



Influence of the Proximal Margin Length on Local Anastomotic Recurrence in Adenocarcinoma of the Gastroesophageal Junction: A Single-center Experience

Adel Zeinalpour¹, MD; Nasser Malekpour Alamdari¹, MD; Barmak Gholizadeh¹, MD; Saeidreza Ghaderi¹, MD; Hamed Ebrahimibagha^{1*}, MD

¹Department of General Surgery, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

*Corresponding author:

Hamed Ebrahimibagha, MD;
7th Floor, Bldg No.2 SBUMS, Arabi Ave, Daneshjoo Blvd, Velenjak, Post Code:
19839-63113, Tehran, Iran. Tel.: +98 21 22439770;
Email: H.ebrahimi97@sbmu.ac.ir

Received: 2023-08-23

Revised: 2023-09-16

Accepted: 2023-09-27

Abstract

Background: Curative resection with adequate margins is a treatment principle in gastroesophageal junction cancers. There is still no comprehensive agreement on the length of the negative proximal margin after total gastrectomy in Siewert II and III tumors. Extending the proximal negative margin in this anatomical region is very difficult in some cases and can cause more complications for the patients. This study aimed to investigate the influence of the negative proximal margin length on the local anastomotic recurrence in gastroesophageal junction (GEJ) adenocarcinoma in a referral cancer center in Iran.

Methods: In a prospective cross-sectional study, 35 patients with GEJ Siewert II and III adenocarcinomas who underwent total radical gastrectomy from 2017 to 2020 were included. Proximal margin length was measured immediately after resection in the operation room. Then, patients were evaluated for local recurrence at the anastomosis site after two years by endoscopic examination. The relationship between negative proximal margin length, local recurrence rate, and overall survival was evaluated.

Results: From 35 patients 29 (82.9%) cases had negative proximal margins, and 6 (17.1%) cases had positive proximal margins. The least negative proximal margin length was 0.1 cm, and the most were 5 cm. The mean margin was 2±1.6 cm. Based on the endoscopic and pathologic findings, the local recurrence at the anastomosis site was 20% in two years of follow-up. The incidence of local tumor recurrence was higher in patients with positive margins versus patients with negative ones (11.4% vs. 8.6%, P=0.007). There was no significant relationship between the negative proximal margin length and the incidence of local anastomotic recurrence.

Conclusion: According to our findings, the length of the negative proximal margin has no effect on the rate of local recurrence at the anastomosis site, however it is suggested to reach the negative proximal margin in all tumor stages in total gastrectomy for Siewert II and III gastric cardia tumors.

Keywords: Neoplasm Recurrence, Local, Incidence, Gastrectomy, Anastomosis, Surgical

Please cite this paper as:

Zeinalpour A, Malekpour Alamdari N, Gholizadeh B, Ghaderi SR, Ebrahimibagha H. Influence of the Proximal Margin Length on Local Anastomotic Recurrence in Adenocarcinoma of the Gastroesophageal Junction: A Single-center Experience. *Iran J Colorectal Res.* 2023;11(3):104-109. doi: 10.30476/ACRR.2023.99892.1186.

Introduction

Gastroesophageal junction adenocarcinoma is one of the most prevalent gastrointestinal

cancers, and its incidence has increased dramatically worldwide (1-4). Siewert classification divided the tumors of this region into three types. According to this classification, tumors 1 cm proximal to the

gastroesophageal junction (GEJ) are type I, from 1 cm proximal to 2 cm distal to the GEJ are type II, and distal to 2–5 cm below the GEJ are type III (5). In the case of Siewert type I tumors, the treatment of choice is like esophageal cancers, and esophagectomy is required. In contrast, in the case of type II or III tumors, total gastrectomy is a more appropriate choice (6-8).

