



ORIGINAL ARTICLE

Diagnosis and treatment of esophagogastric junction tumors. Experience at the National Cancer Institute

Diagnóstico y tratamiento de los tumores de la unión esofagogástrica. Experiencia en el Instituto Nacional de Cancerología

Raúl Pinilla-Morales¹ , Silvia Guerrero-Macías² , Jorge Vélez-Bernal³ ,
Julián Meza-Rodríguez⁴ , Jairo Ospina-Gaitán⁵ , Jenith Lagos⁶ ,
Angélica Rodríguez-Peralta⁷ , Ricardo Oliveros-Wilches⁸

1. MD, specialist in General Surgery, and in Gastroenterology and Digestive Endoscopy; Chair, Department of Gastrointestinal Surgery, Instituto Nacional de Cancerología; Assistant Professor, School of Medicine, Universidad Nacional de Colombia, Bogotá, D.C., Colombia.
2. MD, specialist in General Surgery, fellow, Oncologic Surgery, Universidad Militar Nueva Granada, Instituto Nacional de Cancerología, Bogotá, D.C., Colombia.
3. MD, specialist in General Surgery, Instituto Nacional de Cancerología, Bogotá, D.C., Colombia.
4. MD, specialist in General and Oncologic Surgery, Clínica La Estancia, Popayán, Colombia.
5. MD, specialist in General and Gastrointestinal Surgery, and Digestive Endoscopy, Liga de Lucha Contra el Cáncer, Seccional Bogotá, Bogotá, D.C., Colombia.
6. MD, specialist in General Surgery, fellow, Vascular Surgery, Universidad de Antioquia, Medellín, Colombia.
7. MD, Department of Gastrointestinal Surgery, Instituto Nacional de Cancerología, Bogotá, D.C., Colombia.
8. MD, specialist in General and Gastrointestinal Surgery, and Digestive Endoscopy, Department of Gastrointestinal Surgery, Instituto Nacional de Cancerología, Bogotá, D.C., Colombia.

Abstract

Introduction: Proper diagnosis of gastroesophageal junction tumors is essential for the treatment of these patients. The classification proposed by Siewert-Stein defines its own characteristics, risk factors and surgical strategies according to the location. This study describes the characteristics of patients with adenocarcinoma of the esophagogastric junction treated at our institution.

Methods. Retrospective, descriptive, longitudinal study, which includes patients diagnosed with adenocarcinoma of the esophagogastric junction who underwent surgery at the National Cancer Institute in Bogotá, Colombia, between January 2012 and May 2017.

Results. Fifty-nine patients (84.7% men) were operated on, with a mean age of 62.5 years. In their order of frequency, the tumors were type II (57.6%), type III (30.7%) and type I (11.9%). 74.6% received neoadjuvant therapy and total gastrectomy was performed in 73% of the cases. The moderate diagnostic concordance with the Kappa index

Received: 9/8/2022 - Accepted: 11/22/2022 - Published online: 29/04/2023

Corresponding author: Angélica Rodríguez-Peralta, Calle 1 # 9-85, Instituto Nacional de Cancerología, Bogotá, D.C., Colombia.
Tel.: +57 312 5170622. Email: angiemeponasi@hotmail.com

Cite as: Pinilla-Morales R, Guerrero-Macías S, Vélez-Bernal J, Meza-Rodríguez J, Ospina-Gaitán J, Lagos J, Rodríguez-Peralta A, Oliveros-Wilches R. Diagnosis and treatment of esophagogastric junction tumors. Experience at the National Cancer Institute. Rev Colomb Cir. 2023;38:447-58. <https://doi.org/10.30944/20117582.2250>

This is an open Access under a Creative Commons License - BY-NC-ND <https://creativecommons.org/licenses/by-ncnd/4.0/deed.es>

was 0.56, differing from the endoscopic one in 33.9%. 10.2% of the patients presented some type of intraoperative complication. Three-year survival in type II tumors was 89.6% and 100% in those with complete pathologic response.

Conclusion. The use of different strategies is necessary for an adequate diagnostic process in tumors of the esophagogastric junction. In this series, Siewert II patients, those who received neoadjuvant therapy, and those who obtained a complete pathological response had a better three-year survival.

Keywords: esophagogastric junction; esophageal neoplasms; gastric neoplasms; classification; survival.

Resumen

Introducción. El diagnóstico adecuado de los tumores de la unión esofagogástrica es esencial para el tratamiento de estos pacientes. La clasificación propuesta por Siewert-Stein define las características propias, factores de riesgo y estrategias quirúrgicas según la localización. El objetivo de este estudio fue describir las características de los pacientes con adenocarcinoma de la unión esofagogástrica tratados en nuestra institución.

Métodos. Estudio retrospectivo, descriptivo, de corte longitudinal, que incluyó los pacientes con diagnóstico de adenocarcinoma de la unión esofagogástrica intervenidos quirúrgicamente en el Instituto Nacional de Cancerología, Bogotá, D.C., Colombia, entre enero de 2012 y mayo de 2017.

Resultados. Se operaron 59 pacientes (84,7 % hombres), con una edad media de 62,5 años. En su orden de frecuencia los tumores fueron tipo II (57,6 %), tipo III (30,7 %) y tipo I (11,9 %). El 74,6 % recibieron neoadyuvancia y se realizó gastrectomía total en el 73 % de los pacientes. La concordancia diagnóstica moderada con índice Kappa fue de 0,56, difiriendo con la endoscópica en 33,9 %. El 10,2 % de los pacientes presentó algún tipo de complicación intraoperatoria. La supervivencia a tres años en los tumores tipo II fue del 89,6 % y del 100 % en aquellos con respuesta patológica completa.

