DOI: https://doi.org/10.2298/SARH240423052M
UDC: 616.329/.33-006.6

CURRENT TOPIC • АКТУЕЛНА ТЕМА

Gastroesophageal junction cancer – current topic and treatment dilemmas

Nikola Milošević[1], Suzana Stojanović-Rundić[1,2], Srđan Milanović[1], Ebrahim Keramatollah[2,3], Predrag Sabljak[2,3], Ognjan Skrobić[2,3], Miloš Bjelović[4]

[1]Institute for Oncology and Radiology of Serbia, Belgrade, Serbia;
[2]University of Belgrade, Faculty of Medicine, Belgrade, Serbia;
[3]University Clinical Centre of Serbia, Clinic for Digestive Surgery – First Surgical Clinic, Belgrade, Serbia;
[4]Euromedik Hospital, Belgrade, Serbia

SUMMARY
Treatment of gastroesophageal junction carcinomas have been debated for many years. This type of carcinomas has been classified as either gastric or esophageal carcinomas until Siewert's classification was established and they were defined as a distinct entity. Risk factors for the development of these cancers are gastroesophageal reflux and Barrett's esophagus, obesity, *Helycobacter pylori* infection, smoking, and alcohol. Symptoms of this disease include retrosternal pain, dysphagia to aphagia, and weight loss. Esophagogastroduodenoscopy with biopsy and pathohistological verification as well as CT of the chest and abdomen are crucial in establishing the diagnosis. Adenocarcinoma is predominant histological type of these tumors. The stage of the disease is defined by the TNM classification. Treatment of gastroesophageal junction cancer is complex, multidisciplinary, and multimodal, and involves the use of surgery, chemotherapy, and radiotherapy, alone or in different combinations. Surgery is the major treatment modality for these tumors, especially in local stages. Radiotherapy is used in the treatment of these tumors in all stages of the disease, and especially in the multimodal treatment of locally advanced gastroesophageal junction cancer, both preoperatively and postoperatively, usually in combination with chemotherapy. Chemotherapy is used in the treatment of these cancers as preoperative, postoperative and systemic. Immunotherapy and target therapy, as new promising therapy, is usually applied in a systemic and postoperative approach. Future directions in the treatment of these cancers are directed towards new surgical procedures, new types of immunotherapy, as well as new radiotherapy techniques.
Keywords: gastroesophageal junction cancer; surgery; radiotherapy

INTRODUCTION

Gastroesophageal junction (GEJ) carcinomas are relatively rare and aggressive tumors with an increase in the incidence rate in recent decades [1].

Siewert's classification defines them as tumors located within 5 cm of the anatomical cardia (distal or proximal):

1) type I – adenocarcinoma of the distal esophagus with tumor epicenter 1–5 cm above the GEJ,

2) type II – adenocarcinoma of the cardia with the epicenter of the tumor 1–2 cm below the GEJ, and

3) type III – subcardial gastric carcinoma with the epicenter of the tumor 2–5 cm below the GEJ.

Risk factors for GEJ cancers are gastroesophageal reflux and Barrett's esophagus, obesity, *Helicobacter pylori* infection and smoking [2]. The most common symptoms include retrosternal pain, dysphagia to aphagia, regurgitation of the stomach contents and weight loss. The key methods for diagnosing GEJ cancers are esophagogastroduodenoscopy with biopsy and thoracic and abdominal computed tomography. Histopathology with immunohistochemical staining is used for definitive diagnosis and the majority of GEJ cancers are adenocarcinomas, less often they are squamous type. The genome of gastroesophageal carcinoma is complex and includes mutation of the most common genes (especially TP53), high microsatellite instability, and mutation of oncogenic kinases (EGFR, HER2, and MET). According to the TNM staging, GEJ carcinomas can be divided as follows:

1) local (early) stage (Tis-T1 N0 M0),

2) locally advanced stage (T2-4 N1-3 M0), and

3) metastatic stage (T1-4 N1-3 M1).

TREATMENT

The multimodality and multidisciplinarity are necessary in the treatment of GEJ cancer. Surgery, radiotherapy (RT), and chemotherapy (CT) are treatment modalities. The basic principles of treatment are that early GEJ cancers are treated only with surgery, locally advanced cancers with a combination of surgery, CT, and RT, and metastatic cancers with CT or RT. Most widely used recommendations for the treatment algorithm are the National Comprehensive Cancer Network (NCCN) and the European Society of Medical Oncology (ESMO).