Despite many studies, no comprehensive agreement exists on the length of the proximal negative margin after total gastrectomy in such tumors (9-20). Some guidelines suggest 4-6 cm as the negative proximal margin length (21, 22). On the other hand, many studies show that it is enough to reach the negative margin, and a further negative margin length has no effect on the survival of the patients or recurrence rate (23-27). A study has shown that the positive proximal margin (R1 resection) does not influence the survival rate in cases of >3 involved lymph nodes and T3,4 tumors (14). Creating further negative proximal margin requires more complicated operations, such as esophageal resection and anastomosis in the thorax, which could impose more complications on patients, especially in cases of unfavorable patients' general conditions and high-risk surgeries.

There are few studies on the effect of negative margin and its length on the local recurrence rate at the anastomosis site. This study aimed to investigate the influence of the negative proximal margin length on the local anastomotic recurrence in GEJ adenocarcinoma in a referral cancer center in Iran.

Patients and Methods

Study Design

We designed a cross-sectional study on the new patients diagnosed with gastroesophageal junction tumors. We included patients with tumors 1 cm above to 5 cm below the GEJ (Siewert II and III). All of the included patients underwent total gastrectomy in Shahid Modarres Hospital, Tehran, Iran, from 2017 to 2020. The patients with comorbidities such as diabetes, ischemic heart disease, and a history of prior cancer were excluded from the study. Other exclusion criteria were stage IV tumors, Siewert I tumors, subtotal gastrectomy surgeries, non-adenocarcinoma tumors, and thoracotomy for more resection, intra-thoracic anastomosis. We used the census method and included all patients who fulfilled our criteria. The study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences (ethical code: IR.SBMU.MSP.REC.1398.471).

Study Process

After obtaining written informed consent from patients and routine preoperative preparations, patients underwent total radical gastrectomy and modified D2 lymphadenectomy. In addition, 2 cm

of the distal esophagus and 2 cm of the post-pyloric duodenum were resected. The proximal margin was sent for the frozen section during the operation, and after being sure about negative margins, the reconstruction was performed with the Roux-en-Y esophagojejunostomy technique. The anastomosis was done either by hand-sewing or using a circular stapler. If positive margins were reported on the frozen section, the proximal margin was re-excised with a margin of 1 cm, and then the anastomosis was performed. After the specimen excision, the gastroesophageal junction was opened longitudinally, and the distance from the tumor to the cut end of the esophagus was measured and recorded.

Patients were followed up postoperatively after 1, 6, 12, 18 and 24 months. We evaluated them regarding dysphagia and local recurrence symptoms. In the case of positive symptoms, an upper endoscopy was done, and a biopsy was taken from the site of anastomosis. Eventually, all symptom-free patients underwent upper endoscopy at the end of two years.

Statistical Analysis

Demographic and clinicopathological information were collected and analyzed using SPSS-22. The data distribution was evaluated by checking the skewness, kurtosis, and standard deviation (SD). Parametric, non-parametric, and qualitative data are presented as mean±standard deviation (SD), median (range), and number (percentages) as appropriate. The Kolmogorov-Smirnov test assessed the data distribution and showed that the distribution was asymmetric. We used Pearson's chi-squared, Mann-Whitney, and Fisher's Exact test for data analysis, and a P-value less than 0.05 was considered statistically significant.

Results

Forty-four patients were included in the study. Nine patients did not complete the follow-up period, from whom seven cases died in the postoperative period or two years follow-up, and two of them had Squamous cell carcinoma (SCC) in the permanent pathology. Of the remaining 35 patients, 21 (60%) were men, and 14 (40%) were women. Regarding age, 57.1% of patients were 65 or younger, and 42.9% were older than 65. According to the Siewert classification, 57.1% of cases were in the Siewert II class, and 42.9% were in Siewert III. All of the patients underwent total gastrectomy with D2 lymph node dissection and reconstruction with Roux-en-Y esophagojejunostomy. Patients' demographic and clinicopathologic data are shown in Table 1.