Conclusión. Es necesario el uso de diferentes estrategias para un proceso diagnóstico adecuado en los tumores de la unión esofagogástrica. En esta serie, los pacientes Siewert II, aquellos que recibieron neoadyuvancia y los que obtuvieron una respuesta patológica completa, tuvieron una mejor supervivencia a tres años.

Palabras clave: unión esofagogástrica; neoplasias esofágicas; neoplasias gástricas; clasificación; supervivencia.

Introduction

Gastric cancer corresponds to the fourth cause of cancer mortality worldwide, while esophageal cancer occupies the sixth position. In Western countries its incidence has increased rapidly due to a higher prevalence of gastroesophageal reflux disease^{1,2,3}. The literature in Latin America is very limited in this regard. In a reference institution in Brazil, a prevalence of 15% was reported in biopsies of esophageal and stomach lesions, and other series describe the experience in some cancer centers, with outcomes that do not seem to differ from those reported worldwide^{4,5,6}. In Colombia, this esophageal pathology has a lower incidence,

while gastric cancer represents the leading cause of mortality¹.

The implications of an accurate diagnosis in tumors of the esophagogastric junction (EGJ) require knowledge of this pathology, since errors in classification and inadequate choice of treatment are frequent in the management of these patients⁷. Siewert and Stein developed an endoscopic classification, based on the location of the tumor according to the EGJ⁸; however, in the most recent edition of the American Joint Cancer Committee (AJCC), adenocarcinomas of the EGJ are defined as those with center of the tumor 2 cm proximal and distal to the cardia, which can be a complement to

the Siewert classification for surgical decision-making, considering staging tumors found in the first 2 cm of the proximal stomach (types I and II) as esophageal cancers and the most distal as gastric or type III^{9,10} (Table 1).

Traditionally, Siewert I lesions have been treated as esophageal cancer and type III as gastric cancer, but with regard to Siewert II tumors there are still controversies, both in the neoadjuvant management strategy and in the surgical approach until now, without a consensus for its approach¹¹. With neoadjuvant management with chemotherapy, alone or associated with radiotherapy, adequate response rates have been reported with reduction in tumor size, increased rates of R0 resections, and improvement in survival outcomes; however, significant heterogeneity is observed in the studies results, without being able to discriminate these outcomes associated with a specific type of surgical approach¹².

Thoracotomy esophagectomy has been widely accepted as the treatment for Siewert I tumors, as well as total or proximal gastrectomy by abdominal approach for type III. The best surgical strategy for patients with Siewert II tumors has not been defined. A proximal gastrectomy with a transhiatal approach, resecting the mediastinal lymph nodes according to the length of the esophageal compromise, can be an oncological starting point for these lesions¹³; however, taking into account that radical surgery requires a resection with minimal 2 cm free margins proximal and a circumferential margin greater than 1 mm, associated with a lymphadenectomy of more than

15 nodes¹⁴, resection at the level of the esophagus and its anastomosis, in most cases requires an additional thoracic approach¹⁵.

In the initial review, Siewert found no difference in 5-year survival between the thoracic or transhiatal approach⁸. Some studies have sought to find survival benefits according to the surgical approach according to the type of tumor. Parry et al. compared the outcomes according to surgical management (esophagectomy versus gastrectomy) for type II tumors and, although they did not find differences in five-year survival, they reported a greater presentation of positive circumferential border and fewer resected paraesophageal nodes in patients who underwent only gastrectomy¹⁶. Other studies have evaluated the outcomes according to the type of approach in the thorax, finding a greater dissection of mediastinal nodes in the thoracoabdominal approach compared to the transhiatal approach, but with a higher morbidity (49% vs 34%), with no impact on survival for these patients^{17,18,19}.

Recently, Kurokawa et al., based on the involvement of the mediastinal and abdominal lymph nodes, found that a transhiatal abdominal approach is adequate for tumors with esophageal involvement of less than 3 cm, unlike those with a greater esophageal extension, where it is done necessary to add a right thoracic approach¹⁴.

No national publication was found that describes the experience in the management of patients with EGJ tumors. The objective of this work was to present the experience of the National Cancer Institute in Bogotá, Colombia, in the diagnosis and management of patients with EGJ tumors, analyzing one of the series with the highest representation of patients with Siewert type II, in whom there is the greatest controversy regarding its management.

Methods

Retrospective, observational, descriptive, longitudinal study, which included patients diagnosed with adenocarcinoma of the esophagogastric junction, who underwent surgery at the National Cancer Institute between January 2012 and May

Table 1. Siewert-Stein classification for tumors of the esophagus-gastric junction.

