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Gastroesophageal Junction Adenocarcinoma Siewert Type II and III - Surgical Management and Early Postoperative Outcomes. A Single-Center Retrospective Study

Bogdan Filip[1,2], Ana Grigoras[1,2]*, Dragos-Viorel Scripcariu[1,2], Madalina Gavrilescu[1,2], Ionut Hutanu[1,2], Iulian Radu[1,2], Viorel Scripcariu[1,2]

[1]Department of Surgery, Grigore T. Popa University of Medicine and Pharmacy, Iasi, Romania
[2]1st Surgical Unit, Regional Institute on Oncology Iasi, Romania

***Corresponding author:**
Ana Grigoras, MD
Department of Surgery, Grigore T. Popa University of Medicine and Pharmacy, Iasi, Romania
E-mail: grigoras.ana@d.umfiasi.ro

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Rezumat

Adenocarcinomului joncțiunii gastroesofagiene Siewert tip II și III - Managementul chirurgical și rezultatele postoperatorii immediate. Un studiu retrospectiv unicentric

Introducere: Cancerul gastroesofagian presupune o localizare dificilă din punct de vedere al managementului chirurgical. Cele mai bune rezultate pe termen lung sunt obținute prin tratament chirurgical radical, incluzând o limfadenectomie adecvată, ceea ce necesită frecvent adăugarea unui abord toracic. În prezent există încă dezbateri privind managementul chirurgical al tumorilor de tip Siewert II şi III. Scopul acestui studiu a fost analizarea abordului chirurgical din perspectiva morbidității şi a rezultatelor patologice într-o serie continuă de pacienți, într-o manieră comparativă.
Metode: Am realizat o analiză retrospectivă a unei baze de date colectate prospectiv, care a inclus toate neoplasmele gastroesofagiene de tip Siewert II şi III tratate chirurgical intr-un centru terțiar, în perioada ianuarie 2015 – decembrie 2025. Am evaluat caracteristicile pacienților şi ale patologiei neoplazice, abordul chirurgical, complicațiile postoperatorii precoce şi rezultatele patologice finale.
Rezultate: Un total de 95 de pacienți au fost incluşi în studiu. Dintre aceştia, 40 de pacienți (42,1%) au prezentat tumori de tip Siewert II, iar 55 de pacienți (57,9%) adenocarcinoame de tip Siewert III, cu o vârstă medie globală de 66,5 ani (64,58–68,42). Indicele de comorbiditate Charlson nu a evidențiat diferențe semnificative între grupuri; indicele mediu general a fost 4,38 (3,98–4,77), relativ similar în cele două grupuri: 4,4 (3,83–4,96) vs. 4,44 (3,87–5,01), p=0,37. Pentru pacienții cu tumori Siewert II, în 22 de cazuri (55%) s-a practicat un abord chirurgical exclusiv prin laparotomie mediană, în 12 cazuri (30%) un abord toracoabdominal combinat, iar în 6 cazuri (15%) laparotomie mediană asociată cu toracotomie stângă. Opt pacienți (8,4%) au dezvoltat fistulă esojejunala: 3 cazuri (7,5%) pentru tumorile Siewert II şi 5 cazuri (9,1%) pentru tumorile de tip III. Una dintre cele mai frecvente complicații chirurgicale a fost infecția de plagă operatorie, apărută la 20 de pacienți (21%), mai frecvent la pacienții cu tumori de tip Siewert II: 12 cazuri (30%) vs. 8 cazuri (14,5%), p=0,06, fiind mai frecventă la pacienții la care a fost necesară toracotomia. Complicațiile medicale de grad III sau mai mare au fost întâlnite în 30 de cazuri (31,5%), cele mai frecvente fiind complicațiile infecțioase pulmonare, mai frecvente la pacienții cu tumori Siewert II (14 cazuri (35%) vs. 6 cazuri (10,9%), p=0,004).

Răspunsul patologic complet a fost obținut în 6 cazuri (6,3%), mai frecvent în cazul tumorilor Siewert II (5 cazuri (12,5%) vs. 1 caz (1,8%), p=0,03). Pacienții au prezentat o distribuție similară a stadiilor în cele două grupuri, cel mai frecvent fiind stadiul III [50 de cazuri (52,6%)]. De asemenea, au predominat tumorile slab diferențiate [45 de cazuri (47,4%)], cu invazie limfatică microscopică (71,6%) şi invazie vasculară (51,6%).
Concluzii: Trebuie depus orice efort pentru obținerea unei rezecții chirurgicale radicale. În această cohortă, nu s-a observat o creştere semnificativă statistic a complicațiilor globale în rândul pacienților supuşi toracotomiei. Cu toate acestea, trebuie interpretat cu prudență riscul suplimentar al toracotomiei.