On permanent microscopic evaluation, 29 patients (82.9%) had a negative, and six (17.1%) had a positive proximal margin. The least negative proximal margin length was 0.1 cm, and the most was 5 cm. The average margin was 2±1.6 cm. Based on the endoscopic evaluation after two years of follow-up

Table 1: Clinicopathological and surgical-related characteristics for all patients (N=35)

Characteristic	Parameter
Age (Year)	
Mean (mean±SD)	64.7 (61.6)
Age (n, %)	
≤65	20 (57.1%)
>65	15 (42.9%)
Gender (n, %)	
Male	21 (60%)
Female	14 (40%)
Siewert type (n, %)	
II	20 (57.1%)
III	15 (42.9%)
Tumor size, mm, (n, %)	
≤3	9 (25.7%)
>3	26 (74.3%)
Tumor size, mm, (n, %)	
≤6	20 (57.1%)
>6	15 (42.9%)
Tumor size, mm, (n, %)	
≤10	30 (86.7%)
>10	5 (14.3%)
Differentiation status (n, %)	
Well	3 (8.6%)
Moderately	13 (37.1%)
Poor	19 (54.3%)
N Stage (n, %)	
N0	18 (51.4%)
N1	8 (22.9%)
N2	3 (8.6%)
N3	6 (17.1%)
Lymph node invasion (n, %)	
No	21 (60%)
Yes	14 (40%)
Margin type (n, %)	
Negative	29 (82.9%)
Positive	6 (17.1%)
T Stage (n, %)	
T1	16 (45.7%)
T2	10 (28.6%)
T3	3 (8.6%)
T4	6 (17.1%)
Proximal frozen section (n, %)	
Negative	23 (65.7%)
Positive	12 (34.3%)
Length of proximal margin (cm) (mean±SD)	2.1±1.6 (cm)
Operation time (min) (mean±SD)	218.62±81.36 (min)

Table 2: Effect of margin status on recurrence (Mann-Whitney test)

Recurrence	Margin status		P value
	Negative	Positive	
No (28 (80.0%))	26 (74.3%)	2 (5.7%)	0.008
Yes (7 (20.0%))	3 (8.6%)	4 (11.4%)	
Total	29 (82.9%)	6 (17.1%)	

and pathologic findings, the local recurrence at the anastomosis site was 20%. The prevalence of local tumor recurrence was significantly higher in patients with positive margins versus patients with negative ones in permanent section pathologic examination (11.4% versus 8.6%, $P=0.007$).

Although there is a lower local recurrence at the site of anastomosis in patients with a microscopic

negative margin, there was no significant relationship between the length of the negative proximal margin and the prevalence of local recurrence.

We divided the variable of negative proximal margin into three groups, <0.5, 0.5–3, and >3, yet found no relationship between negative proximal margin and local recurrence at the anastomosis site ($P>0.05$ for all).

There was no significant relationship between margin status and the differentiation and T-stage of the tumor ($P>0.05$).

Also, there was no significant relationship between proximal negative margin length and local recurrence based on the T-stage and tumor differentiation ($P>0.05$).

A negative proximal margin was in reverse relation with lymphatic metastasis. In patients with less lymph node involvement (lower N status), the prevalence of a proximal negative margin was higher ($P>0.028$). However, there was no relationship between negative margin length and the N status of the tumor. Also, there was no statistically significant relationship between the length of the negative proximal margin and the rate of local recurrence based on the N status of the tumor. Table 2 shows the results of the relationship between proximal negative margin length and local recurrence rate.

Discussion

Adenocarcinoma of the GEJ is among the most invasive tumors whose incidence is increasing, especially in some specific regions such as Iran (28). Despite significant improvement in diagnosis, management, and surgical techniques, gastric cardia adenocarcinoma accounts for a high mortality and morbidity rate (29). In addition to TNM staging of the tumors, the proximal margin status is one of the most important prognostic factors, especially in Siewert II and III tumors. According to guidelines, reaching the negative proximal margin in total gastrectomy surgery is necessary; traditionally, the negative proximal margin length is 2 to 3 cm in the early stage and 5 to 6 cm in advanced-stage tumors (24). Despite many recent studies, there is still disagreement about the length of the negative proximal margin (17, 23, 24, 26, 27, 30, 31).