Siewert-Stein classification	
Type	Characteristics
I	Tumor located 1-5 cm above the esophagogastric junction, regardless of its invasion
II	Tumor invades the esophagogastric junction and is located 1 cm above and 2 cm below it
III	Tumor that invades the esophagogastric junction and is located 2-5 cm below it

2017. Patients with squamous cell histology and those with lost to follow-up before three years were excluded.

Based on the medical records and taking into account the endoscopic reports, surgical descriptions, surgical pathology reports, and postoperative follow-up, a database was created using the Research Electronic Data Capture (REDCap) platform. For the demographic characterization and description of the population, frequency measures were used for the case of categorical variables and means or medians, with their corresponding dispersion measures in the case of continuous variables. In order to assess the agreement between the endoscopic and pathological classification, agreement coefficients (weighted kappa) were estimated. To describe overall survival, Kaplan Meier curves were used and incidence density rates together with their 95% confidence intervals were reported. All statistical analyzes were performed in the R – Project v4.1.1 software (R Core Team®, 2021).

Results

Clinical features

A total of 59 patients (84.7% men) were included. The mean age was 62.5 years (SD 34–81 years) (Table 2). The mean body mass index (BMI) was 24.6 ± 3.67 Kg/m², with a minimum BMI of 17.6

and a maximum of 34.7 Kg/m². Comorbidities were found in 33 patients (55.9%), with vascular being the most frequent (45.5%); other underlying pathologies corresponded to immunological, endocrinological, neurological and respiratory alterations. According to the Eastern Cooperative Oncology Group (ECOG), the majority of patients (n=36) had a scale of 1 (61%). According to the endoscopic Siewert-Stein classification, the majority of patients (n=34) were type II (57.6%) and 40 patients were in clinical stage III (67.8%).

Neoadjuvant treatment was administered to 44 patients (74.6%), with the CROSS protocol (carboplatin or another platinum + taxane + radiotherapy) being the most frequently used, in 21 patients (47.7%), followed by the CALGB 9781 protocol (cispaltin + 5FU + radiotherapy) in nine (20.4%); doublet (11.3%) or triplet (13.6%) perioperative chemotherapy protocols were applied in a lower percentage. 85% of the Siewert I patients received some chemoradiotherapy scheme; 65% of Siewert II patients received neoadjuvant therapy, as did 23% of Siewert III patients. The median time between neoadjuvant treatment and the time of surgery was 2.7 months (IQR: 1.17), and ranged from 0.9 to 18.1 months. Half of the patients (50.8%) received adjuvant treatment, with the combination of capecitabine and oxaliplatin being the most widely used regimen (43.3%), followed by the McDonald protocol (20%).

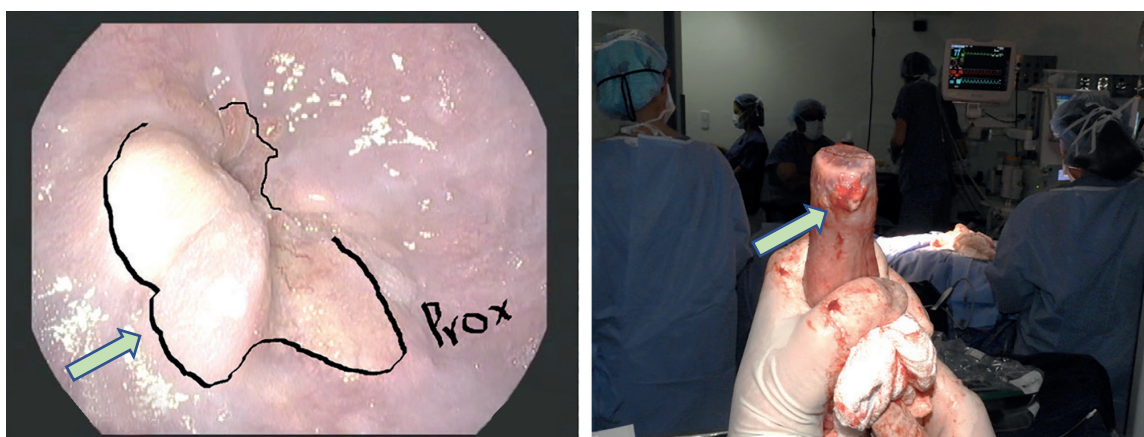


Figure 1. Endoscopic and surgical correlation image of a patient with a Siewert II gastroesophageal junction tumor. Tumor lesion indicated by arrows. Sources: The authors.

Table 2. Demographic, clinical, and surgical characteristics of patients with tumors of the esophagus-gastric junction who underwent surgery at the National Cancer Institute.

Characteristic		Total (n = 59)
Sociodemographic		
Age (years)	Median $\pm$ SD	62.5 $\pm$ 10,0
Sex, n (%)	Male	50 (84.7%)
	Female	9 (15.3%)
Clinics		
Body Mass Index, Kg/m ²	Median $\pm$ SD	24.6 $\pm$ 3.67
Comorbidities, n (%)	Yes	33 (55.9%)
	No	26 (44.1%)
ECOG scale, n (%)	0	22 (37.3%)
	1	36 (61.0%)
	3	1 (1.70%)
ASA clasification, n (%)	I	1 (1.70%)
	II	24 (40.7%)
	III	31 (52.5%)
	IV	3 (5.10%)
Siewert endoscopic classification, n (%)	I	7 (11.8%)
	II	34 (57.6%)
	III	18 (30.5%)
Clinical stage, n (%)	0	1 (1.70%)
	I	4 (6.80%)
	II	6 (10.1%)
	III	40 (67.8%)
Neoadjuvant, n (%)	IV	8 (13.6%)
	Yes	44 (74.6%)
	No	15 (25.4%)
Surgical		
Type of intervention, n (%)		
Open esophagectomy		13 (22.0%)
Laparoscopic esophagectomy		3 (5.10%)
Open total gastrectomy		40 (67.8%)
Laparoscopic total gastrectomy		3 (5.10%)
Operative time (minutes)	Median [IQR*]	245 (50.0)
Intraoperative bleeding (cc)	Median [IQR*]	200 (250)
Intraoperative complications, n (%)	Yes	6 (10.2%)
	No	53 (89.8%)

ECOG=Eastern Cooperative Oncology Group; ASA=American Society of Anesthesiology; SD=Standard deviation. Sources: The authors.

