ORIGINAL ARTICLE

Characteristics and Long-Term Outcome of Adenocarcinoma of the Esophagogastric Junction: A 23-Year Experience at a Tertiary Hospital in Thailand

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Background: Adenocarcinoma of the esophagogastric junction (AEG) has risen significantly worldwide in recent decades. Eastern and western countries report differences in disease characteristics and treatment strategies. However, the Southeast Asian AEG data remains extremely limited.

Objective: To demonstrate the clinicopathological characteristics and surgical treatment outcomes of AEG in Thai patients.

Materials and Methods: The authors conducted retrospective review of 106 AEG patients who underwent curative resection at a university hospital in Thailand between 1998 and 2020. All patients were classified by the Siewert classification. The clinicopathological characteristics, operative outcomes, and survival outcomes were reported and compared between each subtype. The chi-square test was utilized to compare categorical variables, whereas, the one-way ANOVA test was used to analyze continuous data. Survival outcomes were calculated using the Kaplan-Meier method, and the log-rank test was employed to compare the variables that impact survival.

Results: Of 106 patients, 13 patients (12.3%) were classified as Siewert type 1, 56 patients (52.8%) as Siewert type 2, and 37 patients (34.9%) as Siewert type 3 tumors. Most type 1 patients (76.9%) underwent Ivor-Lewis esophagectomy, whereas 60.7% and 81.1% of type 2 and type 3 patients, respectively, received extended gastrectomy. The overall 30-day mortality was 1.9%. The cohort revealed a 5-year survival rate of 25.4%, with a median survival of 17 months. Multivariate analysis showed that poor survival was significantly associated to age older than 65 years (HR 2.54, 95% CI 1.51 to 4.28), higher pN stage (HR 2.63, 95% CI 1.48 to 4.67), and higher histologic grade (HR 2.06, 95% CI 1.25 to 3.39).

Conclusion: The present study is the first study on AEG in Thailand, showing increasing number comparable to those in Western countries. A greater proportion of AEG cases in Thailand were classified as Siewert types 2 and 3. The survival prognosis was still unfavorable and requires improvement in upcoming instances.

Keywords: Adenocarcinoma of the esophagogastric junction; Esophagogastric junction tumor; Esophagogastric junction carcinoma; Southeast Asian; Thailand

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Esophagogastric junction adenocarcinoma (AEG), also known as cardia cancer, is uncommon but associated with low survival rates. It has become a significant issue among foregut diseases in recent decades. The unique and complex nature of this disease due to its location at the transition zone between the esophagus and stomach led to a diagnostic challenge with AEG. The complex etiopathogenesis of AEG can result from three main causes, the development of neoplastic changes in the true cardiac epithelium, progressive dysplastic changes in the proximal gastric mucosa as a result of *Helicobacter pylori* (HP)-induced atrophic gastritis, and Barrett's esophagus transformation due to prolonged acid reflux injury[1,2]. These complexities generated considerable controversy between Eastern and Western countries in terms of classification, etiopathogenesis, and treatment approaches. The incidence of AEG in Western countries has significantly risen over the past few decades, which is consistent with a decline in HP infection and an increase in obesity and gastroesophageal reflux disease (GERD)[3-5]. However, accurately determining the exact incidence of AEG in Eastern population can be challenging because the disease is sometimes classified as gastric cancer and other times as esophageal cancer in various countries.

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The precise global incidence of AEG has been definitively established. Since its proposal in 1987 and adoption worldwide in 1997, the Siewert classification has gained recognition and increased significance in differentiating this tumor from esophageal and gastric cancer[6,7]. Currently, AEG is topographically defined as adenocarcinoma, which its epicenter is located within 5 centimeters (cm) from the esophagogastric junction (EGJ) and categorized by the Siewert classification based on the distance between the tumor epicenter and EGJ. Siewert type 1 refers to a tumor located at the distal esophagus within 1 to 5 cm above the EGJ. Siewert type 2 cancer, also known as "true junctional cancer", has its tumor's epicenter positioned in relation to the EGJ at 1 cm proximally to 2 cm distally. Siewert type 3 infiltrates the junction from below, with the tumor center positioned 2 to 5 cm below the EGJ[6,7].

