15 (16.7)	3 (8.6)	7 (21.9)	5 (21.7)	
Venous invasion (*n* (%))	5 (5.6)	3 (8.6)	1 (3.1)	1 (4.3)	0.597
Perineural invasion(*n* (%))	11 (12.2)	4 (11.4)	4 (12.5)	3 (13)	0.982

Table 4 Postoperative complications

	Total	Type I	Type II	Type III	*P* value
Cases with complication (*n* (%))	28 (31.1)	13 (37.1)	11 (34.4)	4 (17.4)	0.250
Clavien-Dindo grade (*n* (%))					0.462
I	62 (68.9)	22 (62.9)	21 (65.6)	19 (82.6)	
II	8 (8.9)	3 (8.6)	5 (15.6)	0	
III	14 (15.6)	7 (20)	4 (12.5)	3 (13)	
V	6 (6.7)	3 (8.6)	2 (6.3)	1 (4.3)	
Anastomotic leakage	13 (14.4%)	9 (25.7%)	3 (9.4%)	1 (4.3%)	0.046 I:III=0.035
Postoperative hemorrhage	2 (2.2%)	0	1 (3.1%)	1 (4.3%)	0.498
Pulmonary complications	24 (26.7%)	13 (37.1%)	10 (31.3%)	1 (4.3%)	0.017 I:III=0.004 II:III=0.014
Ilius (*n* (%))	1 (1.1)	1 (2.9)	0	0	0.452
Postoperative abdominal collection (*n* (%))	2 (2.2)	1 (2.9)	0	1 (4.3)	0.530
Anastomotic stricture (*n* (%))	2 (2.2)	0	2 (6.3)	0	0.157
Depression (*n* (%))	1 (1.1)	1 (2.9)	0	0	
UTI (*n* (%))	1 (2.2)	0	1 (3.1)	0	0.400
Sepsis (*n* (%))	8 (8.9)	4 (11.4)	4 (12.5)	0	0.219
Diaphragmatic hernia (*n* (%))	1 (1.1)	1 (2.9)	0	0	0.452
Hospital stay	11 (7-65)	12 (8-65)	11 (8-37)	11 (7-36)	0.063
Hospital mortality (*n* (%))	6 (6.7)	3 (8.6)	2 (6.3)	1 (4.3)	0.814
Readmission (*n* (%))	13 (14.4)	6 (17.1)	6 (18.8)	1 (4.3)	0.275

UTI, urinary tract infection.

The survival curves for each Siewert type are shown in (Figs. 1 and 2). Overall survival time and disease-free survival time tended to be lower in type III tumor, although the difference was not statistically significant (Table 5).

Univariate analysis showed that the following seven factors were associated with survival: tumor size (P = 0.014), lymph node metastasis (P = 0.002), presence of Borrmann macroscopic appearance of type II tumors (P = 0.021), and positive resection margin (P = 0.031). Subsequent multivariate analysis confirmed that only tumor size (P = 0.023) and lymph node metastasis (P = 0.020) and presence of Borrmann macroscopic appearance of type II tumors (0.039) were significant and independent prognostic indicators for survival after curative resection for EGC (Table 6 and Figs. 1–6).

Discussion

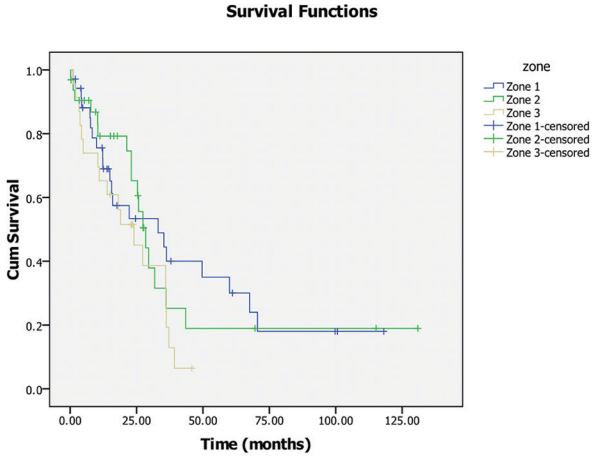
The incidence of EGCs is increasing dramatically in Western countries but not in Eastern countries. In