Surgical management

Total gastrectomy with transabdominal esophageal margin was performed in 43 patients (73%), and in the remaining 16 patients esophagectomy was performed using the McKeown, Ivor Lewis, minimally invasive, or open transhiatal techniques without thoracotomy. The endoscopic classification differed from the intraoperative classification in 38% of the cases, being 43.2% for type II patients, 33% for type I, and 23.5% for type III.

Regarding the Siewert type classification, 66.7% of the patients with type I were treated with esophagectomy by two or three routes and 33.3% by gastrectomy and transabdominal distal esophagectomy. Patients with type II underwent total gastrectomy plus transabdominal distal esophagectomy in 76.7% of cases, 9% with Ivor Lewis esophagectomy, 11.7% with three-way esophagectomy, and only one patient with esophagectomy plus transhiatal gastric ascent. 88.2% of the patients with a Siewert III classification underwent total gastrectomy, with the Ivor Lewis approach or with transhiatal esophagectomy.

The median surgical time was 245 minutes (IQR: 50.0), with a minimum time of 120 and a maximum time of 500 minutes. The average bleeding during the surgical procedure was 200 ml. The most used type of suture was the 25 mm circular stapler in Ivor Lewis type esophagectomy, open total gastrectomy and laparoscopic total gastrectomy.

Early outcomes

Intraoperative complications occurred in six patients (10.2%): bleeding in three, injury to adjacent structures in two, and airway injury in one. After surgery, 28 patients required transfer to the Intensive Care Unit (47.5%) with a mean stay of 9.5 days. Regarding hospital stay, the median was 11 days.

Twenty-two patients (37.3%) presented some type of postoperative complication, with a reoperation rate of 15.3% due to thoracic collection in four patients, anastomotic leak in three, intestinal obstruction in one patient, and

abdominal collection in one. The anastomotic leak rate was 6.8%, with no differences according to the type of approach performed. Complications occurred equally in patients who underwent gastrectomy or transhiatal esophagectomy and 2-way

or 3-way esophagectomy; however, of the total number of patients with cardiopulmonary complications (n=11), 63.6% had had an associated transthoracic approach. Mortality in the first 30 days occurred in two patients (3.4%) (Table 3).

Table 3. Postoperative and pathological characteristics of patients with tumors of the esophagus-gastric junction who underwent surgery at the National Cancer Institute.

Characteristic		Total (n = 59)
Postoperative		
ICU requirement, n (%)	Yes	28 (47.5%)
	No	31 (52.5%)
Hospital stay (días)	Median [IQR*]	11.0 (7.0)
Postoperative complications, n (%)	Yes	22 (37.3%)
	No	37 (62.7%)
Reoperation, n (%)	Yes	9 (15.3%)
	No	50 (84.7%)
Anastomotic leak, n (%)	Yes	4 (6.8%)
	No	55 (93.2%)
Hospital readmission, n (%)	Yes	4 (6.8%)
	No	55 (93.2%)
30-day mortality, n (%)	Yes	2 (3.4%)
	No	57 (96.6%)
Adjuvant treatment, n (%)	Yes	30 (50.8%)
	No	29 (49.2%)
Pathological		
Stage, n (%)	0	3 (5.1%)
	Ia	3 (5.1%)
	Ib	7 (11.9%)
	IIa	7 (11.9%)
	IIb	12 (20.3%)
	IIIa	1 (1.7%)
	IIIb	20 (33.9%)
	IVa	6 (10.2%)
Degree of differentiation, n (%)	Well	5 (8.5%)
	Moderate	26 (44.1%)
	Poor	13 (22.0%)
	Not reported	15 (25.4%)
Positive margin, n (%)	Yes	12 (20.3%)
	No	47 (79.7%)
Number of nodes resected	Median $\pm$ SD	20 $\pm$ 9.56
Pathological Siewert, n (%)	I	6 (10.1%)
	II	29 (49.2%)
	III	20 (33.9%)
	Indeterminate	4 (6.8%)

ICU=Intensive Care Unit; IQR=Interquartile range; SD=Standard deviation. Sources: The authors.

Pathological features

Most of the patients presented pathological stage IIIb (n=20, 33.9%), followed by stage IIb (20.3%). 8.3% of the patients had a complete pathological response, 80% of them had a Siewert type II endoscopic classification and had received neoadjuvant therapy with the CALGB 9781 protocol. The degree of histological differentiation was moderate in 44.1% of the patients.

A positive margin was found in the surgical piece or in the esophageal donut in 12 patients (20.3%): in the esophageal donut in four, in the proximal margin in four, in the circumferential margin in three, and in the distal in one. All patients with a positive proximal margin, including the esophageal donut, were managed with total gastrectomy plus transabdominal distal esophagectomy. Of the patients with a positive circumferential margin, 66.7% had undergone 3-way esophagectomy.