Interestingly, recent reports from Eastern countries indicate a gradual increase in the incidence of AEG, mirroring the trend observed in Western countries[8-11]. This phenomenon can be attributed to the expanding popularity of Westernized and urbanized lifestyles and diets, resulting in a rise in the number of obese individuals and the occurrence of GERD[12,13].

In Thailand, AEG is an uncommon cancer compared to gastric cancer and esophageal squamous cell carcinoma, which are more prevalent. However, there has been a noticeable rise in the occurrence of this condition in clinical practice in recent years. To the authors' knowledge, there is currently no available data on AEG in Thailand, as this specific type of tumor is often misdiagnosed as either distal esophageal cancer or proximal gastric cancer. The present study represented the first comprehensive investigation into the clinicopathological characteristics, distribution, based on the Siewert classification, perioperative, and survival outcomes of AEG in Thai patients.

Material and Methods

The present study was a retrospective cross-sectional study among patients diagnosed with AEG and admitted for curative surgical treatment at a university hospital in Thailand between January 1998 and December 2020. To enhance the accuracy of the incidence of AEG in the present study patients, the authors retrospectively reviewed the medical records of both esophageal and gastric cancer patients identified by ICD-10 codes (C 15.5, C 15.9, C 16.0, and C 16.1). In the present study database, there were 1,597 patients diagnosed with ICD-10 codes for distal esophageal and proximal gastric cancer. Of these, only 132 patients could be classified as AEG according to the Siewert classification. Patients with tumors involving the entire stomach, a prior history of gastric or esophageal cancer, or prior gastric or esophageal surgery were excluded from the present study. The data regarding demographic characteristics, operative details, perioperative outcome, pathological report, and survival outcome were retrieved from electronic medical records. All patients were followed-up until death, or until December 31, 2020.

AEG was defined as an adenocarcinoma with an epicenter within the first and second 5 cm of the EGJ. It was further divided into subtypes using the Siewert classification, which was based on imaging and endoscopic findings. A computed tomography (CT) scan and, in selected cases, diagnostic laparoscopy were the optional methods for determining clinical staging. All patients were assessed by a multidisciplinary conference to formulate an appropriate course of treatment. Before surgery, the operative approach was planned for individual patients based on the Siewert subtypes and length of esophageal invasion, aiming to obtain an R0 resection. The surgical approach was esophagectomy for Siewert types 1 and some type 2 tumors with distal esophageal invasion greater than 2 cm, and total gastrectomy and transhiatal distal esophagectomy, or extended gastrectomy, for most type 2 and type 3 tumors. Proximal gastrectomy was performed selectively in the early stages of the disease, for clinical T1 lesion. The authors obtained photographs and documented the morphological features of all the excised specimens. Subsequently, all surgical specimens were sent to the pathologist for full examination. Based on the preoperative evaluation, intraoperative findings, and final pathological report, the Siewert subtypes of all patients were determined retrospectively to reach a more accurate subtype of the tumor during the present study. The prolonged duration of data collection in the present study resulted in changes in stages regarding the staging system. During the authors' analyses, Siewert type 1, and 2 patients were classified according to the AJCC Eighth TNM staging system for esophageal cancer. Siewert type 3 patients were classified according to the AJCC Eighth TNM staging of gastric cancer. Follow-up evaluations were performed at 3-month intervals during the initial 2-year period following surgery and subsequently at 6-month intervals for the following three years. Overall survival was determined by measuring the time from the operation until either the occurrence of death or the most recent

follow-up contact.

Clinicopathological data were descriptively analyzed and presented as appropriate in terms of mean, median, frequency, and percentage. The chi-square test or Fisher's exact test was used to assess the comparison of clinicopathological variables, as considered appropriate. The continuous data were compared using one-way ANOVA for parametric data and the Kruskal-Wallis test for non-parametric data. Survival outcomes were calculated by the Kaplan-Meier method and compared by the log-rank test. A Cox proportional hazard regression model was used to analyze multivariable relationships between covariates and survival using a stepwise procedure (the value of 0.2 was considered for entry into the model). A p-value less than 0.05 was considered statistically significant. All data were analyzed using IBM SPSS Statistics, version 27.0 (IBM Corp., Armonk, NY, USA).