Another issue in gastric cardia tumors is the limitation in the length of the negative proximal margin, which is challenging due to its anatomical position. Suppose we want to do a larger distal esophageal resection and give more margins. In that case, we need higher anastomosis in the posterior mediastinum, which increases the risk of anastomosis leak or need for thoracoabdominal incision or left thoracotomy for intrathoracic anastomosis, imposing more complications on the patients (32). There are many studies concerning the effect of negative margin on the overall survival; most of them state that the negative margin length does not affect the overall survival. However, there are few studies on the effect of negative margin length on the local recurrence rate at the site of anastomosis, which was the purpose of this research.

Mine et al., in their study in 2013, found that a minimum negative proximal margin length of 2 cm is necessary and sufficient for Siewert II and III tumors (33). In another study by Kim et al., published

in 2014, a positive proximal margin was associated with a poor prognosis. Further negative proximal margin lengths were not recommended and did not affect the overall survival and local recurrence (24). In another study by Feng et al. in 2016, the negative proximal margin length had no effect on the survival rate of patients undergoing total gastrectomy, and only reaching a negative microscopic margin was sufficient for the treatment (23). Schoenfeld et al. conducted a study on 91 patients in 2016, and they showed that a positive margin increased recurrence and decreased survival even in the case of postoperative aggressive adjuvant therapy (34).

In the study of Koumariou et al. in 2019, the rate of microscopic margin involvement was reported at 18.9%, which worsened the prognosis of patients, and the importance of achieving a negative proximal margin was shown (35). Niclauss et al., in 2019, systematically reviewed the results of 13 articles. They recommended the length of the negative proximal margin between 2 and 6 cm but did not consider the effect of neoadjuvant therapy on the proximal margin. This study investigated the effect of margin on the overall survival rate, not just local recurrence at the anastomotic site (36).

In the study by Kim et al. 2020, the average margin length in advanced gastric cancers after total gastrectomy was 3.5 cm. They examined the proximal margin length in ≤ 1.0 cm, 1.1-3.0 cm, 3.1-5.0 cm, and >5.0 cm groups. The researchers concluded that the negative proximal margin length was not a prognostic factor in gastric cancers and did not affect patients' local recurrence and recurrence-free survival (37). A meta-analysis and systematic review study by Jiang et al. in 2021 showed that a positive margin (R1 resection) is associated with lower five-year survival and overall survival, and surgeons should try to perform an R0 resection with a negative proximal margin (20).

The results of our study on the patients with gastric cardia cancer undergoing neoadjuvant chemoradiotherapy indicate that a positive proximal margin is associated with a very high local recurrence rate at the anastomotic site, and surgeons must always try to reach the negative proximal margin. On the other hand, our experience, similar to the results of most recent studies and other similar studies in this field, shows that achieving the negative proximal margin in Siewert II and III gastric cardia tumors is enough, regardless of the size and stage of the tumor, and trying to reach to more negative margin length does not affect the local recurrence. On the other hand, creating proximal negative margins can impose more complications on the patients (25-27).

In contrast to the studies that investigated the prognostic effect of the positive proximal margin only in stages I and II of gastric cancer and did not consider any effect of the positive proximal margin in stages III and IV (38), in our study, we showed that the positive proximal margin in all stages of gastric

cardia cancer increases local recurrence at the site of anastomosis, and re-excision to achieve a clear margin is strongly recommended for all patients.

To improve the results, it may be better that the re-excised specimen be sent again for a frozen section during the operation to ensure the negative margin and then do the anastomosis. However, in a few cases, permanent pathology reported proximal margin involvement, opposite to the frozen section results (39, 40).

The advantages of this study include consideration of the effect of preoperative chemo-radiotherapy, evaluation of local recurrence at the anastomosis site by endoscopy and biopsy, measurement of proximal margin by the surgeon before fixing the specimen in formalin, and evaluation of the relationship between the negative margin and its length and the tumor stage.