Cuvinte cheie: cancer gastroesofagian, clasificarea Siewert, toracotomie, morbiditate

Abstract

Background: Gastroesophageal cancer represents a challenging localisation in terms of operative management. The best long-term results is given by the complete resection of the tumour with an adequate lymphadenectomy which often requires the addition of a thoracic approach. Currently there is still debate regarding the surgical management of Siewert type II and III tumours. The aim of this study was to analyse the surgical approach in terms of morbidity and pathological results on a continuous series of patients, in a comparative manner.
Methods: We performed a retrospective analysis on a prospective collected database that included all the gastro-esophageal tumours from January 2015 and December 2025. We selected only the Siewert type II and III tumours. We presented the patients and tumour characteristics, the surgical approach, early postoperative complications and final pathological results.
Results: A total of 95 patients were included in the study, 40 patients (42.1%) presented Siewert type II tumours and 55 patients (57.9%) had Siewert type III adenocarcinomas with an overall mean age of 66.5 years (64.58-68.42). The Charlson comorbidity index showed no differences, overall mean index was 4.38(3.98-4.77), relatively similar in the two groups 4.4 (3.83-4.96) vs 4.44 (3.87-5.01), p=0.37. For patients with Siewert II tumours in 22 cases (55%) an approach only through a median laparotomy was chosen, a combined thoracoabdominal approach 12 cases (30%), median laparotomy and left thoracotomy [6 cases (15%)]. There were 8 patients (8.4%) that developed esojejunal fistula, 3 cases (7.5%) for Siewert II tumours and 5 cases (9.1%) for type III tumours. One of the most common surgical complications was surgical site infection in 20 patients (21%), more frequent in patients with Siewert type II tumours, 12 cases (30%) vs. 8 cases (14.5%), p=0.06, more frequent in patients in which a thoracotomy was required. Overall grade III and above medical complications were encountered in 30 cases (31.5%), the most common were pulmonary infectious complications, more frequent in patients with Siewert II tumours [14 cases (35%) vs 6 cases (10.9%), p=0.004]. Complete pathological response was obtained in 6 cases (6.3%), more common for Siewert II tumours [5 cases (12.5%) vs. 1 case (1.8%), p=0.03]. Patients had a similar stage distribution in the two groups, the most common was stage III [50 cases (52.6%)] and more frequent had poorly differentiated tumours [45 cases (47.4%)] with microscopic lymphatic invasion (71.6%) and vascular invasion (51.6%).
Conclusion: Any attempt should be made to obtain complete surgical resection. In this cohort, no statistically significant increase in overall complications was observed among patients undergoing thoracotomy. However, this finding should be interpreted with caution and should not be considered evidence that thoracotomy carries no additional risk.

Keywords: gastroesophageal cancer, Siewert classification, thoracotomy, morbidity

Introduction

The incidence of gastroesophageal junction adenocarcinoma varies by geographical region, sex and age, worldwide estimates are 1-6 cases per 100,000 person-year (1), with an actual incidence in Western countries of 2-6/100,000, especially in older white males (2). Moreover, in East Asia, overall gastric cancer incidence is high, but gastroesophageal adenocarcinoma rates are lower (1-3/100,000) (3). There is an actual increase in incidence of actual cardia tumour incidence with lower rates of non-cardia gastric cancer in most regions (4). Currently there are many attempts to better classify this particular tumour location which sometimes it is recognised and treated as esophageal cancer and in other cases as gastric cancer. One of the oldest and most used classification is proposed by Siewert in 1988 (5). This classification includes data from preoperative imaging studies, endoscopy and intraoperative findings. Type I are distal esophageal adenocarcinomas, located 1-5 cm above the gastro-esophageal junction, frequently associated with Barrett oesophagus and are usually treated as oesophageal cancer. Type II are true cardia tumours

with tumour epicentre located 1cm above and 2 cm below to the gastroesophageal junction and have an intermediate biological behaviour, clinical management includes either esophagectomy or total gastrectomy depending on tumour extension. Type III are subcardial gastric adenocarcinomas located 2-5 cm below the gastroesophageal junction and are managed like gastric cancers. In Japan for cardia tumours it is used the Nishi classification, based on the center of the tumour, 2 cm above and below the normal anatomical gastroesophageal junction (6). Nishi's proposal has 5 types depending on the proximal or distal relative extent.