The present study was approved by the Institutional Review Board Committee of the Faculty of Medicine, Chulalongkorn University (IRB No. 236/64). The informed consent was waived due to its retrospective study type.

Results

Of the 1,597 patients diagnosed with adenocarcinoma of the distal esophagus and gastric cancer at the present study hospital in a 23-year period, there were 132 patients (8.3%) classified as AEG by the Siewert classification and were candidates for curative surgery at the time of diagnoses. During the study period, there was an upward trend in the number of AEG patients who underwent surgical resection, from an average of three-point-three cases per year between 1998 and 2008 to an average of eight cases per year between 2009 and 2019 as displayed in Figure 1. However, only 106 cases (80.3%) underwent successful curative resection and were included in the final analysis. Of the 106 resected patients, 13 patients (12.3%) were classified as Siewert type 1, 56 patients (52.8%) as Siewert type 2, and 37 patients (34.9%) as Siewert type 3 tumors. More than half of the resected patients were male, with 63.2%, and the mean age of this cohort was 64.1 years. Almost 60% of the patients were diagnosed with stage 3 disease. Most patients (85.8%) in the present study underwent upfront surgery.

There were no significant differences in age, gender, American Society of Anesthesiologists (ASA) classification, clinical stage, pathological T stage, pathological N stage, resection margin status,

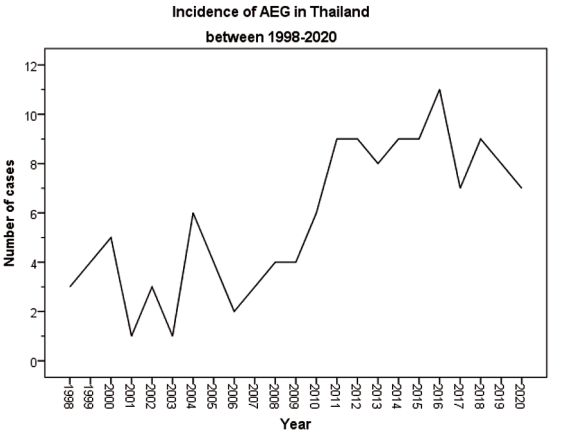

Figure 1. Time trends in incidence of adenocarcinoma of the esophagogastric junction in Thai patients.

* Period 2020 under the lockdown policy due to COVID-19 pandemic

number of metastatic and harvested lymph nodes, and overall pathologic stage between the 3 subtypes, as demonstrated in Table 1. Type 3 tumors revealed a higher histologic grade and exhibited a significantly higher rate of R2 resection.

Ten patients (76.9%) with type 1 tumors had transthoracic esophagectomy, and the other three patients had proximal gastrectomy because their disease was in early stage (T1a lesion). Total gastrectomy with distal esophagectomy was the most common procedure in 60.7% of type 2 patients and 81.1% of type 3 patients. Only 17.9% of type 2 patients required esophagectomy to obtain a negative proximal margin. Operative time, length of intensive care unit (ICU) stays, and re-operation rate were significantly higher in type 1 patients. No significant differences were observed in intraoperative blood loss, length of hospital stays, surgical complications, or 30-day mortality rates among the three subtypes. Other operative details and perioperative outcomes are shown in Table 2. In the present study, the overall 30-day mortality rate occurred in two patients, accounting for 1.9% of the total. Both patients presented with type 3 tumors and underwent total gastrectomy with distal esophagectomy. One patient, found to have multiple liver metastases during the operation, experienced liver failure 20 days after the procedure. Another patient died on the ninth day after surgery due to acute respiratory distress syndrome caused by aspiration.