Received • Примљено: April 23, 2024
Revised • Ревизија: June 17, 2024
Accepted • Прихваћено: June 24, 2024
Online first: July 1, 2024

Correspondence to:
Nikola MILOŠEVIĆ
Institute for Oncology and Radiology of Serbia
Pasterova 14
11000 Belgrade, Serbia
milosevicnikola43@gmail.com

Early stage

Local (early) GEJ carcinomas includes Tis and T1a-b N0 stage of disease.

The primary approach in early stage of the disease is radical surgery and includes endoscopic techniques such as endoscopic mucosal resection and endoscopic submucosa dissection (ESD), as well as classical surgical techniques such as esophagectomy with gastrectomy and lymphadenectomy.

Endoscopic mucosal resection is an option for T1a lesions smaller than 10–15 mm and ESD may be considered in T1a lesions larger than 15 mm [3]. If after endoscopic resection histopathology parameters show poor differentiation, lymphovascular invasion, or positive margins, further steps may include adjuvant radiochemotherapy (RCT).

For T1b GEJ cancers esophagectomy is indicated, but for T1b cancers with favorable histopathological pattern (well-differentiated, smaller than 2 cm and without LVI) ESD may be a good alternative to esophagectomy. Two types of esophagectomy are used, transthoracic (Ivor-Lewis procedure) and transhiatal. The radicality of surgery is imperative due to the significant deep and *per continuitatem* spread of these tumors (significantly more in type I and II than in type III) [4]. The consensus in surgical treatment of GEJ type I cancer is esophagectomy with transthoracic approach [5]. GEJ type II carcinomas are true junctional tumors, so the choice of surgical approach is very controversial. Two types of surgery are used, total gastrectomy with transhiatal distal esophagectomy and transmediastinal esophagectomy with proximal gastrectomy [6]. Total gastrectomy with distal esophagectomy is needed for GEJ type III carcinomas [6]. Lymphadenectomy implies a dissection of mediastinal and abdominal lymph nodes ("two-field"). Recommendations for lymphadenectomy in GEJ type I cancer are upper, middle, and lower mediastinal and abdominal dissection, in type II are upper, middle, and lower mediastinal and abdominal dissection, and in type III these are lower mediastinal and abdominal dissection [7].

In recent years, newer surgical procedures in the treatment of GEJ carcinoma such as robot-assisted, hybrid, and minimally invasive esophagectomies may have the potential to achieve better results compared to conventionally accepted surgical techniques [8].

Locally advanced stage

Locally advanced GEJ carcinomas include T2-T4 N0-3 stage of the disease.

For patients who are medically fit and present with good performance status (ECOG PS 0–1) with potentially resectable locally advanced disease stage T2-T4a, indication is preoperative RCT with/without surgery, perioperative CT with surgery or neoadjuvant/perioperative immune checkpoint inhibitors therapy with/without surgery. T4b tumors with involvement of the surrounding organs are unresectable, so that patients, if they are medically fit with ECOG PS 0–2 are candidates for definitive CRT or CT.

Today, a standard in the treatment of a locally advanced GEJ carcinoma is a multimodal approach (a combination of RT, CT, and surgery). Even though RCT provides higher rates of complete pathologic response and better locoregional control then perioperative CT, survival in both types of therapy is similar [9]. The ESOPEC-trial [10], which compares these two modalities in neoadjuvant setting in patients with esophageal adenocarcinoma, is in progress, and results are expected. For GEJ adenocarcinomas preoperative RCT is generally used in the USA, while perioperative CT is favored in most European countries, but for GEJ squamous cell carcinomas, preoperative RCT is the standard of care in general. The most important study that established the benefit of preoperative RCT is the Dutch CROSS trial [11], with over 300 patients that compared the five-year survival of two groups of patients, treated with surgery alone or with a combination of preoperative RCT (CT with paclitaxel/carboplatin and 3D conformal RT with TD 41,4 Gy) and surgery. The percentage of R0 resection was 92% *vs*. 69%, five-year survival was 43.2 *vs*. 27.1 months (RCT and surgery group *vs*. surgery group), pCR was 23%, and grade III toxicity was up to 10%. The most relevant study on the role of perioperative CT in gastric and GEJ cancer is MAGIC trial [12], with 500 patients, which compares two groups of patients treated with surgery alone and patients treated with perioperative CT (epirubicin/CDDP/5-FU) with surgery. The results showed acceptable toxicity (0.3–23.8% of hematological grade III and 2.6-6.4% of non-hematological grade III), and five-year survival rate of 36% *vs*. 23% in favor of the CT group.