All the actual classification of this localisation refers only to the centre of the tumour and do not consider the longitudinal tumoral infiltration, especially at the level of the esophagus. The dissection of the distal esophagus is the most crucial element to have a negative resection margin and to perform a safe anastomosis in the posterior lower mediastinum. If those conditions are not met it is recommended to perform a thoracotomy for better exposure and safe technique. The general principles of surgical resection are: complete resection with negative longitudinal and circumferential margins, to limit the resection of normal esophagus, adequate lymphadenectomy in upper abdomen and lower mediastinum and the performance of a safe functional anastomosis. The most important prognostic factor is the extent of lymphatic spread, the most common site for metastatic lymphnodes are in the paracardial region, lesser curvature and coronary artery. For Siewert type I and II there is a higher incidence of mediastinal lymph nodes metastases. A large retrospective study showed that for type I the rate of mediastinal lympnodes spread is 32%, for type II of 16% and 12% for type III tumours (7). Those results are confirmed by a Japanese study, moreover there is a lower chance for distal gastric metastatic lymphnodes (8). Current recommendations for advanced cT3 or resectable cT4 tumours are abdomino-transhiatal total gastrectomy with distal esophageal resection for type III tumours, abdomino-thoracic subtotal esophagectomy with proximal gastric resection or abdomino-transhiatal/transthoracic total gastrectomy and esophagectomy with gastric/jejunal esophagostomy for type II tumours and total esophagectomy with limited proximal gastrectomy with high intrathoracic or cervical anastomosis (9) The only difficult choice is for advanced true cardia tumours (type II) in which tumour and patient's anatomical characteristic are the key factors in order to perform a safe resection and anastomosis. Other key factors that influence the decision for a specific approach are the mobility of the jejunum and the length of the mesentery or the vascularisation of small bowel, the disposition of visceral adiposity, the localisation of mediastinal enlarged lymphnodes and the possibility of a intraoperative frozen section evaluation of the esophagus. The advantages of the radical gastrectomy with Roux-en-Y esophagojejunostomy are the surgery takes place only in the abdomen, it allows a complete D2 lymphadenactomy; the downsize is the higher risk of R1 esophageal resection rate, the limited mediastinal lymphadenectomy and the risk of a difficult anastomosis due to jejunal particularities. The addition of a thoracotomy increases the risk of pulmonary complications and the risk of hiatal herniation of bowel, but it allows an accurate mediastinal lymphadenectomy and safe anastomosis with a lower rate of R1 resection margin. The cranial transection line for the esophagus needs to be at least at 2cm on the in situ specimen to limit the possible positive resection margin (10).

The aim of this study was to present in a comparative manner the treatment options and results for Siewert type II and III tumours in terms of surgical approach, resection, reconstruction, in a tertiary referral centre for digestive malignancies. We also presented the early postoperative outcomes and pathological results following radical surgery.

Material and Methods

This was a retrospective study on a prospective collected database that includes all the patients diagnosed with gastric or gastroesophageal junction cancer in which surgery was performed between January 2015 and December 2025 in the 1st Surgical Department of Regional Institute of Oncology Iasi, which is a tertiary referral centre for gastro-intestinal malignancies. We included in the analysis only the patients with Siewert type II (cardia tumours with its epicentre located between 1cm above and 2 cm below the anatomical esophagogastric junction) and type III (subcardial cancer with epicentre located 2-5 cm below the gastroesophageal junction) (11) The inclusion criteria were age > 18 years, positive diagnosis of gastric or gastro-oesophageal junction adenocarcinoma, complete preoperatory stadialisation and surgery with curative intent. Exclusion criteria were any other pathological subtype (such as neuroendocrine tumours or gastrointestinal stromal tumour), incomplete clinical stadialisation or missing data, patients with metastatic disease and palliative type of surgery.

Preoperative workup included endoscopy with tumour biopsy and complete description of the localisation of the tumour. All the patients were submitted to a thoracic and abdominal computer

tomography to establish the local and regional extent of the disease. For patients that developed a suspected distant metastatic lesion on tomography, a PET-CT was performed to guide the treatment. All patients were discussed in a multidisciplinary meeting and a decision to perform upfront surgery, or perioperative chemotherapy was considered based on clinical staging, patient comorbidities and patient's preferences. In cases in which neoadjuvant chemotherapy was indicated a restaging tomography of the chest, abdomen and pelvis was performed 2 weeks after the last session of chemotherapy and in the absence of tumour progression with extended local invasion or of metastatic disease the patient became a candidate to radical surgery. Preoperative evaluation included also a cardiac and pulmonary functional evaluation at the discretion of the anaesthesiologists.

Patients considered for thoracotomy underwent a more thorough evaluation of pulmonary function.

In all patients a total esogastrectomy with D2 lymphadenectomy was done, no proximal gastrectomy was performed. The extent of longitudinal oesophageal resection was done according to the preoperative imaging studies (mainly thoraco-abdominal tomography that indicates the extent of distal esophageal involvment) the intraoperative findings. One of the first steps of the intervention after the initial exploration of the liver and the peritoneal cavity is the assessment of the actual localisation of the tumour and the extent of esophageal involvement. By incising the oesophageal hiatus, a distal mediastinal oesophageal dissection was performed with periesophageal lymphadenectomy (lymph nodes no. 110 and no. 111), this also allowed a distal mobilisation of the oesophagus. Based on the patient's anatomical particularities (such as a shorter part of the abdominal esophagus) and on the tumour characteristics (cranial extension in the distal part of the thoracic esophagus or difficulties in transhiatal dissection of the distal esophagus due to the lateral extension of the tumor), a left thoracotomy was performed in order to allow adequate longitudinal esophageal mobilization and to facilitate the creation of the esophagojejunal anastomosis.