The overall 5-year survival rate of the entire cohort was 25.4%, with a median survival duration of 17 months. Based on the survival curves shown in Figure 2, there was no significant difference in 5-year

Table 1. Demographic data according to Siewert classification

Clinicopathological features	Total (n=106)	Type 1 (n=13)	Type 2 (n=56)	Type 3 (n=37)	p-value
Sex; n (%)					0.067
Male	67 (63.2)	12 (92.3)	33 (58.9)	22 (59.5)	
Female	39 (36.8)	1 (7.7)	23 (41.1)	15 (40.5)	
Age at surgery (years); mean (SD)	64.1 (12.8)	63.9 (9.3)	64.6 (13.9)	63.3 (12.3)	0.894
BMI (kg/m^2); median [IQR]	20.7 [4.5]	22.5 [6.6]	20.4 [4.1]	21.1 [5.8]	0.656
ASA class; n (%)					0.267
Class I	29 (27.4)	1 (7.7)	16 (28.6)	12 (32.4)	
Class II	57 (53.8)	10 (76.9)	31 (55.4)	16 (13.2)	
Class III	20 (18.9)	2 (15.4)	9 (16.1)	9 (24.3)	
Clinical stage; n (%)					0.595
Stage I	6 (5.7)	2 (15.4)	3 (5.4)	1 (2.7)	
Stage II	32 (30.2)	4 (30.8)	16 (28.6)	12 (32.4)	
Stage III	63 (59.4)	7 (53.8)	33 (58.9)	23 (62.2)	
Stage IV	5 (4.7)	0 (0)	4 (7.1)	1 (2.7)	
Neoadjuvant therapy; n (%)					0.551
None (upfront surgery)	91 (85.8)	10 (76.9)	48 (85.7)	33 (89.2)	
Neoadjuvant therapy	15 (14.2)	3 (23.1)	8 (14.3)	4 (10.8)	

SD=standard deviation; IQR=interquartile range; BMI=body mass index; ASA=American Society of Anesthesiologists

Table 2. Perioperative outcome and pathological characteristics of patients with adenocarcinoma of esophagogastric junction, categorized according to Siewert classification

Factors	Total (n=106)	Type 1 (n=13)	Type 2 (n=56)	Type 3 (n=37)	p-value
Operative procedure; n (%)					<0.001*
Esophagectomy	20 (18.9)	10 (76.9)	10 (17.9)	0 (0.0)	
Total gastrectomy with distal esophagectomy	64 (60.4)	0 (0.0)	34 (60.7)	30 (81.1)	
Proximal gastrectomy	22 (20.8)	3 (23.1)	12 (21.4)	7 (18.9)	
Surgical approach; n (%)					<0.001*
Transhiatal	86 (81.1)	3 (23.1)	46 (82.1)	37 (100)	
Transthoracic	20 (18.9)	10 (76.9)	10 (17.9)	0 (0.0)	
Lymphadenectomy; n (%)					<0.001*
D1 plus lymphadenectomy	22 (20.8)	3 (23.1)	12 (21.4)	7 (18.9)	
D2 lymphadenectomy	64 (60.4)	0 (0.0)	34 (60.7)	30 (81.1)	
2-field lymphadenectomy	20 (18.9)	10 (76.9)	10 (17.9)	0 (0.0)	
Reconstruction; n (%)					<0.001*
Esophagogastric anastomosis	35 (33)	12 (32.9)	17 (30.4)	6 (16.2)	
Esophagojejunostomy anastomosis	64 (60.4)	1 (7.7)	34 (60.8)	29 (78.4)	
Jejunal interposition	4 (3.8)	0 (0.0)	4 (7.1)	0 (0.0)	
Colon interposition	1 (0.9)	0 (0.0)	1 (1.8)	0 (0.0)	
No anastomosis performed	2 (1.9)	0 (0.0)	0 (0.0)	2 (5.4)	
Pathological T stage; n (%)					0.120
pT1	11 (10.4)	3 (23.1)	6 (10.7)	2 (5.4)	
pT2	19 (17.9)	3 (23.1)	10 (17.9)	6 (16.2)	
pT3	38 (35.8)	6 (46.2)	22 (39.3)	10 (27.0)	
pT4	38 (35.8)	1 (7.7)	18 (32.1)	19 (51.4)	
Pathological N stage; n (%)					0.318
pN0	33 (31.1)	5 (38.5)	19 (33.9)	9 (24.3)	

IQR=interquartile range; ICU=intensive care unit
* Statistically significant

Table 2. (continued)