The disadvantages of the present study include the small number of cases, the short duration of patients' follow-up, not increasing the margin length in the case of esophagojejunostomy with circular stapling, not evaluating the overall survival rate, not considering the effect of adjuvant chemotherapy regimen, and performing the re-excision and anastomosis without a second pathology report if the first frozen section was positive.

Conclusion

In total gastrectomy for Siewert II and III gastric

cardia tumors, reaching a negative proximal margin in all tumor stages is necessary. However, the length of the negative proximal margin does not affect the local recurrence rate at the anastomosis site. According to the results of this study, performing a total gastrectomy with a negative proximal margin might be sufficient for these tumors with no need for a thoracoabdominal incision or left thoracotomy for more proximal incision or esophagectomy. However, creating a maximum negative proximal margin in the abdomen may be reasonable depending on the patient's condition before and during surgery and the likelihood of complications.

Acknowledgment

The authors of the present study would like to thank the Shahid Modarres Educational Hospital staff, who helped us execute this study.

Authors' Contribution

Study conception and design: Adel Zeinalpour, Nasser Malekpour Alamdari, Barmak Gholizadeh; drafting of the manuscript and acquisition of data: Saeidreza Ghaderi, Hamed Ebrahimibagha; critical revision: Barmak Gholizadeh. All authors revised successive versions of the manuscript and approved the final version for publication.

Conflict of interest: None declared.

References

- Devesa SS, Blot WJ, Fraumeni JF, Jr. Changing patterns in the incidence of esophageal and gastric carcinoma in the United States. *Cancer*. 1998;83(10):2049-53.
- Bollschweiler E, Wolfgarten E, Gutschow C, Hölscher AH. Demographic variations in the rising incidence of esophageal adenocarcinoma in white males. *Cancer*. 2001;92(3):549-55.
- Steevens J, Botterweck AA, Dirx MJ, van den Brandt PA, Schouten LJ. Trends in incidence of oesophageal and stomach cancer subtypes in Europe. *European journal of gastroenterology & hepatology*. 2010;22(6):669-78.
- Siewert JR, Hölscher AH, Becker K, Gössner W. [Cardia cancer: attempt at a therapeutically relevant classification]. *Der Chirurg; Zeitschrift für alle Gebiete der operativen Medizin*. 1987;58(1):25-32.
- Siewert JR, Stein HJ. Classification of adenocarcinoma of the oesophagogastric junction. *The British journal of surgery*. 1998;85(11):1457-9.
- Hosokawa Y, Kinoshita T, Konishi M, Takahashi S, Gotohda N, Kato Y, et al. Clinicopathological features and prognostic factors of adenocarcinoma of the esophagogastric junction according to Siewert classification: experiences at a single institution in Japan. *Annals of surgical oncology*. 2012;19(2):677-83.
- Rüdiger Siewert J, Feith M, Werner M, Stein HJ. Adenocarcinoma of the esophagogastric junction: results of surgical therapy based on anatomical/topographic classification in 1,002 consecutive patients. *Annals of surgery*. 2000;232(3):353-61.
- Suh YS, Han DS, Kong SH, Lee HJ, Kim YT, Kim WH, et al. Should adenocarcinoma of the esophagogastric junction be classified as esophageal cancer? A comparative analysis according to the seventh AJCC TNM classification. *Annals of surgery*. 2012;255(5):908-15.
- Chen JD, Yang XP, Shen JG, Hu WX, Yuan XM, Wang LB. Prognostic improvement of reexcision for positive resection margins in patients with advanced gastric cancer. *European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology*. 2013;39(3):229-34.
- Nagata T, Ichikawa D, Komatsu S, Inoue K, Shiozaki A, Fujiwara H, et al. Prognostic impact of microscopic positive margin in gastric cancer patients. *Journal of surgical oncology*. 2011;104(6):592-7.
- Cho BC, Jeung HC, Choi HJ, Rha SY, Hyung WJ, Cheong JH, et al. Prognostic impact of resection margin involvement after extended (D2/D3) gastrectomy for advanced gastric cancer: a 15-year experience at a single institute. *Journal of surgical oncology*. 2007;95(6):461-8.
- Wang SY, Yeh CN, Lee HL, Liu YY, Chao TC, Hwang TL, et al. Clinical impact of positive surgical margin status on gastric cancer patients undergoing gastrectomy. *Annals of surgical oncology*. 2009;16(10):2738-43.
- Sun Z, Li DM, Wang ZN, Huang BJ, Xu Y, Li K, et al. Prognostic significance of microscopic positive margins for gastric cancer patients