We preferred a mechanical esojejunal end-to-side anastomosis, only in cases of technical difficulties a hand sewn anastomosis was performed. In all patients a feeding jejunostomy was placed at the end of intervention. All the patients were kept a jeun for 7 days and oral liquid, followed by solid foods were reinitiated after a radiological control of the integrity of the anastomosis.

We recorded all the complications following surgery and we classified them according to the Dindo-Clavien classification (12) we included in the analysis only grade III and above complications. Fistula (anastomotic leak) was defined as the presence of turbid fluid, intestinal content or oral intake on drainage tube accompanied by signs of inflammation (fever, abdominal pain, elevated leucocyte count or C-reactive protein and procalcitonin).

Pathological evaluation of surgical specimen included a complete macroscopic characterisation regarding the epicentre of the tumour and the microscopical evaluation categorised the tumour as differentiated (well differentiated, moderate differentiated or papillary) and undifferentiated (poorly cohesive or signet cell carcinoma). For TNM staging, the 8th edition of the American Joint Committee on Cancer TNM Staging Manual for esophageal and gastric cancers was used (13).

We recorded the clinical and tumour characteristics for the patients with Siewert type II/III tumours (gender, age, tumour site, histological classification, biological parameters, comorbidities, surgical approach, postoperative complications and final pathological examination).

Continuous data was presented as means with standard deviation or (95% confidence interval) and compared using Student t-test or Mann-Whitney U test. Categorial data was presented as numbers and percentages and the chi-squared or Fisher exact test was used to compare proportions. A p-value of < 0.05 was considered statistically significant. All statistical analysis was performed using MedCalc version 23.4 (MedCalc Software, Ostend, Belgium). A multivariate analysis, which would involve further subdivision of the dataset, presents limited value. The only multivariate analysis was done regarding Charlson score and the previous tumour history.

The study was conducted with approval from de University of Medicine and Pharmacy in Iasi, with compliance to the ethical standards of the institutional research committee and all the patients provided a written informed consent at the beginning of the treatment.

Results

During the study period, there were 147 patients diagnosed with gastroesophageal adenocarcinoma that were admitted in the 1st Surgical Unit of the Regional Institute of Oncology Iasi. Of those patients in 34 cases (23.12%) a palliative procedure was performed (diagnostic laparoscopy to confirm the peritoneal carcinomatosis or feeding gastrostomy or jejunostomy). There were 17 patients (11.56%) diagnosed with Siewert type I adenocarcinoma and were not included in the analysis. A total of 95 patients

were included in the study, 40 patients (42.1%) presented Siewert type II tumours and 55 patients (57.9%) had Siewert type III adenocarcinomas. Baseline characteristics of the patients are shown in *Table 1*. The mean age of all cases was 66.5 years (64.58-68.42), without statistical difference in between the two groups, 63.9 (61.5-66.3) vs 67.1 (62.4-71.8). There was a higher percentage of male patients in both subgroups (72.6% males vs 27.4% females). Regarding the Charlson comorbidity index there were no differences, overall mean index was 4.38 (3.98-4.77), relatively similar in the two groups 4.4 (3.83-4.96) vs 4.44 (3.87-5.01), p=0.37. The most common preexistent condition was the presence of a cardiac disease, overall 57.9% of cases, equally distributed. The only statistically significant medical condition was the presence of a pulmonary disease 11 patients in total (11.58%), but more frequent in the Siewert III group 10 (18.2%) vs. 1 (2.5%), p=0.02 in the Siewert II group. There were no difference in the incidence of hepatic or renal diseases or in term of previous malignancies. The two groups had similar levels of hemoglobin and albumin, there was a difference in terms of CA19-9 levels, patients with Siewert II tumours had statistically significant higher levels 71.6 (11.46-131.81) vs. 34.63 (16.56-52.71), p<0.001. Based on clinical evaluation, neoadjuvant treatment was used in 42 cases (44.2%), more frequent for Siewert II tumours (23 cases (57.5%) vs. 19 cases (34.5%)). The addition of radiotherapy to chemotherapy was done in 2 cases.

Details regarding the surgical technique are presented in *Table 2*. Most patients in the Siewert III group had a total gastrectomy with distal oesophageal resection through a median laparotomy 52 cases (94.6%). In 2 cases a continuous thoracoabdominal approach was used and in 1 case a median laparotomy and a lower left thoracotomy was performed. For patients with Siewert II tumours only in 22 cases (55%) an approach by a median laparotomy was chosen, more often a combined thoracoabdominal approach 12 cases (30%), median laparotomy and left thoracotomy (6 cases (15%)).