Factors	Total (n=106)	Type 1 (n=13)	Type 2 (n=56)	Type 3 (n=37)	p-value
Pathological N stage; n (%) (continued)					
pN1	17 (16.0)	3 (23.1)	9 (16.1)	5 (13.5)	
pN2	25 (23.6)	4 (30.8)	14 (25.0)	7 (18.9)	
pN3	31(29.3)	1 (7.7)	14 (25.0)	16 (43.2)	
Pathological stage (AJCC 8th edition); n (%)					0.474
Stage I	14 (11.9)	3 (23.1)	7 (12.5)	4 (10.8)	
Stage II	13 (11.0)	1 (7.7)	10 (17.9)	2 (5.4)	
Stage III	63 (53.5)	8 (61.5)	31 (55.4)	24 (64.9)	
Stage IV	16 (13.6)	1 (7.7)	8 (14.3)	7 (18.9)	
Histologic grade; n (%)					0.008*
G1/2	56 (52.8)	9 (69.2)	35 (62.5)	12 (32.4)	
G3/4	50 (47.2)	4 (30.8)	21 (37.5)	25 (67.6)	
Resection margin status; n (%)					0.001*
R0 resection	78 (73.6)	11 (84.6)	48 (85.7)	19 (51.4)	
R1 resection	23 (21.7)	2 (15.4)	8 (14.3)	13 (35.1)	
R2 resection	5 (4.7)	0 (0.0)	0 (0.0)	5 (13.5)	
Proximal margin; n (%)					0.115
Negative	94 (88.7)	11 (84.6)	53 (94.6)	30 (81.1)	
Positive	12 (11.3)	2 (15.4)	3 (5.4)	7 (18.9)	
Circumferential margin; n (%)					0.099
Negative	93 (87.7)	12 (92.3)	52 (92.9)	29 (78.4)	
Positive	13 (12.3)	1 (7.7)	4 (7.1)	8 (21.6)	
No. of harvested nodes; median [IQR]	18.5 [18]	19 [20]	19.5 [17]	15 [22]	0.822
No. of metastatic nodes; median [IQR]	3 [9]	1 [5]	2.5 [7]	5 [14]	0.087
Operative time (minutes); median [IQR]	298 [156]	405 [107]	271 [150]	295 [90]	0.035*
Operative blood loss (mL); median [IQR]	550 [700]	900 [1,080]	500 [600]	700 [1,095]	0.344
ICU stays (days); median [IQR]	1.5 [2]	3 [5]	1 [1]	1 [2]	0.023*
Hospital stays (days); median [IQR]	21 [20]	33 [32]	19.5 [17]	22 [21]	0.084
Surgical complications; n (%)					
Anastomotic leakage	8 (7.5)	3 (23.1)	2 (3.6)	3 (8.1)	0.064
Intraabdominal collection	14 (13.2)	2 (15.4)	7 (12.5)	5 (13.5)	0.957
Surgical site infection	7 (6.6)	0 (0.0)	5 (8.9)	2 (5.4)	0.472
Re-operation; n (%)	3 (2.8)	3 (23.1)	0 (0.0)	0 (0.0)	<0.001*
30-day mortality; n (%)	2 (1.9)	0 (0.0)	0 (0.0)	2 (5.4)	0.151
Disease-free survival (months); median	14	23	12	15	0.456
Overall survival (months); median	17	24	16	16	0.455

IQR=interquartile range; ICU=intensive care unit

* Statistically significant

survival rates according to the Siewert subtypes of 30.8%, 28.7%, and 16.2% for types 1, 2, and 3, respectively (p=0.26). The median survival times for each subtype were 24, 16, and 16 months for type 1, type 2, and type 3 patients, respectively. Patients with negative lymph nodes (pN0, n=33) had a better survival rate than those with positive lymph nodes (pN1-3, n=73), with 5-year survival rates of 50.4% and 14.2%, respectively (p<0.001), as displayed in Figure 3. In addition, the number of metastatic lymph nodes significantly influenced the survival outcome (p<0.001). The higher 5-year survival rate in patients who underwent R0 resection was revealed compared to non-R0 resection patients at 30.2% versus 7.7% (p=0.027). The Cox proportional hazard regression was used to assess prognostic factors including age, gender, Siewert subtypes, operative approach, neoadjuvant treatment, histologic grade, and resection margin status. The multivariate analysis revealed that age older than 65 years old (HR 2.54, 95% CI 1.51