- with potentially curative resection. *Annals of surgical oncology*. 2009;16(11):3028-37.
14. Bickenbach KA, Gonen M, Strong V, Brennan MF, Coit DG. Association of positive transection margins with gastric cancer survival and local recurrence. *Annals of surgical oncology*. 2013;20(8):2663-8.
 15. Woo JW, Ryu KW, Park JY, Eom BW, Kim MJ, Yoon HM, et al. Prognostic impact of microscopic tumor involved resection margin in advanced gastric cancer patients after gastric resection. *World journal of surgery*. 2014;38(2):439-46.
 16. Postlewait LM, Squires MH, 3rd, Kooby DA, Poultides GA, Weber SM, Bloomston M, et al. The importance of the proximal resection margin distance for proximal gastric adenocarcinoma: A multi-institutional study of the US Gastric Cancer Collaborative. *Journal of surgical oncology*. 2015;112(2):203-7.
 17. Bissolati M, Desio M, Rosa F, Rausei S, Marrelli D, Baiocchi GL, et al. Risk factor analysis for involvement of resection margins in gastric and esophagogastric junction cancer: an Italian multicenter study. *Gastric cancer : official journal of the International Gastric Cancer Association and the Japanese Gastric Cancer Association*. 2017;20(1):70-82.
 18. Kim BS, Oh ST, Yook JH, Kim HS, Lee IS, Kim BS. Appropriate gastrectomy resection margins for early gastric carcinoma. *Journal of surgical oncology*. 2014;109(3):198-201.
 19. Kim Y, Squires MH, Poultides GA, Fields RC, Weber SM, Votanopoulos KI, et al. Impact of lymph node ratio in selecting patients with resected gastric cancer for adjuvant therapy. *Surgery*. 2017;162(2):285-94.
 20. Jiang Z, Liu C, Cai Z. Impact of Surgical Margin Status on Survival in Gastric Cancer: A Systematic Review and Meta-Analysis. 2021;28:10732748211043665.
 21. Japanese gastric cancer treatment guidelines 2014 (ver. 4). *Gastric cancer : official journal of the International Gastric Cancer Association and the Japanese Gastric Cancer Association*. 2017;20(1):1-19.
 22. Ajani JA, Barthel JS, Bekaii-Saab T, Bentrem DJ, D'Amico TA, Das P, et al. Gastric cancer. *Journal of the National Comprehensive Cancer Network : JNCCN*. 2010;8(4):378-409.
 23. Feng F, Tian Y, Xu G, Liu S, Liu Z, Zheng G, et al. The length of proximal margin does not influence the prognosis of Siewert type II/III adenocarcinoma of esophagogastric junction after transhiatal curative gastrectomy. *SpringerPlus*. 2016;5:588.
 24. Kim MG, Lee JH, Ha TK, Kwon SJ. The distance of proximal resection margin does not significantly influence on the prognosis of gastric cancer patients after curative resection. *Annals of surgical treatment and research*. 2014;87(5):223-31.
 25. Lee CM, Jee YS, Lee JH, Son SY, Ahn SH, Park DJ, et al. Length of negative resection margin does not affect local recurrence and survival in the patients with gastric cancer. *World journal of gastroenterology*. 2014;20(30):10518-24.
 26. Ohe H, Lee WY, Hong SW, Chang YG, Lee B. Prognostic value of the distance of proximal resection margin in patients who have undergone curative gastric cancer surgery. *World journal of surgical oncology*. 2014;12:296.
 27. Jang YJ, Park MS, Kim JH, Park SS, Park SH, Kim SJ, et al. Advanced gastric cancer in the middle one-third of the stomach: Should surgeons perform total gastrectomy? *Journal of surgical oncology*. 2010;101(6):451-6.