On average, the number of lymph nodes resected was 20 (SD: 9.56), with a minimum number of three and a maximum of 47. The number of lymph nodes resected was higher in classification III (mean=22, SD: 8.64); 22 patients (37.3%) had a lymphadenectomy with less than 15 nodes. Regarding the approach route, the average number of nodes resected was 21.1 in patients undergoing

total gastrectomy by transhiatal approach, with less than 15 nodes in 30.4% of cases. In patients undergoing 2-way esophagectomy, the average was 10.8 nodes, with 80% of lymphadenectomies having fewer than 15 nodes. In patients undergoing 3-way esophagectomy, the average was 19, with less than 15 in 42.8% of patients.

The Siewert pathological classification had a moderate concordance, with a Kappa index of 0.56 (95% CI: 0.33–0.79), differing from the endoscopic findings in 33.9% of the patients, which was higher for the patients with Siewert I (66%) and II (32.4%) and less in type III (23.5%). The concordance of the intraoperative classification with the pathological one was greater, differing only in 15.2% of the patients, with less disagreement when compared with the endoscopic diagnosis in type II tumors (16% vs 32.4%) (Table 4).

The median extension of the resected esophagus was 37.5 mm (SD: 10-150 mm); in the case of the proximal resection margin, the median was 24 mm (IQR: 26.2), with a minimum size of 3 and a maximum of 120 mm.

Long-term outcomes

The median follow-up period was 31.5 months (IQR: 39.0). There was a relapse in 16 patients (27%); of these, 43% had presented some early

Table 4. Concordance in relation to the type of endoscopic and pathological Siewert classification in patients diagnosed with adenocarcinoma of the esophagogastric junction.

		Pathological			
		I	II	III	Total
Endoscopic	I	4	1	1	6
	II	2	23	7	32
	III	0	5	12	17
Total		6	29	20	55

$\kappa = 0.56 \rightarrow 95\% \text{ CI } [0.33 - 0.79]$

kappa value (κ):	Match strength:
< 0.01	Poor
0.01 – 0.20	Weak
0.41 – 0.60	Moderate
0.61 – 0.80	Good
0.81 – 100	Very good

Sources: The authors.

postoperative complication. Only two of them had a positive margin (proximal and circumferential). The median number of lymph nodes resected for these patients was 19.5, with no difference with the patients who did not relapse (19.8). Two patients (12.5%) had a Siewert type I classification, 10 type II (62.5%) and four type III patients (25%). 75% of the patients who relapsed had been managed with total gastrectomy plus transhiatal distal esophagectomy. As an important finding, it was found that, of the patients treated with 3-way esophagectomy, 43% presented relapse, while only 14% of those operated with the Ivor Lewis technique had it.

Overall survival, defined as the time elapsed from the date of surgery to the date of death (or last contact), at two years was 74.9% (95% CI: 63.9–88.0) and at three years of 68.2% (95% CI: 55.5–83.9). Three-year overall survival for patients with Siewert type I was 68.6% (95% CI: 40.3–100), for type II it was 89.6% (95% CI: 79.0–100), and 51.8% for type III (95% CI: 32.4–82.7). In patients who received neoadjuvant therapy, survival was 76.3% (95 % CI: 63.7–91.4) and 70.9% (95 % CI: 50.4–99.8) in those who did not. All patients with pathologic complete response were alive and relapse-free at the time of data collection.

Survival in relation to the type of surgical treatment received was 65.3% (95% CI: 44.5–95.8) for patients who underwent esophagectomy and 78.5% (95% CI: 66.2–93.1) in patients managed with total gastrectomy. Patients with a positive margin presented a survival lower than that reported for the series in general, with 41.6% at three years. Of the 59 patients, 16 died (27.1%). Among the variables associated with an increase in mortality, it was found that half of the patients with lymphadenectomy with fewer than 15 nodes and all the patients with relapse died in the three-year follow-up.

Discussion

The incidence of tumors of the esophagogastric junction has been increasing worldwide, and a progressive increase is estimated until the year

2030 ⁶. In this series, a predominance of male patients was observed, with an average age of presentation (62.5 years), similar to that reported in studies characterizing the European and North American populations ²⁰⁻²².

In the 1980s, given the increasing confusion of the specific area of the EGJ as a zone beyond an anatomical structure, Siewert *et al.* proposed a classification for tumors in this location, with the intention of dividing this zone into three types of tumors, each with different characteristics, risk factors and surgical strategies. In our series, the distribution in the classification of these patients is striking, with more than 60% endoscopically diagnosed as Siewert II, compared to the Chilean series published in 2010, where 70% of the patients were classified as Siewert III ⁴. However, recent publications emphasize that type II tumors are the true tumors of the cardia, and this group that requires further study due to its difficulties in surgical and multimodal management.

Given the difficulty of adequately classifying these tumors, we wanted to analyze the concordance of the endoscopic, intraoperative, and pathological Siewert classification. In this series, endoscopy achieved an adequate classification when compared with the pathology report in 20 patients (66%), a result similar to those reported in other studies ^{23,24}. In addition, endoscopy was found to be more effective for classifying type III tumors (76.5%).

When the intraoperative diagnosis made by the surgeon was compared with the pathology report, this presented a concordance of 85%, with a more significant difference in favor of type II tumors (84% vs 67.6%) compared with the endoscopic diagnosis, which is expected given the possibility of a better anatomical evaluation.