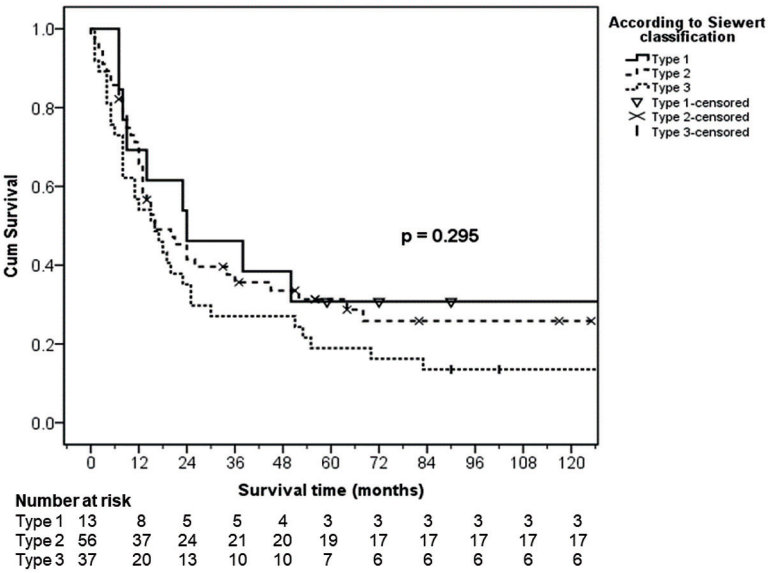

Figure 2. Kaplan-Meier curves of overall survival, categorized according to Siewert classification.

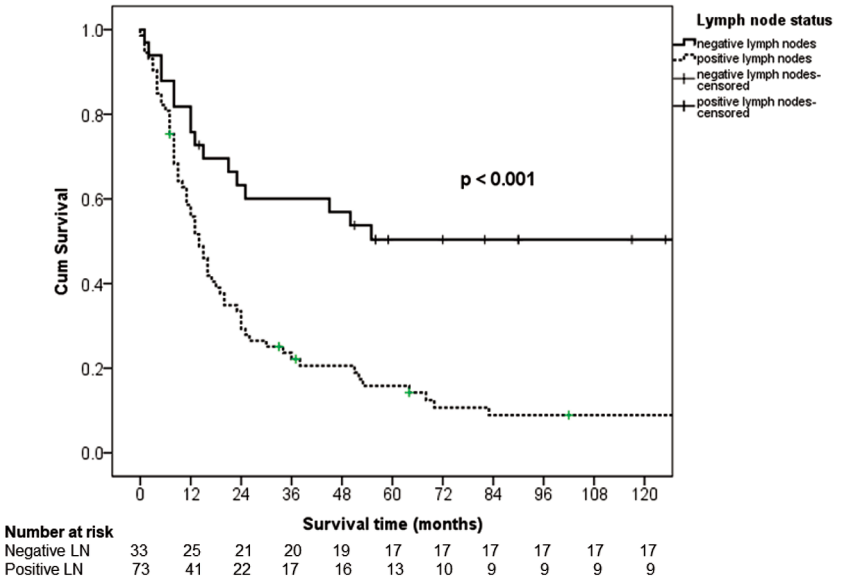

Figure 3. Kaplan-Meier curves of 106 patients of adenocarcinoma of the esophagogastric junction, categorized according to lymph node metastases.

LN=lymph node

to 4.28, p<0.001), pathologic lymph node stage (HR 2.63, 95% CI 1.48 to 4.67, p=0.001), and histologic grade (HR 2.06, 95% CI 1.25 to 3.39, p=0.004) were independent prognostic factors affecting the survival outcome after surgery, as shown in Table 3.