The combination of radiotherapy and CT enhances the effect of the therapy. The most modern radiotherapy techniques include intensity modulated radiotherapy (IMRT) and volumetric modulated arc therapy (VMAT) [13]. Radiotherapy doses in preoperative RCT are ~ 41.4–50.4 Gy in ~ 23–28 fractions.

After preoperative RCT, if there is local disease (partial tumor regression or stable disease), patients are referred for surgery. However, in the case of a complete clinical response, patients can undergo esophagectomy or continue to follow-up [14].

Perioperative CT with FLOT (5-fluorouracil, leucovorin, oxaliplatin, and docetaxel) has become the gold standard treatment for medically fit patients with operable gastroesophageal adenocarcinoma [15]. In patients who are intolerant to multiple agents, HT with 5FU/CDDP can be used [16]. Perioperative CT is incorporated in guidelines such as ESMO and NCCN, but preoperative RCT is emerging as the standard in the treatment of locally advanced GEJ carcinomas [17, 18]. Preferred regimens combination of cytostatic drugs in preoperative RCT are 5-FU/CDDP and paclitaxel/carboplatin.

Definitive radiotherapy is performed less often on GEJ cancer patients who are considered medically unfit for surgery, in unresectable disease (cT4b stage) cases, and on patients with resectable disease who decline surgery. RT technics and a combination of cytostatic drugs are the same as in preoperative RCT, and RT doses are 45–54 Gy in 25–30 fractions.

In postoperative approach after esophagectomy, further therapy depends on previous therapy (preoperative CT/RCT), margin resection status, nodal status, number of extracted lymph nodes, tumor stage, tumor differentiation, and tumor invasion [17, 18].

In general, there is no consensus in adjuvant treatment of GEJ cancers. Although most patients with locally advanced disease receive preoperative therapy, postoperative RCT remains a standard of care for GEJ/gastric cancers in the USA. Postoperative CT is a standard of care in the East [19].

Research that can serve as a landmark regarding the application of postoperative RCT in GEJ cancers is INT 0116/SWOG 9008 trial [20]. In this trial, surgery or surgery plus postoperative RCT have been used in over 500 patients with gastric or GEJ cancer (RT with 45 Gy in 25 fractions and CT with 5-fluorouracil/leucovorin). Three-year survival was 50% *vs*. 41% in favor of the RCT group, and local and regional relapse was reduced in the RCT group (19% *vs*. 29% and 65% *vs*. 72%). The radiation techniques used in postoperative RT are also IMRT and VMAT, and the doses are also in the range of 45–50.4 Gy in 25–28 fractions.

The use of adjuvant CT after surgery is established after the CLASSIC trial [21], which included 1000 patients with gastric and GEJ cancer and showed enhanced five-year survival in patients who had postoperative CT over the patients who had only surgery. Preferred combination of cytostatic drugs in postoperative CT are also 5-FU/CDDP and paclitaxel/carboplatin.

Advancements in radiotherapy techniques are improving tumor delineation (RT planning based on MRI and PET), reducing interfraction motion (using IGRT and 4DCT) and intrafraction motion (respiratory-gated RT), increasing the dose to the tumor [simultaneous integrated boost (SIB) technique of RT] [22]. Recently, proton therapy has shown promising results especially in sparing of organs at risk.

In the treatment of GEJ cancers, immunotherapy with monoclonal antibodies is used, such as trastuzumab and "checkpoint" inhibitors such as pembrolizumab and nivolumab.

Adjuvant nivolumab after surgery in patients with esophageal and GEJ cancers, who had received neoadjuvant RCT and have evidence of residual pathological disease in the resection specimen (>ypT1 and/or >ypN1) leads to significant improvement in disease-free survival [23].

Metastatic stage

Metastatic GEJ carcinomas include T1-T4 N1-N3 M1 stage of the disease.

CT with/without immunotherapy is the standard of treatment in metastatic disease, followed by palliative radiotherapy. Patients with good ECOG PS (0–2) are considered for systemic CT.

Combination treatments with two drugs (fluoropyrimidines + platinum) are the treatment standard, combinations with three drugs (5-FU + platinum + docetaxel) are controversial but could be applied in patients with excellent ECOG PS, while monotherapy (fluoropyrimidine, irinotecan, weekly taxane) could be the choice in patients with poor ECOG PS [24]. Adding transtuzumab to standard CT in the first-line setting led to improved outcomes in patients with HER2-positive, advanced GEJ cancers [25]. Nivolumab in combination with standard first-line CT demonstrate superior results [26]. Both paclitaxel and irinotecan are reasonable second-line treatment options because there is no statistically significant difference between them in the overall survival [25].