1996, Siewert categorized EGCs into three subtypes based on the anatomic location of the tumor center to the cardia [1–5]. These tumors show a high incidence of early lymphatic dissemination and lymph node metastases [5–8]. In Eastern countries, the ratios of esophageal cancer, EGCs, and gastric cancer were 20.2, 4, and 75.8%, respectively, and in Western countries the ratios were 23.9, 35.9, and 40.2% [4,10,11,19–23]. In our study, the ratios of true esophageal cancer, EGCs, and true gastric cancer were 46 (11.7%), 90 (22.8%), and 258 (65.5%). Thirty-five (38.9%) patients had type I, 32 (35.6%) patients had type II, and 23 (25.6%) patients had type III tumor. These findings differ from reports in Western nations and in Eastern nations. The incidence of Siewert type I tumors is more frequent in our study (38.9%) than in Eastern countries (3.4%) and Western countries (20.3%) [2–5]. The high frequency of type I EGCs may be explained by a higher prevalence of gastroesophageal reflux, obesity, and *Helicobacter pylori* infection [1,19–25].

In this study, 62 (68.9%) patients who had EGCs were men and the male-to-female ratio was 2.2: 1. There were no significant differences in age, sex, and Borrmann macroscopic types between the three subtypes. Zhang *et al* [19]. reported that no significant differences were found in age and sex among the three types of EGC cancers. Type III tumors were larger and associated with more weight loss compared with type I and type II tumors. Five-year survival rates were 15, 21, and 0% for types I, II and III, respectively. Lymph node metastasis, lymphovascular infiltration, large tumor size, and Borrmann type II were significant and independent factors for poor prognosis after R0 resection of the tumor.

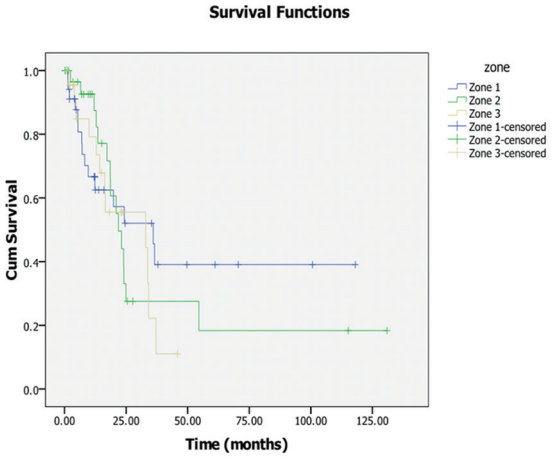
Management of patients with EGCs continues to be a matter of debate. Despite their rising incidence, there are marked difference in the definition of EGCs, the selection of surgical approach, and surgical outcomes. The surgical approaches to these tumors have been controversial. The selection

Figure 1



Actuarial survival (Kaplan–Meier analysis) after resection of esophagogastric cancer (EGC): influence of zone.

Figure 2



Actuarial survival (Kaplan–Meier analysis) after resection of esophagogastric cancer (EGC): overall disease-free survival influence of zone.