In all cases a D2 lymphadenectomy was performed, a spleen preserving D2 lymphadenectomy was done in 69 cases (72.6%). There were 16 cases (16.8%) of multivisceral resection, excluding the spleen, among those the most common resection organs were part of the diaphragmatic hiatus in 12 cases, diaphragm 2 cases, liver 2 cases and pancreatic resection in 2 cases.

Early postoperative results are presented in *Table 3*. There were 8 patients (8.4%) that developed eso-jejunal fistula, in 7 cases it was a clinically diagnosed fistula and in 1 case a radiological diagnosed fistula. There were no differences in terms of incidence between the

Table 1. Patient's characteristics

	Total (N=95)	Siewert II tumours (N=40)	Siewert III tumours (N=55)	p-value
Age	66.5 (64.58-68.42)	63.9 (61.5-66.3)	67.1 (62.4-71.8)	0.54
Sex				0.81
M	69 (72.6%)	30 (75%)	39 (70.9%)	
F	26 (27.4%)	10 (25%)	16 (29.1%)	
Charlson score	4.38 (3.98-4.77)	4.4 (3.83-4.96)	4.44 (3.87-5.01)	0.37
Cardiac disease	55 (57.9%)	22 (54.7)	30 (57.9%)	0.86
Diabetes	22 (23.2%)	10 (25%)	12 (21.8%)	0.9
Pulmonary diseases	11 (11.58%)	1 (2.5%)	10 (18.2%)	0.02
Hepatic diseases	12 (12.6%)	7 (1.8%)	5 (9.1%)	0.36
Renal disease	15 (15.8%)	9 (22.5%)	6 (10.9%)	0.21
Neurological disease	12 (12.6%)	6 (15%)	6 (10.9%)	0.77
Previous/synchronous malignancies	7 (7.4%)	4 (10%)	3 (5.5%)	0.66
Hb	12.1 (11.1-13.1)	12.4 (11.8-13.1)	11.8 (11.2-12.4)	0.45
Albumine	4.32 (4.22-4.42)	4.39 (4.29-4.52)	4.27 (4.13-4.41)	0.87
ACE	3.39 (1.43-5.34)	3.21 (0.06-6.46)	3.48 (0.86-6.09)	0.97
CA 19-9	47.73 (24.05-71.4)	71.6 (11.46-131.81)	34.63 (16.56-52.71)	p<0.001
Neoadjuvant treatment	42 (44.2%)	23 (57.5%)	19 (34.5%)	0.04

Table 2. Surgical approach

	Total cases	Siewert II tumours	Siewert III tumours	p-value
Thoracoabdominal approach	14 (78.9%)	12 (30%)	2 (3.6%)	<0.005
Median laparotomy and left thoracotomy	7 (7.4%)	6 (15%)	1 (1.8%)	0.07
Median laparotomy	74 (77.9%)	22 (55%)	52 (94.6%)	<0.005
Splenectomy	26 (27.4%)	12 (30%)	14 (25.4%)	0.79
Multivisceral resections	16 (16.8%)	7 (17.5%)	9 (16.4%)	0.89

Table 3. Early postoperative results

	Total number of cases	Siewert II tumours	Siewert III tumours	p-value
Esojejunal fistula	8 (8.4%)	3 (7.5%)	5 (9.1%)	0.92
Duodenal stump fistula	4 (4.2%)	1 (2.5%)	3 (5.5%)	0.36
Abdominal collection	10 (10.5%)	4 (10%)	6 (10.9%)	0.88
Wound infection	20 (21%)	12 (30%)	8 (14.5%)	0.06
Medical complications	30 (31.5%)	18 (45%)	12 (21.8%)	0.01
Pulmonary complications	20 (21%)	14 (35%)	6 (10.9%)	0.004
Cardiovascular complications	10 (10.5%)	3 (7.5%)	7 (12.7%)	0.41
Sepsis	13 (13.7%)	4 (10%)	9 (16.4%)	0.37
Death	4 (4.2%)	2 (5%)	2 (3.6%)	0.74

two groups, 3 cases (7.5%) for Siewert II tumours and 5 cases (9.1%) for type III tumours. In all cases a conservative treatment was initiated, no invasive manoeuvres were required. Overall, in 4 cases (4.2%) a duodenal fistula was encountered. More frequent an abdominal collection was diagnosed in 10 cases (10.5%), in 6 cases in patients either with esophagojejunal or duodenal stump fistula and in 4 cases in patients with sepsis of unknown origin. In 3 cases a surgical drainage was required.