 28. Correa P, Chen VW. Gastric cancer. *Cancer surveys*. 1994;19-20:55-76.
 29. Leers JM, DeMeester SR, Chan N, Ayazi S, Oezcelik A, Abate E, et al. Clinical characteristics, biologic behavior, and survival after esophagectomy are similar for adenocarcinoma of the gastroesophageal junction and the distal esophagus. *The Journal of thoracic and cardiovascular surgery*. 2009;138(3):594-602; discussion 1-2.
 30. Squires MH, 3rd, Kooby DA, Poultides GA, Pawlik TM, Weber SM, Schmidt CR, et al. Is it time to abandon the 5-cm margin rule during resection of distal gastric adenocarcinoma? A multi-institution study of the U.S. Gastric Cancer Collaborative. *Annals of surgical oncology*. 2015;22(4):1243-51.
 31. Kim JH, Park SS, Kim J, Boo YJ, Kim SJ, Mok YJ, et al. Surgical outcomes for gastric cancer in the upper third of the stomach. *World journal of surgery*. 2006;30(10):1870-6; discussion 7-8.
 32. Clemente-Gutiérrez U, Sánchez-Morales G, Santes O, Medina-Franco H. Clinical usefulness of extending the proximal margin in total gastrectomies for gastric adenocarcinoma. *Revista de gastroenterología de México (English)*. 2019;84(2):136-42.
 33. Mine S, Sano T, Hiki N, Yamada K, Kosuga T, Nunobe S, et al. Proximal margin length with transhiatal gastrectomy for Siewert type II and III adenocarcinomas of the oesophagogastric junction. *The British journal of surgery*. 2013;100(8):1050-4.
 34. Schoenfeld JD, Wo JY, Mamon HJ, Kwak EL, Mullen JT, Enzinger PZ, et al. The Impact of Positive Margins on Outcome Among Patients With Gastric Cancer Treated With Radiation. *American journal of clinical oncology*. 2016;39(3):243-7.
 35. Koumariou A, Krivan S, Machairas N, Ntavatzikos A, Pantazis N, Schizas D, et al. Ten-year survival outcomes of patients with potentially resectable gastric cancer: impact of clinicopathologic and treatment-related risk factors. *Annals of gastroenterology*. 2019;32(1):99-106.
 36. Niclauss N, Jung MK, Chevally M, Mönig SP. Minimal length of proximal resection margin in adenocarcinoma of the esophagogastric junction: a systematic review of the literature. *Updates in surgery*. 2019;71(3):401-9.
 37. Kim A, Kim BS, Yook JH, Kim BS. Optimal proximal resection margin distance for gastrectomy in advanced gastric cancer. *World journal of gastroenterology*. 2020;26(18):2232-46.
 38. Aurello P, Magistri P, Nigri G, Petrucciani N, Novi L, Antolino L, et al. Surgical management of microscopic positive resection margin after gastrectomy for gastric cancer: a systematic review of gastric R1 management. *Anticancer research*. 2014;34(11):6283-8.
 39. Squires MH, 3rd, Kooby DA, Pawlik TM, Weber SM, Poultides G, Schmidt C, et al. Utility of the proximal margin frozen section for resection of gastric adenocarcinoma: a 7-Institution Study of the US Gastric Cancer Collaborative. *Annals of surgical oncology*. 2014;21(13):4202-10.
 40. Kasakura Y, Fujii M, Mochizuki F, Imai S, Kanamori N, Suzuki T. Clinicopathological features of the superficial spreading type of early gastric cancer. *Gastric cancer : official journal of the International Gastric Cancer Association and the Japanese Gastric Cancer Association*. 1999;2(2):129-35.