Table 5 Long-term follow-up and oncologic outcome

	Total	Type I	Type II	Type III	*P* value
Follow-up period (months)	17.68 (0.2-130.92)	14.95 (1-118.1)	22.16 (0.2-130.92)	18.99 (0.95-45.83)	0.966
Median overall survival time (months)	28.28	30.67	30.19	24.08	0.237
Overall survival rate					0.408
1-year survival rate	57%	55%	66%	50%	
3-year survival rate	24%	41%	21%	4%	
5-year survival rate	13%	15%	21%	0	
Median overall disease-free survival time (months)	24.92	34.13	21.63	24.95	0.754
Overall disease-free survival rate					0.702
1-year disease-free survival rate	51%	60%	40%	52%	
3-year disease-free survival rate	28%	41%	26%	7%	
5-year disease-free survival rate	24%	41%	18%	0%	

of the surgical approach for resection of GEJ carcinoma should be tailored for achieving macroscopic and microscopic tumor resection with lymphadenectomy [1,26,27]. The surgical approaches for achieving R0 resection for GEJ carcinoma differs widely from esophagectomy transthoracic or transhiatal to total gastrectomy with transhiatal resection [1–3,19–22]. Many studies reported that the surgical approach should be based on obtaining at least 6 cm safety margin to avoid residual tumor [1,23–26].

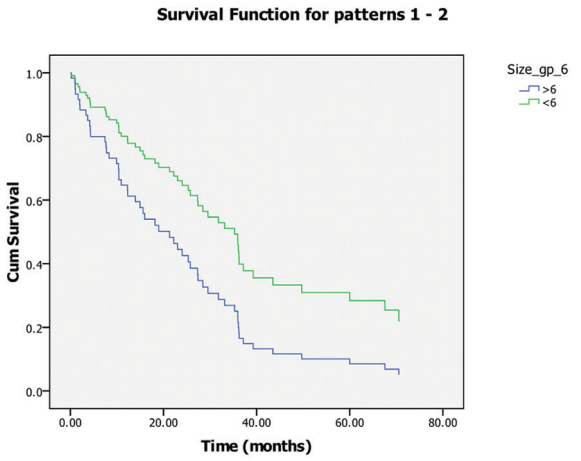
In the present study, the majority of patients with type III carcinomas underwent total gastrectomy with distal esophagectomy using an abdominal approach. Thoracotomy was required in 74.3% of type I patients but only in 28.1% of type II patients and 13% of

Table 6 Univariate and multivariate predictors of overall survival

Variables	No	Univariate analysis *P* value (HR (95% CI))	Multivariate analysis *P* value (HR (95% CI))
Age			
<60	72	0.715 (1.13 (0.59-2.14))	
>60	18		
Sex			
Male	62	0.534 (1.20 (0.67-2.14))	
Female	28		
Siewert type			
Type I or II	67	0.094 (1.63 (0.92-2.90))	
Type III	23		
Histologic grade			
G1, G2	76	0.153 (1.60 (0.84-3.05))	
G3, G4	14		
Venous invasion			
Negative	85	0.687 (1.27 (0.39-4.11))	
Positive	15		
Perineural invasion			
Negative	79	0.699 (1.18 (0.50-2.78))	
Positive	11		
T stage			
T1, T2	47	0.067 (1.65 (0.97-2.81))	
T3, T4	43		
Cut margin			
Negative	70	0.031 (1.98 (1.06-3.67))	0.171 (1.58 (0.82-3.02))
Positive	20		
Tumor size (cm)			
<6	58	0.014 (1.96 (1.14-3.35))	0.019 (1.93 (1.11-3.33))
>6	32		
N stage			
+ LN	62	0.002 (2.68 (1.42-5.07))	0.009 (2.40 (1.24-4.63))
– LN	28		
Borrmann			
II	16	0.021 (2.07 (1.11-3.85))	0.019 (2.12 (1.33-3.99))
I, III, and IV	74		

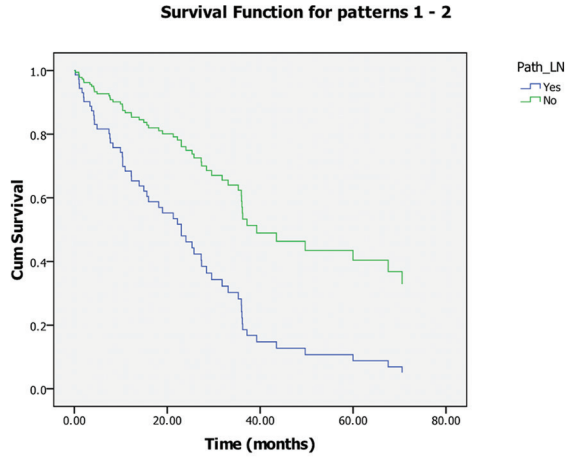
CI, confidence interval; HR, hazard ratio.