One of the most common surgical complications was wound infection in 20 patients (21%), more frequent in patients with Siewert type II tumours, 12 cases (30%) vs. 8 cases (14.5%), p=0.06, more frequent in patients in which a thoracotomy was required. Overall grade III and above medical complications were encountered in 30 cases (31.5%), the most common were pulmonary infectious complications, more frequent in patients with Siewert II tumours (14 cases (35%) vs 6 cases (10.9%), p=0.004). Pulmonary complication were observed in 8 patients with additional thoracotomy and in 6 patients with only median laparotomy. Death occurred in 4 cases (4.2%) equally distributed in the two groups, the causes of death were: pulmonary sepsis in 2 cases, myocardial infarction in 1 case and stroke in 1 case.

Final pathological examination results are presented in *Table 4*. Complete pathological response was obtained in 6 cases (6.3%), more common for Siewert II tumours [5 cases (12.5%) vs. 1 case (1.8%), p=0.03]. Patients had a similar stage distribution in the two groups, the most common was stage III [50 cases (52.6%) and more frequent had poorly differentiated tumours (45 cases (47.4%)] with microscopic lymphatic invasion (71.6%) and vascular invasion (51.6%). The mean number of resected lymph nodes was 36.71 (33.47-39.9) equally distributed in the two groups, and the mean number of positive lymph nodes was 6.38 (4.35-8.42), with lower numbers in Siewert II group [5.9 (2.2-9.7) vs. 6.7 (4.3-9.05), p=0.05]. The R1 resection rate was 5.26% (5 patients), in 3 cases for Siewert II tumours and 2 cases of Siewert III tumours.

We performed a univariate analysis of factors involved in the development of a postoperative complication (we included all complications), as seen in *Table 5*. The only statistically significant factor was the Charlson comorbidity index 4.88 (4.18-5.58) vs. 4.06 (3.60-4.53), p=0.04. Even by introducing the

Table 4. Final pathological evaluation of resection specimens

	Total number of cases	Siewert II tumours	Siewert III tumours	p-value
Grading				
G1	10(10,5%)	3(7,5%)	7(12,7%)	0,41
G2	27(28,4%)	14(35%)	13(23,6%)	0,22
G3	45(47,4%)	20(50%)	25(45,4%)	0,66
Gx	11(11,6%)	3(7,5%)	8(14,5%)	0,28
L1	68(71,6%)	30(75%)	38(69,1%)	0,61
V1	49(51,6%)	20(50%)	29(52,7%)	0,65
Pn1	47(49,5%)	20(50%)	27(49,1%)	0,79
Complete response	6(6,3%)	5(12,5%)	1(1,8%)	0,03
Stage 1	10(10,5%)	4(10%)	6(10,9%)	0,88
Stage II	29(30,5%)	12(30%)	17(30,9%)	0,92
Stage III	50(52,6%)	19(47,5%)	31(56,4%)	0,39
Mean nr of lymphnodes	36,71(33,47-39,9)	36,6(30,8-42,4)	36,8(32,9-40,6)	0,09
Mean nr of positive lymphnodes	6,38(4,35-8,42)	5,9(2,2-9,7)	6,7(4,3-9,05)	0,05
R1 resection	5(5,26%)	3(7,5%)	2(3,6%)	0,4

Table 5. Univariate analysis of factor involved in the occurrence of a postoperative complication

	Complications N=36 (37.9%)	Without complications N=59 (62.1%)	p-value
Age	68.16 (65.18-71.14)	65.49 (62.95-68.02)	0.18
Sex			0.52
M	28	41	
F	8	18	
Charlson score	4.88 (4.18-5.58)	4.06 (3.60-4.53)	0.04
Cardiac disease	22 (61.11%)	30 (50.84%)	0.44
Hypertension	23 (63.88%)	35 (59.32%)	0.82
Diabetes mellitus	11(30.55%)	11(18.64%)	0.27
Pulmonary conditions	7 (19.44%)	4 (6.77%)	0.12
Hepatic diseases	4 (11.11%)	8 (13.55%)	0,97
Chronic renal diseases	8 (22.22%)	7 (11.86%)	0.29
Previous/synchronous tumours	1(2.77%)	7 (11.86%)	0.08
Hb	11.68 (10.84-12.51)	12.31 (11.82-12.80)	0.15
Albumine	4.35 (4.17-4.53)	4.30 (4.19-4.42)	0.66
ACE	2.23 (1.14-3.32)	4.14 (0,95-7.32)	0.34
CA 19-9	44.92 (11.67-78.18)	49.11 (16.75-81.57)	0.86
Neoadjuvant treatment	13 (36.11%)	29 (49.15%)	0.30
Thoracotomy	11(30.55%)	10 (16.94%)	0.12
Splenectomy	7(19.44%)	19 (32.2%)	0.26
Multvisceral resection	5 (13.88%)	11(18.64%)	0.75
R1 resection	3 (8.33%)	2 (3.38%)	0.29