This discrepancy indicates that the use of combined tools for preoperative classification and evaluation should be favored, taking into account that an inadequate diagnosis could lead to a change in the indication of the type of neoadjuvant management and implications for the possibility of adjuvant treatment. On the other hand, the planning of the surgical approach, transabdomi-

nal or thoracoabdominal, is based on the length of the esophageal compromise of more or less 3 cm, which would determine the extension of the lymphadenectomy according to the recommendations of the Yamashita and Kurokawa publications based on the compromised lymphatic system of EGJ tumors^{14,25}.

Multimodal management of patients with EGJ tumors is currently the standard in locally advanced stages, due to high treatment failure rates with surgical management alone. Neoadjuvant management, with or without radiotherapy, is recommended in patients with stages higher than T3 and N+, achieving an increase in the rate of R0 resections and survival benefits of 49 vs 24 months²⁴. In this series, 74.6% of the patients received neoadjuvant management, being more frequent for Siewert I and II locally advanced patients. The frequency of complete pathological response was 8.3%, with 80% of type II tumors. These results, which correspond to a group of patients with adenocarcinoma, are close to what has been reported in some studies for this subgroup (9-18%), but differ from the complete pathological response rates reported in other studies that included patients with squamous cell carcinomas and adenocarcinomas (26-28%)^{26,27}.

Surgical management in this series of patients is consistent with what has been reported in the literature, with a tendency towards a thoracoabdominal approach with two or three-way esophagectomy for Siewert I tumors and total gastrectomy for type III tumors. On the other hand, there is a tendency to manage with total gastrectomy and transabdominal esophageal margin for Siewert II tumors (76.7%), a distribution similar to that found in other studies²⁸. However, to date, the evidence supporting esophagectomy or total gastrectomy for this group of patients remains heterogeneous and the two systematic reviews with this objective reported similar three-year and five-year survival rates for both approaches, with differences that do not exceed 10%^{19,29}.

The rate of complications in this study (37.3%) does not differ from others¹⁸. Contrary to other series where an increase in morbidity greater than 50% has been described for the transthoracic

approach, in this series no significant differences were found between the types of approaches and the presentation of complications; only cardiopulmonary complications were more frequent in the transthoracic approach, with implications for hospital stay and the need for additional interventions during hospitalization.

One of the most studied complications in these patients is anastomotic leak; however, we identified only 6.7%, a value lower than the 12% mentioned in other series^{18,30}, and no association was found with the type approach performed or an impact on relapse or survival.

The outcomes of cancer patients are directly related to non-curative resections, therefore, achieving an R0 resection is the main objective in the surgical treatment of EGJ tumors. Some minimum standards have been described, one of which is the extension of the proximal margin greater than 5 cm in vivo or 2 cm ex-vivo^{11,31}. In this study, the data for this variable were obtained from the pathology report with a median greater than 2 cm, and an incidence of positive margins (longitudinal or circumferential) of 20%, finding an association with the transabdominal route in all cases, which reflects the technical difficulty that this approach may have in achieving a safe margin in some patients with Siewert II tumors. The literature reports an incidence of positive margins in the range of 3-40%³², with a negative impact on long-term outcomes, especially in patients in early stages. Likewise, for this series, the three-year survival was significantly lower in these patients compared to the general group (41.6% vs 68.2%), unrelated to locoregional relapse.

Another of the standards in the surgical management of EGJ tumors is radical lymphadenectomy, emphasizing not only the need for a minimum of 15 resected nodes, but also a dissection according to the location of the tumor and its esophageal extension. This objective, as well as the adequate margin, has been studied in relation to the type of approach, since the transabdominal route could limit the dissection of the middle and superior mediastinal nodes, underestimating their compromise^{11,31}. For this series, the average number of nodes resected was 20 and 37% of patients with

a lymphadenectomy of less than 15 nodes were reported, being more frequent for the 2-way and 3-way esophagectomy approach; however, this variable had no association with locoregional or distant relapse.

Conclusions

Despite the fact that the results of this series correspond to a retrospective study, they provide valuable information that is easily reproducible in other institutions in the country. In this series we found that mortality was directly related to relapse, while the variables associated with greater survival were Siewert II tumors, patients who received neoadjuvant therapy, and those who presented a complete pathological response. We also found that despite having a lower lymphadenectomy in the combined approach and a more frequent positive margin in the transabdominal approach, the difference in survival was not significant with that reported in other studies. Therefore, we could conclude that it is not just one, but several factors that together influence the oncological outcomes of patients.

Compliance with ethical standards

Informed consent: This research followed the principles established in the guidelines of Good Clinical Practices of the International Committee for Harmonization and the ethical principles of the Declaration of Helsinki, and in accordance with resolution 008430 of 1993 of the Ministry of Health of the Republic of Colombia, considered a study without risk. The Research Ethics Committee of the National Cancer Institute approved this research work.

Conflict of interest: none declared by the authors.

Funding: The financing resources of this research project come entirely from contributions of the authors.

Author's contributions

- Conception and design of the study: Raúl Pinilla-Morales, Jorge Vélez-Bernal.
- Acquisition of data: Jorge Vélez-Bernal, Julián Meza-Rodríguez, Jairo Ospina-Gaitán, Jenith Lagos, Angélica Rodríguez-Peralta.
- Data analysis and interpretation: Raúl Pinilla-Morales, Silvia Guerrero-Macías, Ricardo Oliveros-Wilches, Angélica Rodríguez-Peralta.