Figure 3



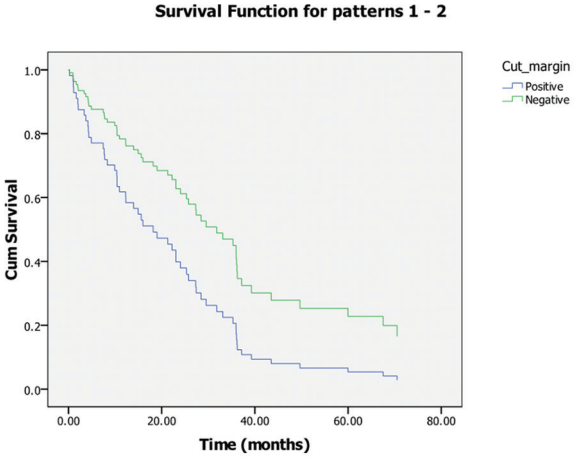
Actuarial survival (Kaplan–Meier analysis) after resection of esophagogastric cancer (EGC): influence of tumor size.

Figure 4



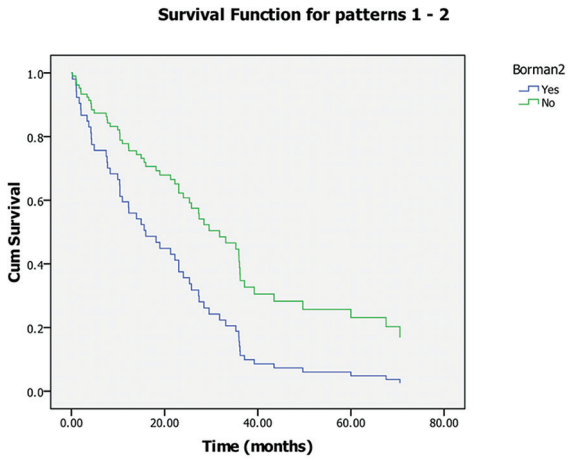
Actuarial survival (Kaplan–Meier analysis) after resection of esophagogastric cancer (EGC): influence of LN status.

Figure 5



Actuarial survival (Kaplan–Meier analysis) after resection of esophagogastric cancer (EGC): influence of safety margin.

Figure 6



Actuarial survival (Kaplan-Meier analysis) after resection of esophagogastric cancer (EGC): influence of the presence of Borrmann II.

type III patients. In recent years, total gastrectomy has emerged as the standard procedure to treat type III EGCs [19]. Abdominal total gastrectomy is frequently performed for GEJ carcinoma in east country, whereas thoracoabdominal approach is frequently performed in the west [11–15,19].

Hasegawa *et al* [11]. reported that postoperative morbidities were reported in 40% of type I cases, but only in 21.9% of type II cases and 8.3% of type III cases. In our study, at least one postoperative complication was observed in 37.1% of patients with type I, 34.4% of patients with type II, and 17.4% of patients with type III. The differences in surgical approaches may be the cause of these differences.

In our study, the tumor differentiation was more in type II tumors than in type III tumors. Siewert *et al*.[7] found that the difference of differentiation among subtypes is present. Hasegawa *et al* [11]. reported that the grade of differentiation was poor in type III tumors than in type II tumors. Zhang *et al* [19]. reported that type III tumors were more larger, deeper, and aggressive compared with type II tumors, with a higher rate of lymph node metastases and are more difficult to diagnose early. Siewert type I tumors are usually associated with intestinal metaplasia and Barrett's esophagus and Siewert type III is subcardiac gastric carcinoma infiltrating EGJ and usually undifferentiated [1,26,27].