Charlson score and the previous tumour history (p=0.08) in the multivariate analysis, we found no statistically significant factors associated with the development of a complication. Thoracotomy was not statistically associated with overall postoperative complications in the univariate analysis (p=0.12)

Discussions

Gastroesophageal junction adenocarcinoma represents a particular type of malignancy that raises important therapeutic challenges regarding the surgical approach and the extent of lymphadenectomy. The local and regional extension of this tumour seems to be relatively similar for type I Siewert tumours as the oesophageal cancer and for type III tumours as gastric tumours. For true cardia tumours there is a debate whether should be treated either by thoracoabdominal approach or by only abdominal approach with total gastrectomy and distal esophageal resection. Since most of the cases present in advanced stages, peri-operative chemotherapy emerged as a therapeutic approach to improve long-term outcomes of these patients. The rational for preoperative chemotherapy is to obtain tumour downstage, increase the chance to perform a R0 resection, and to treat the micrometastatic disease. Those principles are confirmed by the results of UK MAGIC trial which showed that the combination of 3 cycles of epirubicin, cisplatin and 5-fluorouracil (ECF) versus surgery alone increased overall survival from 23% to 36% (14), the ACCORD-07 trial (15) and moreover the AIO-FLOT4 study that showed the superiority of infusional 5-Fluorouracil, Leucovorin, Oxaliplatin and Docetaxel (16) and imposed as the standard of treatment this regimen. There are studies that showed that total neoadjuvant treatment can safely be applied for patients with gastric or gastro-esophageal junction cancer (17). In our study we had overall 44.2% patients that were submitted to neo-adjuvant treatment, in the first part of the study the ECF regimen, and in the latter the FLOT regimen, moreover patients with cardia tumours (57.5%). For patients with neoadjuvant treatment, we obtained a complete pathological response in 6 patients (6.3%) with a higher percentage for Siewert II tumours (12.5%). Based on the results of our study, the addition of neoadjuvant chemotherapy did not increase the overall risk of postoperative complications. Due to the long period of study, the chemotherapy regimens were not the same, in the first part of the study ECF regimen was used, and in the last 4 years the treatment shifted towards FLOT regimen. Another explanation was that patients were referred for surgical treatment from other institutions in which chemotherapy was performed. Imunnotherapy, especially Durvalumab, was not used in our patients, mainly because it was not reimbursed by the healthcare system.

Currently there is the agreement that for Siewert type III tumours an extended gastrectomy with limited dissection of the distal esophagus represents the best approach. A macroscopic resection margin at least 2-4 cm seems to give the best long term results (overall survival and progression free survival), with the highest chance of a R0 resection rate especially for tumours smaller than 4 cm and intestinal type histology (18). In our study for type III tumours, we preferred the abdominal approach with radical gastrectomy and at least 4 cm of macroscopic free length of the esophagus to reduce the rate of R1 resection margins. During the study period there was no routine intraoperatory histopathological evaluation of the resection status of the esophagus, and an acceptable 4-5 cm distance from the superior margin of the tumour was safe for the transection. Despite this, there were 5 cases (5.26%) in which a longitudinal R1 resection margin was proven on final pathological evaluation, equally distributed in the two subgroups, which suggest that the addition of a thoracotomy did not decrease the rate of R1 longitudinal resection rate. None of the patients presented positive circumferential resection margins. The management of those patients consisted of chemoradiotherapy in 4 cases, only chemotherapy in 1 case and surgical reresection was

performed in 3 cases, by using an abdominal and thoracic approach. For type II tumours (true cardia tumours), we prefer to begin the intervention by an abdominal approach with initial dissection at the level of the hiatus and based on the tumour characteristics and on the anatomical particularities of the patients an initial attempt to dissect the distal part of the mediastinal esophagus is performed. If an accurate length of the esophagus is obtained, often by a surgical enlargement of the hiatus, the intervention continues only in abdominal approach. For the rest of the cases an additional left thoracotomy is performed for the esophageal dissection, lymphadenectomy and a safe anastomosis. An international survey regarding the worldwide trend in surgical techniques for gastro-esophageal cancer showed that for type II tumours 66% of responders prefer extended gastrectomy, 27% esophagectomy and 7% total gastrectomy (19). Moreover, Siewert III tumours were treated by gastrectomy in 90% of responders, esophagectomy in 6% and extended gastrectomy in 4%. Up to this moment there is no evidence for a superiority of a specific approach in terms of survival, oncological outcome and quality of life, all the data are based on retrospective studies. Currently there is an ongoing trial (CARDIA trial) (20), which is a randomized, multi-national trial comparing transthoracic esophagectomy with transhiatal extended gastrectomy for Siewert II tumours. There are few randomised trials regarding the surgical approach for Siewert type II tumours, one of them was JCOG9502, which was a Japanese phase III trial, that included 167 patients with type II and III tumours randomised for left thoracoabdominal or abdominal transhiatal approach (20). Transhiatal approach was associated with better 5-year overall survival (52.3% vs. 37.9%), lower morbidity (34% vs. 49%), and lower pneumonia rates (4% vs. 13%). This established TH as standard for tumors with ≤ 3 cm esophageal involvement — but the trial specifically excluded patients with > 3 cm invasion, leaving that subgroup unresolved. Currently there is an ongoing trial (CARDIA trial) (21), which is a randomized, multi-national trial comparing transthoracic esophagectomy with transhiatal extended gastrectomy for Siewert II tumours, without long-term data result. Although it was not a randomised study, the JGCA-JES nation-wide prospective study (22), used a therapeutic efficacy index to define which lymph node station are worth dissecting and proposed tailoring of the surgical approach based on esophageal length invasion, trans-hiatal for an invasion less than 2 cm , either approach for 2-3 cm invasion and transthoracic for over 3 cm invasion. In our study nearly half of the patients required a left thoracotomy (55% of cases) either by a separated thoracotomy (15%) or by a continuous laparotomy and thoracotomy (30% of cases).