Discussion

Esophageal and gastric cancers are the leading causes of mortality and morbidity worldwide. According to Global Cancer Statistics (GLOBOCAN) 2020 data, they are ranked as the seventh and fifth most common cancers globally, respectively[14]. In developed countries, the incidence of esophageal cancer has shifted over recent decades, with adenocarcinoma becoming more prevalent than squamous cell carcinoma. This change is attributed

Table 3. Univariate and multivariate analysis by Cox regression methods for overall survival

Variables; unfavorable/favorable factors	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Age (years); >65/<65	1.76 (1.13 to 2.74)	0.012*	2.54 (1.51 to 4.28)	<0.001*
Sex; female/male	0.98 (0.62 to 1.55)	0.931		
Siewert classification; type 1/2/3	1.56 (0.75 to 3.30)	0.229		
Treatment approach; neoadjuvant therapy/ upfront surgery	0.93 (0.48 to 1.80)	0.835		
Operative approach; TT/TH	0.54 (0.28 to 1.02)	0.056*	1.09 (0.54 to 2.23)	0.808
Resection margin; non-R0/R0 resection	1.69 (1.05 to 2.73)	0.031*	1.59 (0.91 to 2.76)	0.102
Histologic grade; G3-4 / G1-2	2.05 (1.31 to 3.22)	0.002*	2.06 (1.25 to 3.39)	0.004*
Pathologic N stage; pN1-3/ pN0	2.88 (1.65 to 5.02)	<0.001*	2.63 (1.48 to 4.67)	0.001*

CI=confidence intervals; HR=hazard ratio; TT=transthoracic approach; TH=transhiatal approach

* Statistically significant

to increased GERD and Barrett's esophagus incidence, coupled with a decreased prevalence of HP infection[3-5]. While gastric cancer is more prevalent in Eastern countries compared to Western countries, the incidence of gastric cancer in Asian countries has been quite steady during the last decades[9]. However, from recent studies, the incidence of esophageal adenocarcinoma (EAC) in Asian countries has been gradually increasing, similar to that in Western countries, because of the westernized diet and lifestyle, which led to an increased prevalence of obesity and GERD, which were like the trend in Western countries[8-11]. Surgical cases of AEG, including Barrett's EAC, in Japan increased from 2.3% of all gastric cancers between 1962 and 1965 to 10.0% of all gastric cancers between 2001 and 2005[8].

The present study currently serves as the first report on AEG in Thailand and in the Southeast Asia region. Historically, patients were commonly misclassified as having gastric or EAC. Nevertheless, the widespread worldwide adoption of the Siewert classification enabled the comparison of findings from different studies. The authors had also implemented this classification system in their institution. It has been observed that the distribution of the Siewert subtypes differs significantly between populations in the West and the East. In Western countries, the distribution of the three types was equivalent, while in Eastern countries, types 2 and 3 were more prevalent[15-17]. According to the authors' findings, type 2 and type 3 tumor comprised the majority of AEG in Thai patients, mirroring pattern observed in other Asian countries. The proportions of Thai patients categorized as type 1, 2, and 3 were 12.3%, 52.8%, and 34.9%, respectively. The lower incidence of type 1 tumors in Thai population can be attributed to a lesser incidence of GERD, a lower prevalence of obesity, and a higher rate of HP infection resulting from delayed eradication of HP compared to other developed countries[18].

The current study revealed distinct epidemiological and clinicopathological variations among the three subtypes. Type 3 tumors exhibit a more aggressive nature compared to type 1 and type 2 tumors, as evidenced by a significantly higher histologic grade and a tendency to have a greater number of metastatic lymph nodes. Despite the aggressive nature of type 3 tumors, the present study surprisingly showed no significant difference in overall survival among each Siewert subtype. These findings in survival outcomes are consistent with the results previously reported in other Asian countries[16,17,19]. However, they differ from a previous Western study by Siewert et al. that demonstrated better survival in type 1 and type 2 tumors than in type 3[15]. Multivariate analysis identified that age older than 65 years, pathologic lymph node stage, and histologic grade as independent predictors of poor survival outcome in the present study patients. These results are consistent with findings reported in prior studies[20-23].

Regarding the surgical approach for type 2 tumors, which is a controversial issue between Western and Eastern practices: In Western countries, type 2 tumors are managed similarly to type 1 tumors by performing esophagectomy. However, in Asian countries, type 2 tumors are managed similarly to type 3 tumors and distal gastric cancer[2]. The authors suggest that Thai patients are more likely to develop type 2 tumors due to gastric intestinal metaplasia from chronic HP gastritis than Barrett's esophagus, which is more common in Western populations. Endoscopic evidence of atrophic gastritis supported this hypothesis, despite the fact that the majority of

type 2 patients in the present study lacked a history or evidence of GERD. Consequently, the authors decided to approach type 2 in a similar fashion to type 3, predominantly by performing gastrectomy. Nevertheless, individuals with esophageal invasion more than 2 cm were scheduled for esophagectomy, as this significantly increased the probability of a positive proximal margin and mediastinal lymph node metastases[24-26]. The findings of the present study supported this hypothesis by demonstrating that type 2 tumors exhibit characteristics and prognosis more closely resembling type 3 tumors than type 1 tumors.