- Drafting the manuscript: Raúl Pinilla-Morales, Silvia Guerrero-Macías, Jorge Vélez, Angélica Rodríguez-Peralta.
- Critical review: Raúl Pinilla-Morales, Ricardo Oliveros-Wilches, Silvia Guerrero-Macías.

References

1. International Agency for Research on Cancer. IARC: Global Cancer Observatory, Cancer Today: GCO. Fecha de consulta 20 de julio de 2022. Disponible en: <https://gco.iarc.fr/today>
2. Zhang Y. Epidemiology of esophageal cancer. *World J Gastroenterol.* 2013;19:5598-606. <http://dx.doi.org/10.3748/wjg.v19.i34.5598>
3. Arnold M, Laversanne M, Brown LM, Devesa SS, Bray F. Predicting the future burden of esophageal cancer by histological subtype: international trends in incidence up to 2030. *Am J Gastroenterol.* 2017;112:1247-55. <https://doi.org/10.1038/ajg.2017.155>
4. De Barros SG, Vidal RM, Luz LP, Ghisolfi ES, Barlem GG, Komlós F, et al. Prevalência de adenocarcinoma do esôfago e da junção esofagogástrica durante 10 anos num centro de referência para câncer no sul do Brasil. *Arq Gastroenterol.* 1999;36:32-6. <https://pubmed.ncbi.nlm.nih.gov/10511877/>
5. Ulloa-Ochoa P, Palomeque-Bueno J, Vecilla-Chancay J. Adenocarcinoma de la unión esofagogástrica y su resolución quirúrgica en Guayaquil, Ecuador. *Revista Médica Sinergia.* 2019;4:e276. <https://doi.org/10.31434/rms.v4i9.276>
6. Butte JM, Becker F, Visscher A, Waugh E, Meneses M, Court I, et al. Adenocarcinoma of the esophagogastric junction: retrospective analysis of 39 patients. *Rev Med Chile.* 2010;138:53-60. <https://dx.doi.org/10.4067/s0034-98872010000100007>
7. Grotenhuis BA, Wijnhoven BP, Poley JW, Hermans JJ, Biermann K, Spaander MC, et al. Preoperative assessment of tumor location and station-specific lymph node status in patients with adenocarcinoma of the gastroesophageal junction. *World J Surg.* 2013;37:147-55. <https://doi.org/10.1007/s00268-012-1804-9>
8. Siewert JR, Stein HJ. Classification of adenocarcinoma of the oesophagogastric junction. *Br J Surg.* 1998;85:1457-9. <https://doi.org/10.1046/j.1365-2168.1998.00940.x>
9. Escrig-Sos J, Gómez-Quiles L, Maiocchi K. The 8th edition of the AJCC-TNM classification: New contributions to the staging of esophagogastric junction cancer. *Cir. Esp.* 2019;97:432-7. <https://doi.org/10.1016/j.ciresp.2019.03.006>
10. Kumagai K, Sano T. Revised points and disputed matters in the eighth edition of the TNM staging system for gastric cancer. *Jpn J Clin Oncol.* 2021;51:1024-7. <https://doi.org/10.1093/jjco/hyab069>