The lymphatic flow of any type of EGCs is directed toward the abdominal lymph node (pericardia, lesser curvature, greater curvature, para-aortic lymph node). Metastases to lower mediastinal lymph node commonly occurred in all types of EGCs, and so dissection of this area is necessary in all types of EGCs. Nodal metastases to upper and middle mediastinal from type II and type III is uncommon and so thoracotomy and mediastinal lymphadectomy are not required in both types [1,11–15,26,27]. In this study, lymph node metastases were more frequently noticed in type III tumors than in other types. Abdominal lymph node metastases were frequently affected in types II and III. Mediastinal lymph node metastases frequently occurred in types I and II. This could be explained by the difference in the number of cases that underwent thoracotomy [11–15,17]. Zhang and colleagues reported that 72.8% of patients had lymph node metastases and the frequency of lymph node metastases was higher in types II and III. The common nodal involvement were paracardiac (67.3%), lesser curvature (66.5%), greater curvature (12.9%), paraesophageal (2.9%), and left gastric (2.5%) [19].

Carcinoma of GEJ are biologically aggressive and usually diagnosed at late stage, and so the prognosis is bad even after curative resection. Overall survival time and disease-free survival time tended to be lower in type III tumor, although the difference was not statistically significant. This may be related to the nature of type III tumors, which include cardia cancer centered 2–5 cm below the EGJ that enlarges, and then infiltrates the EGJ. It may also be more difficult to diagnose early cancer around the cardia than in the distal esophagus by means of screening endoscopy [13]. Compared with type III cancer, type I or II cancers might be diagnosed earlier when the tumor is small, given the tumor's proximity to the esophageal junction and the earlier appearance of signs of obstruction [12]. This trend has been reported by other groups [12,13,25]. In contrast, Chung *et al* [1]. reported that type I has poorer prognosis. Fang *et al* [10]. reported similar survival rates between types II and III (59.6 vs. 63.5%). Indeed, the Siewert type remains an anatomic classification and should not be confused with a prognostic classification. It can be used in the preoperative assessment for the determination of the surgical approach [10].

We reported hospital death in 6.7% of cases. This rate is higher than the rate reported by Siewert and colleagues, which was 3.8%. This may attributed to preoperative nutritional status, liver condition, and age of presentation of our Egyptian patients. In present study, pulmonary and anastomotic leakage complications were more common in type I tumors. This may be related to thoracotomy, which was performed in most type I tumors.

Preoperative chemoradiotherapy (CRT) followed by surgery is the standard treatment for resectable EGCs in Western countries. The preoperative CRT increased R0 resection compared with surgery alone and improved 5-year overall survival (47% surgery with CRT vs. 34% surgery alone). In Eastern countries, postoperative adjuvant chemotherapy is the standard treatment for resectable EGCs as it improves 5-year overall survival (71.7% in the postoperative chemotherapy group vs. 61.1% in the surgery alone group) [1–5,23–25].

The present study has some limitations as it is a retrospective study and single center experiences. Although it was carried out in a referral specialized center, the number of patients still small. Our center is a referral specialized center for Delta area in Egypt (more than 6 governments). This study reveals experience of EGJ in Egypt in middle east.

Conclusion

The incidence of EGCs is increasing dramatically in Western countries but not in Eastern countries. The selection of the surgical approach for resection of GEJ carcinoma should be tailored for achieving macroscopic and microscopic tumor resection. The surgical approach should be based on obtaining at least 6 cm safety margin. In all, 1-, 3-, and 5-year disease-free survival rates for all patients were 51, 28, and 24%, respectively. Tumor size and lymph node metastasis and presence of Borrmann macroscopic appearance of type II tumors were significant and independent prognostic indicators for survival after curative resection for EGC. Overall survival time and disease-free survival time tended to be lower in type III tumor.

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Conflicts of interest

There are no conflicts of interest.

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