The first clinical trials on the application of immunotherapy based on human dendritic cells showed good tolerance and prolonged survival time in patients with gastrointestinal tract cancers, but the application is still a great challenge [27].

More than 40% of patients with metastatic cancer receive palliative radiotherapy [28]. Indications are local recurrence, bleeding, obstruction, pain, and bone and brain metastases, and radiation doses are 8 Gy in one fraction, 16 Gy in four fractions, 20 Gy in five fractions, or 30 Gy in 10 fractions.

CONCLUSION

Treatment of GEJ cancers is complex and involves the use of RT, CT, surgery, and immunotherapy alone or in different combinations. Surgery is the first choice of GEJ cancer treatment, especially in the localized stage of the disease. RT has a significant role in the treatment of these tumors in all stages of the disease, especially in locally advanced cancers in the neoadjuvant approach, usually in combination with CT, but also in the adjuvant approach. The modern RT techniques have enabled the application of higher doses of radiation with significant protection of the surrounding healthy tissues in this region, leading to a significant reduction in the toxicity of RT alone or in combination with CT. Various CT regimens are unavoidable in the treatment of GEJ cancer in a neoadjuvant, adjuvant, or systemic approach. Immunotherapy as a new promising therapy is being imposed in the treatment of these cancers. The future of treatment of these cancers is directed toward new surgical procedures, wider application of immunotherapy, as well as new RT techniques.

Ethics: This article was written in accordance with the ethical standards of the institutions and the journal.

Conflict of interest: None declared.