11. Hayashi T, Yoshikawa T. Optimal surgery for esophagogastric junctional cancer. *Langenbecks Arch Surg.* 2022;407:1399-1407. <https://doi.org/10.1007/s00423-021-02375-7>
12. Zhao X, Ren Y, Hu Y, Cui N, Wang X, Cui Y. Neoadjuvant chemotherapy versus neoadjuvant chemoradiotherapy for cancer of the esophagus or the gastroesophageal junction: A meta-analysis based on clinical trials. *PLoS One.* 2018;13:e0202185. <https://doi.org/10.1371/journal.pone.0202185>
13. Kurokawa Y, Takeuchi H, Doki Y, Mine S, Terashima M, Yasuda T, et al. Mapping of lymph node metastasis from esophagogastric junction tumors: a prospective nationwide multicenter study. *Ann Surg.* 2021;274:120-7. <https://doi.org/10.1097/sla.0000000000003499>
14. Mine S, Sano T, Hiki N, Yamada K, Kosuga T, Nunobe S, Yamaguchi T. Proximal margin length with transhiatal gastrectomy for Siewert type II and III adenocarcinomas of the oesophagogastric junction. *Br J Surg.* 2013;100:1050-4. <https://doi.org/10.1002/bjs.9170>
15. Okereke IC. Management of gastroesophageal junction tumors. *Surg Clin North Am.* 2017;97:265-75. <https://doi.org/10.1016/j.suc.2016.11.004>
16. Parry K, Haverkamp L, Bruijnen RC, Siersema PD, Ruurda JP, van Hillegersberg R. Surgical treatment of adenocarcinomas of the gastro-esophageal junction. *Ann Surg Oncol.* 2015;22:597-603. <https://doi.org/10.1245/s10434-014-4047-1>
17. Hulscher JB, van Sandick JW, de Boer AG, Wijnhoven BP, Tijssen JG, Fockens P, et al. Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the esophagus. *N Engl J Med.* 2002;347:1662-9. <https://doi.org/10.1056/nejmoa022343>
18. Sasako M, Sano T, Yamamoto S, Sairenji M, Arai K, Kinoshita T, et al; Japan Clinical Oncology Group (JCOG9502). Left thoracoabdominal approach versus abdominal-transhiatal approach for gastric cancer of the cardia or subcardia: a randomised controlled trial. *Lancet Oncol.* 2006;7:644-51. [https://doi.org/10.1016/s1470-2045\(06\)70766-5](https://doi.org/10.1016/s1470-2045(06)70766-5)
19. Heger P, Blank S, Gooßen K, Nienhüser H, Diener MK, Ulrich A, et al. Thoracoabdominal versus transhiatal surgical approaches for adenocarcinoma of the esophagogastric junction-a systematic review and meta-analysis. *Langenbecks Arch Surg.* 2019;404:103-13. <https://doi.org/10.1007/s00423-018-1745-3>
20. Verlato G, De Manzoni G. Epidemiology and risk factors. In: Giacopuzzi S, Zanoni A, de Manzoni G, eds. *Adenocarcinoma of the Esophagogastric Junction.* Cham: Springer; 2017. https://doi.org/10.1007/978-3-319-28776-8_1
21. Carneiro F, Moutinho C, Pera G, Caldas C, Fenger C, Offerhaus J, et al. Pathology findings and validation of gastric and esophageal cancer cases in a European cohort (EPIC/EUR-GAST). *Scand J Gastroenterol.* 2007;42:618-27. <https://doi.org/10.1080/00365520601101641>
22. El-Serag HB, Mason AC, Petersen N, Key CR. Epidemiological differences between adenocarcinoma of the oesophagus and adenocarcinoma of the gastric cardia in the USA. *Gut.* 2002;50:368-72. <https://doi.org/10.1136/gut.50.3.368>
23. Pedrazzani C, Bernini M, Giacopuzzi S, Pugliese R, Catalano F, Festini M, et al. Evaluation of Siewert classification in gastro-esophageal junction adenocarcinoma: What is the role of endoscopic ultrasonography? *J Surg Oncol.* 2005;91:226-31. <https://doi.org/10.1002/jso.20302>
24. Chevallay M, Bollschweiler E, Chandramohan SM, Schmidt T, Koch O, Demanzoni G, et al. Cancer of the gastroesophageal junction: a diagnosis, classification, and management review. *Ann N Y Acad Sci.* 2018;1434:132-8. <https://doi.org/10.1111/nyas.13954>
25. Yamashita H, Seto Y, Sano T, Makuuchi H, Ando N, Saako M, et al. Results of a nation-wide retrospective study of lymphadenectomy for esophagogastric junction carcinoma. *Gastric Cancer.* 2017;20(Suppl 1):69-83. <https://doi.org/10.1007/s10120-016-0663-8>
26. Charalampakis N, Tsakatikas S, Schizas D, Kykalos S, Tolia M, Fioretzaki R, et al. Trimodality treatment in gastric and gastroesophageal junction cancers: Current approach and future perspectives. *World J Gastrointest Oncol.* 2022;14:181-202. <https://doi.org/10.4251/wjgo.v14.i1.181>
27. Kamarajah SK, Griffiths EA; Oesophago-Gastric Anastomotic Audit (OGAA) Collaborative, Writing group list in the end of manuscript & co-authors listed in the Appendix. Postoperative and pathological outcomes of CROSS and FLOT as neoadjuvant therapy for esophageal and junctional adenocarcinoma: an international cohort study from the Oesophagogastric Anastomosis Audit (OGAA). *Ann Surg.* 2022; Online ahead of print. <https://doi.org/10.1097/sla.0000000000005394>
28. Kamarajah SK, Phillips AW, Griffiths EA, Ferri L, Hofstetter WL, Markar SR. Esophagectomy or total gastrectomy for Siewert 2 Gastroesophageal Junction (GEJ) Adenocarcinoma? A registry-based analysis. *Ann Surg Oncol.* 2021;28:8485-94. <https://doi.org/10.1245/s10434-021-10346-x>
29. Haverkamp L, Ruurda JP, van Leeuwen MS, Siersema PD, van Hillegersberg R. Systematic review of the surgical strategies of adenocarcinomas of the gastroesophageal junction. *Surg Oncol.* 2014;23:222-8. <https://doi.org/10.1016/j.suronc.2014.10.004>
30. Takeuchi M, Kawakubo H, Matsuda S, Mayanagi S, Irino T, Okui J, et al. Association of anastomotic leakage with long-term oncologic outcomes of patients with esophagogastric junction cancer. *World J Gastrointest Surg.* 2022;14:46-55. <https://doi.org/10.4240/wjgs.v14.i1.46>

31. Groth SS, Virnig BA, Whitson BA, DeFor TE, Li ZZ, Tuttle TM, *et al.* Determination of the minimum number of lymph nodes to examine to maximize survival in patients with esophageal carcinoma: data from the Surveillance Epidemiology and End Results database. *J Thorac Cardiovasc Surg.* 2010;139:612-20.
<https://doi.org/10.1016/j.jtcvs.2009.07.017>
32. Barbour AP, Rizk NP, Gonen M, Tang L, Bains MS, Rusch VW, Coit DG, Brennan MF. Adenocarcinoma of the gastroesophageal junction: influence of esophageal resection margin and operative approach on outcome. *Ann Surg.* 2007;246:1-8.
<https://doi.org/10.1097/01.sla.0000255563.65157.d2>