One of the most severe complication following an extended gastrectomy is the occurrence of a esojejunal anastomosis fistula and this can lead to an increased hospital stay and overall mortality (21). A recent systematic review that included 16 studies with 42489 patients showed an anastomotic leakage rate between 2.1-16.2%, among the risk factors were age, BMI, impaired respiratory function, prognostic nutritional index, alcohol consumption, chronic renal failure, diabetes, mixed-histology type on multivariate analysis (21). Another important factor for the occurrence of this complications can be the duration of surgery, operative time seems to be an independent risk factor (22) , and the surgeon experience, higher leak rates were found in less experienced surgeons (23). In our study the overall esojejunal anastomotic leak rate was 8,4% , in line with other published studies, interestingly a higher percentage for Siewert III tumours (9.1%) than for type II (7.5%), but without statistical significance. One explanation for these results can be that the Siewert III tumours tent to be more advanced, with a difficult intraoperative management. One interesting result in our study is that the rate of medical complications differ with tumour locations. The higher rate of medical and especially pulmonary complications in type II tumours would be explained by the higher percentage of thoracotomies in this subgroup, but there have been 8 patients that developed pulmonary infection in thoracotomy group compared with 6 patients with infectious pulmonary complication and only median abdominal incision. Although the addition of a thoracotomy seems to decrease the rate of a anastomotic fistula by providing a better visualisation during the performance of the anastomosis and the direct visualisation of its integrity, this can induce a higher chance for a pulmonary complication.

Study Limitations

This study has several drawbacks, one of them is the retrospective character, and this can increase selection bias. Other limitations of this study are the fact that we could not obtain in all patients data regarding estimated blood loss and intraoperative anastomotic difficulties which can impair the post-operative course of the patient. Also, the length of hospital stay was not one of our main focus. Although the surgeries in this series of patients were performed by mainly 3 surgeons with high expertise and experience in upper gastro-intestinal surgery, intra-operative assessment of the anastomotic tension remains subjective and could not be objectively assessed in this study. Moreover, in none

of the patients an intraoperative frozen section pathological evaluation of the resected esophagus was performed. The extent of longitudinal resection was chosen based on the macroscopic cranial margin of the tumour; a clearance of approximatively 5 cm was considered to be safe. The advantage of this study is that includes a continuous series of patients, with a relatively similar preoperative evaluation and a uniform surgical treatment by a highly experienced and dedicated team. Nevertheless, another drawback is the lack of long-term oncological outcome, in terms of overall survival, recurrence pattern and disease-free interval. No actual data was available for all patients to perform such analysis and this will be the scope of another study.

Conclusion

In conclusion, this study presents our postoperative outcomes in patients with gastroesophageal cancer according to the surgical approach. In patients with Siewert type II and III gastroesophageal junction tumours, the addition of a thoracotomy is sustained by the higher possibility of negative longitudinal resection margins, a secure anastomosis, and adequate lymphadenectomy. In this cohort, no statistically significant increase in overall complications was observed among patients undergoing thoracotomy. However, this finding should be interpreted with caution and should not be considered evidence that thoracotomy carries no additional risk. A higher rate of pulmonary complications was observed. Particularly in Siewert type II tumours, a thoracotomy may be considered based on preoperative assessment and intraoperative findings. In cases with more extensive gastric involvement, total gastrectomy with Roux-en-Y esophagojejunostomy may be required.

Conflicts of Interest

All authors declare no conflicts of interest regarding this article.

Ethical Statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Regional Institute of Oncology Iasi (protocol 60/ 27 February 2026). The requirement for individual informed consent was waived due to the retrospective nature of the study. All included patients had previously provided consent for data collection at the time of admission to the Regional Institute of Oncology, Iasi.

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