Evaluation of surgical margins of laparoscopic gastric cancer surgery: Single-center results

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ABSTRACT

Introduction: Surgical margin positivity incidence is reported between 5 snd 20% in gastric cancer surgery. Although some studies showed that presence of positive surgical margins affects overall survival negatively, others reported no effect. The aim of this study is to investigate the relationship between surgical margin and the survival of patients who underwent laparoscopic gastrectomy in our clinic.

Materials and Methods: Between 2015 and 2022 years, patients who underwent laparoscopic gastrectomy because of gastric cancer were included in this study. Surgical resection margin (diameter) width, micro-scopic evaluation of the surgical margin, pathological tumor stage, resected lymph nodes numbers and involvement, and overall survival were analyzed.

Results: After patients with benign disorders and inadequate lymph nodes resection were excluded from the study, 136 patients were included the study. Median surgical margin length width? was 2.3 (0.1-10) cm, and 13 (9.6%) patients had positive surgical margin after pathological evaluation. Median survival was 51.00 ± 18.56 months in patients with positive surgical margins and 46.00 ± 2.99 months in patients with negative surgical margins (p=0.977). The 1, 3, and 5-year survival rates of patients with negative versus positive surgical margins (78.9% vs. 69.2%, p=0.426), (46.3% vs. 46.2%, p=0.990), and (17.1% vs. 30.8%, p=0.225), respectively. Surgical margin was positive in 3 (7.7%) patients with proximal tumors, and in 10 (10.3%) patients with distal located tumors.

Conclusion: While most studies emphasized surgical margin positivity in proximal tumors, the rate of distal surgical margin positivity was found to be higher in this study. In conclusion, no correlation was found between surgical margin positivity and overall survival.

Keywords: Distal, Gastric cancer, Minimally invasive, Proximal, Resection

Introduction

According to Globocan 2020 data, stomach cancer is the fifth cancer most common cancer in the world and the fourth most common reason for cancer-related death.^[1] The most important goal in gastric cancer surgery is RO

resection, meaning without microscopic tumors on the resection margins, and with adequate lymphadenectomy. On the other hand, positive surgical margin or R1 resection means inadequate surgery. Surgical margin positivity incidence has changed from between 5 and 20% due to





The aims of this study were firstly to evaluate the positivity rate of surgical margins in gastric cancer patients who underwent laparoscopic gastrectomy in our clinic. The second aim was to investigate the relationship between surgical margins and patient survival and the factors affecting it.

Materials and Methods

Between 2015 and 2022 years, patients who underwent laparoscopic gastrectomy because of gastric cancer were included in this study. Patients who had inadequate lymph node resection numbers (<15 lymph nodes) for evaluation of tumor involvement were excluded from the study. Patient demographic data, concomitant disease, tumor location, neoadjuvant chemotherapy status, surgery type, complications, length of stay, surgical resection margin diameter and microscopic evaluation, pathological tumor stage, resected lymph nodes numbers, and overall survivals were all analyzed. The study was approved by the ethics comity of Inonu University (Approval No: 2023/703).

Statistical Analysis

The analyses were performed using SPSS v23. Compliance of numerical data with normal distribution was checked by Kolmogorov–Smirnov test. Continuous numerical variables were analyzed with the Mann–Whitney U test. The median, minimum, and maximum values of these variables were presented. Chi-square analysis was performed for categorical variables. Frequency and percentage values of these variables were presented. Univariate logistic regression analysis was performed for each variable by taking the variables with statistically significant P values in similar variables. The effect of surgical margin positivity on overall survival was analyzed using the Kaplan–Meier method and log-rank test. P<0.05 was considered statistically significant.

Results

Between 2015 and 2018 years, 260 patients underwent laparoscopic gastrectomy for gastric pathologies. After benign disorders and inadequate lymph nodes, harvested patients were excluded from the study, 136 patients were included in the study. Eighty-seven (64%) patients were male and median age was 62 years (range 26–91). Other demographic dates are listed in Table 1. Ninety-seven

Table 1. Demographical variables of patients				
	Median (min-max)	Count (%)		
Age, years	62 (26–91)			
Gender				
Male		87 (64.0)		
Female		49 (36.0)		
BMI, kg/m ²	25.06 (15.8–45)			
ASA				
1		16 (11.8)		
2		88 (64.7)		
3		31 (22.8)		
4		1 (0.7)		
HT				
Absence		99 (72.8)		
Presence		37 (27.2)		
DM				
Absence		119 (87.5)		
Presence		17 (12.5)		
COPD				
Absence		127 (93.4)		
Presence		9 (6.6)		
CAD				
Absence		126 (92.6)		
Presence		10 (7.4)		
CEA	1.94 (0.1–363.2)			
CA 19-9	8.56 (0.1–2157)			
Neoadjuvant				
Chemotherapy				
Absence		121 (89.0)		
Presence		15 (11.0)		
Perioperative	100 (0–900)			
bleeding, ml				
Operative Time	300 (120–720)			
Location				
Upper		39 (28.7)		
Distal		97 (71.3)		
Complication				
Absence		105 (77.2)		
Presence		31 (22.8)		

BMI: Body mass index; HT: Hypertension; DM: Diabetes mellitus; COPD: Chronic obstructive pulmonary disease; CAD: Coronary artery disease; ASA: American society of anesthesiologists.