Furthermore, a significant majority (82.1%) of the patients with type 2 tumors underwent curative gastrectomy, whereas a smaller proportion (17.9%) required esophagectomy. All patients with type 3 tumors underwent gastrectomy.

Multimodal treatment is currently considered the gold standard for managing locally advanced AEG, supported by clear advantages identified in randomized controlled studies[27-29]. However, perioperative chemotherapy and neoadjuvant chemoradiation were not initially considered as standard treatments in the early phase of the present study because of its long timeframe. Primary resection has consistently been the dominant treatment approach in the present study hospital, as indicated by 86% of the patients who underwent this approach. Predictably, primary resection achieved curative results in just 80% of patients in the present study, leading to an unfavorable 5-year survival rate. In previous decades, the high unresectable rate was the main concern, prompting a modification of practice in response to well-established evidence. However, a consensus on the optimal choice between perioperative chemotherapy and neoadjuvant chemoradiation is yet to be established. The ongoing trial results will help to find the best neoadjuvant treatment for locally advanced AEG by comparing neoadjuvant chemoradiation with the current best choice of perioperative chemotherapy (FLOT regimen)[30,31].

While the present study revealed similarities between type 2 and 3 tumors and distal gastric cancer, the current information may not be sufficient to determine whether type 2 tumors constitute an aggregation of esophageal and gastric cancer types or represent a distinct histological entity. In the authors' future research, it is crucial to conduct a comprehensive investigation into the mucosal changes occurring on both the esophageal and gastric sides, along with exploring the consequences of HP infection. Moreover, incorporating molecular studies into future research is of great significance[32,33].

The primary limitation of the current study was its retrospective design. The study did not include information on patients with unresectable conditions, which could lead to selection biases and make it challenging to accurately determine the total number of cases of AEG. Additionally, the lengthy duration of the study meant that treatment approaches evolved over time, necessitating caution in interpreting the results.

Conclusion

In conclusion, the present study contributes to the knowledge gap in existing literature for the Southeast Asian region on AEG, revealing an increasing number of patients mirroring global trends and distinct epidemiological and clinicopathological characteristics in Thailand. Findings in the present study stress the importance of region-specific insights, calling for further molecular studies and comprehensive investigations into AEG pathogenesis in Thai population, which may be different from the Western population. The current study emphasizes the importance of remaining vigilant in adjusting interventions according to emerging evidence to achieve the most favorable outcomes for AEG patients in Thailand.

What is already known on this topic?

The worldwide incidence of AEG has risen over the past few decades. When categorized by the Siewert classification, AEG displays distinct characteristics between Western and Eastern populations. Western populations predominantly present with Siewert type 1 and type 2, whereas Eastern populations primarily consist of type 2 and type 3. This variation has sparked debates regarding the tumor's etiopathogenesis, surgical strategies, and neoadjuvant treatments.

What does this study add?

The distribution and clinicopathological characteristics of AEG in Thai patients, closely mirroring those in other Asian countries, with Siewert type 2 being the most common subtype. Type 2 tumors show similarities to type 3 rather than type 1, which differs from what is typically seen in Western populations. Implying that guidelines based only on Western contexts may not be entirely applicable to Thai patients. The consistently low survival rates in Thai patients emphasize the necessity to implement

neoadjuvant treatment strategies. This approach is supported by evidence from multiple randomized controlled trials, with the goal of improving long-term survival results.

Authors' contributions

Made substantial contributions to conception and design of the study and edited manuscript: TC. Analyzed data, performed a literature review, and wrote the manuscript: CT. Collected and analyzed data: SB.

Availability of data and materials

Research data are stored in an institutional repository and will be shared upon request to the corresponding author.

Conflicts of interest

All authors declared that there are no conflicts of interest.

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