REFERENCES

1. Oberoi M, Noor MS, Abdelfatah E. The Multidisciplinary Approach and Surgical Management of GE Junction Adenocarcinoma. Cancers (Basel). 2024;16(2):288. [DOI: 10.3390/cancers16020288] [PMID: 38254779]
2. Manabe N, Matsueda K, Haruma K. Epidemiological Review of Gastroesophageal Junction Adenocarcinoma in Asian Countries. Digestion. 2022;103(1):29–36. [DOI: 10.1159/000519602] [PMID: 34718236]
3. Joseph A, Raja S, Kamath S, Jang S, Allende D, McNamara M, et al. Esophageal adenocarcinoma: A dire need for early detection and treatment. Cleve Clin J Med. 2022;89(5):269–79. [DOI: 10.3949/ccjm.89a.21053] [PMID: 35500930]
4. Jovanovic I, Alempijević T, Milosavljević T, Popović D, Bjelovic M, Micev M, et al. Clinicopathological Characteristics of Barrett's Carcinoma, Cardia Carcinoma Type II and Distal Gastric Carcinoma: Influence of Observed Parameters on the Five-Year Postoperative Survival of Patients. Serbian Archives of Medicine. 2009;137(5–6):249–54. [DOI: 10.2298/SARH0906249J]
5. Räsänen JV, Kauppi JT. Selection of surgical approach for esophageal cancer at esophagogastric junction. Shanghai Chest. 2019;3:49. [DOI: 10.21037/shc.2019.08.10]
6. Oo AM, Ahmed S. Overview of gastroesophageal junction cancers. Mini-invasive Surg. 2019;3:13. [DOI: 10.20517/2574-1225.2019.02]
7. Schuring N, van Berge Henegouwen MI, Gisbertz SS. History and evidence for state of the art of lymphadenectomy in esophageal cancer surgery. Dis Esophagus. 2024;37(4):doad065. [DOI: 10.1093/dote/doad065] [PMID: 38048446]
8. Hayami M, Ndegwa N, Lindblad M, Linder G, Hedberg J, Edholm D, et al. Population-Based Cohort Study from a Prospective National Registry: Better Long-Term Survival in Esophageal Cancer After Minimally Invasive Compared with Open Transthoracic Esophagectomy. Ann Surg Oncol. 2022;29(9):5609–21. [DOI: 10.1245/s10434-022-11922-5] [PMID: 35752726]
9. Laxague F, Schlottmann F. Esophagogastric junction adenocarcinoma: Preoperative chemoradiation or perioperative chemotherapy? World J Clin Oncol. 2021;12(7):557–64. [DOI: 10.5306/wjco.v12.i7.557] [PMID: 34367928]
10. Hoeppner J, Lordick F, Brunner T, Glatz T, Bronsert P, Röthling N, et al. ESOPEC: prospective randomized controlled multicenter phase III trial comparing perioperative chemotherapy (FLOT protocol) to neoadjuvant chemoradiation (CROSS protocol) in patients with adenocarcinoma of the esophagus (NCT02509286). BMC Cancer. 2016;16:503. [DOI: 10.1186/s12885-016-2564-y] [PMID: 27435280]
11. Shapiro J, van Lanschot JJB, Hulshof MCCM, van Hagen P, van Berge Henegouwen MI, Wijnhoven BPL, et al. CROSS study group. Neoadjuvant chemoradiotherapy plus surgery versus surgery alone for oesophageal or junctional cancer (CROSS): long-term results of a randomised controlled trial. Lancet Oncol. 2015;16(9):1090–8. [DOI: 10.1016/S1470-2045(15)00040-6] [PMID: 26254683]
12. Cunningham D, Allum WH, Stenning SP, Thompson JN, Van de Velde CJ, Nicolson M, et al. MAGIC Trial Participants. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. N Engl J Med. 2006;355(1):11–20. [DOI: 10.1056/NEJMoa055531] [PMID: 16822992]
13. Mileusnic D, Kolarević G, Arsovski O, Kostovski A. Performance Procedures of Modern Techniques Transcutaneous Radiotherapy and Brachyterapy. In: Mileusnic D, Marosevic G, Durbaba M. Radiation oncology. Faculty of Medicine, University of Banja Luka; 2020. p. 61–8.
14. Park J, Yea JW, Oh SA, Park JW. Omitting surgery in esophageal cancer patients with complete response after neoadjuvant chemoradiotherapy: a systematic review and meta-analysis. Radiat Oncol. 2021;16(1):219. [DOI: 10.1186/s13014-021-01947-7] [PMID: 34775988]
15. Giommoni E, Lavacchi D, Tirino G, Fornaro L, Iachetta F, Pozzo C, et al. Results of the observational prospective RealFLOT study. BMC Cancer. 2021;21(1):1086. [DOI: 10.1186/s12885-021-08768-7] [PMID: 34625033]
16. Ahmad MU, Javadi C, Poultsides GA. Neoadjuvant Treatment Strategies for Resectable Proximal Gastric, Gastroesophageal Junction and Distal Esophageal Cancer. Cancers (Basel). 2022;14(7):1755. [DOI: 10.3390/cancers14071755] [PMID: 35406527]
17. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology. Esophageal and Esophagogastric Junction Cancers. Version 3; 2024. Available from: https://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf
18. Obermannová R, Alsina M, Cervantes A, Leong T, Lordick F, Nilsson M, et al; ESMO Guidelines Committee. Oesophageal cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol. 2022;33(10):992–1004. [DOI: 10.1016/j.annonc.2022.07.003] [PMID: 35914638]
19. Greally M, Agarwal R, Ilson DH. Optimal management of gastroesophageal junction cancer. Cancer. 2019;125(12):1990–2001. [DOI: 10.1002/cncr.32066] [PMID: 30973648]
20. Macdonald JS, Smalley SR, Benedetti J, Hundahl SA, Estes NC, Stemmermann GN, et al. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. N Engl J Med. 2001;345(10):725–30. [DOI: 10.1056/NEJMoa010187] [PMID: 11547741]
21. Noh SH, Park SR, Yang HK, Chung HC, Chung IJ, Kim SW, et al. CLASSIC trial investigators. Adjuvant capecitabine plus oxaliplatin for gastric cancer after D2 gastrectomy (CLASSIC): 5-year follow-up of an open-label, randomised phase 3 trial. Lancet Oncol. 2014;15(12):1389–96. [DOI: 10.1016/S1470-2045(14)70473-5] [PMID: 25439693]
22. Chandra RA, Keane FK, Voncken FEM, Thomas CR Jr. Contemporary radiotherapy: present and future. Lancet. 2021;398(10295):171–84. [DOI: 10.1016/S0140-6736(21)00233-6] [PMID: 34166607]
23. Kelly RJ, Ajani JA, Kuzdzal J, Zander T, Van Cutsem E, Piessen G, et al. CheckMate 577 Investigators. Adjuvant Nivolumab in Resected Esophageal or Gastroesophageal Junction Cancer. N Engl J Med. 2021;384(13):1191–203. [DOI: 10.1056/NEJMoa2032125] [PMID: 33789008]
24. Pericay C, Macías-Declara I, Arrazubi V, Vilà L, Marín M. Treatment in esophagogastric junction cancer: Past, present and future. Cir Esp (Engl Ed). 2019;97(8):459–64. [DOI: 10.1016/j.ciresp.2019.03.016] [PMID: 31155142]
25. Tabernero J, Hoff PM, Shen L, Ohtsu A, Shah MA, Siddiqui A, et al. Pertuzumab, trastuzumab, and chemotherapy in HER2-positive gastric/gastroesophageal junction cancer: end-of-study analysis of the JACOB phase III randomized clinical trial. Gastric Cancer. 2023;26(1):123–31. [DOI: 10.1007/s10120-022-01335-4] [PMID: 36066725]
26. Janjigian YY, Shitara K, Moehler M, Garrido M, Salman P, Shen L, et al. First-line nivolumab plus chemotherapy versus chemotherapy alone for advanced gastric, gastro-oesophageal junction, and oesophageal adenocarcinoma (CheckMate 649): a randomised, open-label, phase 3 trial. Lancet. 2021;398(10294):27–40. [DOI: 10.1016/S0140-6736(21)00797-2] [PMID: 34102137]
27. Ni L. Advances in Human Dendritic Cell-Based Immunotherapy Against Gastrointestinal Cancer. Front Immunol. 2022;13:887189. [DOI: 10.3389/fimmu.2022.887189] [PMID: 35619702]
28. Williams GR, Manjunath SH, Butala AA, Jones JA. Palliative Radiotherapy for Advanced Cancers: Indications and Outcomes. Surg Oncol Clin N Am. 2021;30(3):563–80. [DOI: 10.1016/j.soc.2021.02.007] [PMID: 34053669]

Карцином гастроезофагеалног споја – актуелна тема и дилеме у лечењу

Никола Милошевић[1], Сузана Стојановић-Рундић[1,2], Срђан Миланović[1], Ебрахим Кераматолах[2,3], Предраг Сабљак[2,3], Огњан Скробић[2,3], Милош Бјеловић[4]

[1]Институт за онкологију и радиологију Србије, Београд, Србија;
[2]Универзитет у Београду, Медицински факултет, Београд, Србија;
[3]Универзитетски клинички центар Србије, Клиника за дигестивну хирургију – Прва хируршка клиника, Београд, Србија;
[4]Болница „Еуромедик", Београд, Србија

САЖЕТАК

Карциноми гастроезофагеалног споја дуго су изазивали дилеме и класификовани су као карциноми желуца или једњака све до Сивертове класификације када су дефинисани као посебан ентитет. Фактори ризика за развој карцинома гастроезофагеалног споја су гастроезофагеални рефлукс и Баретов једњак, гојазност, инфекција бактеријом *Helycobacter pylori*, пушење и алкохол. Симптоми ове болести укључују ретростернални бол, дисфагију до афагије, регургитацију желудачног садржаја и губитак тежине. Езофагогастродуоденоскопија са биопсијом и патохистолошком верификацијом, као и компјутеризована томографија грудног коша и абдомена кључне су у постављању дијагнозе. Аденокарцином је доминантни хистолошки тип ових тумора. Стадијум болести се дефинише *TNM* класификацијом. Лечење карцинома гастроезофагеалног споја је комплексно, мултидисциплинарно и мултимодално и подразумева примену хирургије, хемиотерапије и радиотерапије, самостално или у различитим комбинацијама. У мултимодалном лечењу локално узнапредовалог карцинома гастроезофагеалног споја постоје дилеме као што су оптималан хируршки приступ и терапијски редослед. Хирургија је главни начин лечења ових тумора, посебно у локалним стадијумима. Радиотерапија се користи у лечењу ових тумора у свим стадијумима болести, а посебно у мултимодалном лечењу локално узнапредовалог карцинома гастроезофагеалног споја, преоперативно и постоперативно, најчешће у комбинацији са хемиотерапијом. Хемиотерапија се користи у свим облицима у лечењу ових карцинома као преоперативна, постоперативна и системска. Имунотерапија и циљна терапија, као најновији облици лечења, обично се примењују системски и постоперативно. Будући правци у лечењу ових карцинома су усмерени ка новим хируршким процедурама, новим типовима имунотерапије, као и новим техникама радиотерапије.

Кључне речи: карцином гастроезофагеалног прелаза; хирургија; радиотерапија