(71.3%) patients had tumors originating from the distal stomach. Median tumor diameter was 5.5 cm (0.1–19), median surgical margin length was 2.3 (0.1–10) cm. Median harvested lymph nodes and metastatic lymph nodes numbers were 30 (15–85) and 5 (0–44), respectively. Twentynine (21.3%) patients had early-stage tumor and 33 (24.3%) patients had no lymph node metastasis. The results of the pathologies of the specimens are shown in Table 2. Thirteen (9.6%) patients had a positive surgical margin after pathological evaluation. The characteristics of patients with positive and negative surgical margins are summarized in Table 3. There were no differences in the T stages and lymphatic metastases of patients with and without positive surgical margins. There was no significant difference in the number of lymph nodes removed and the metastatic rates of these lymph nodes in patients with positive and negative surgical margins. Median survival was 51.00±18.56 months in patients with positive surgical margins and 46.00±2.99 months in patients with negative surgical margins, p=0.977 (Table 4). The 1, 3, and 5-year survival rates of patients with negative versus positive surgical margins were (78.9% vs. 69.2%, p=0.426), (46.3% vs. 46.2%, p=0.990), and (17.1% vs. 30.8%, p=0.225), respectively (Table 4 and Fig. 1).

When we classified according to tumor localization, preoperative CEA and CA 19-9 levels of patients with distal localization were significantly lower than patients with proximal tumors, respectively (p=0.018, p=0.012). The duration of operation and the amount of intraoperative bleeding in distal localized tumors were less than for proximal localized tumors (p<0.001). Patients with proximal tumors received more neoadjuvant chemotherapy (p=0.004). When we compared proximally and distally located tumors as being of early or advanced stages, no differences were found in the tumor T stages. Surgical margin was positive in 3 (7.7%) patients with proximal tumors, and in 10 (10.3%) patients with distal tumors. Detailed characteristics of the patients according to distal and proximal location are summarized in Table 5.

Discussion

In this study, the median tumor-free margin was 2.3 cm in patients who underwent laparoscopic gastrectomy. The positive surgical margin rate was 9.6%. There was no significant difference between the number of lymph nodes removed and their metastatic rates. The presence of a positive surgical margin did not have a significant effect on overall survival (p=0.97). The rate of positive surgical marginal margi

Median Count (%) (min-max) 5.5(0.1-19)Tumor Size, cm **Negative Surgical** 2.3(0.1-10)Margin Diameter (cm) Surgical Margin Positive 13 (9.6) Negative 123 (90.4) Tstage Τ1 29 (21.3) T2 9 (6.6) Т3 36 (26.5) 60 (44.1) T4a T4b 2(1.5)T early/late stage T1 28 (20.6) T1-2-3 108 (79.4)

Table 2. Pathological outcomes of patients

Harvesting Total LAP	30 (15–85)
Positive LAP	2.5 (0-44)
Nstage	
N0	33 (24.3)
N1	35 (25.7)
N2	15 (11.0)
N3a	30 (22.1)
N3b	23 (16.9)
TNMstage	
1a	20 (14.7)
1b	9 (6.6)
2a	10 (7.4)
2b	20 (14.7)
3a	29 (21.3)
3b	23 (16.9)
3c	25 (18.4)
LVI	
Absence	29 (21.3)
Presence	107 (78.7)
PNI	
Absence	52 (38.2)
Presence	84 (62.8)

LVI: Lymphovascular invasion; PNI: Perineural invasion.

gins was higher in patients with distal tumors than those with proximal locations (10.3% vs. 7.7%).

The aim of optimal gastric surgery is to remove the tumor

Table 3. Analysis of continuous variables and categorical data by surgical margin					
	Surgical Margin Status			р	
	Negative surgical margin		Positive surgical margin		
	Median (min-max)	Count (%)	Median (min-max)	Count (%)	-
Age, years	63 (29–91)		60 (34–79)		0.486*
Male		77 (62 6)		10 (76 0)	0 306
Female		11 (02.0) 16 (37.1)		3 (23 1)	0.300
BMI kg/m ²	25.0 (15.8-45)	40 (31.4)	26.8 (23-35.1)	5 (23.1)	0 046*
ΔSΔ	23.0 (13.0 43)		20.0 (23 33.1)		0.040"
1		15 (12 2)		1 (7 6)	0 211
2		82 (66 7)		6 (46 2)	0.211
3		25 (20.3)		6 (46 2)	
4		1 (0.8)		0(0)	
HT		(0.0)		0 (0)	
Absent		88 (71.5)		11 (84.6)	0.314
Present		35 (28.5)		2 (15.4)	
DM		()		_(,	
Absent		108 (87.8)		11 (84.6)	0.741
Present		15 (12.2)		2 (15.4)	
COPD		. ,		. ,	
Absent		114 (92.7)		13 (100.0)	0.313
Present		9 (7.3)		0 (0)	
CAD					
Absent		114 (92.7)		12 (92.3)	0.961
Present		9 (7.3)		1 (7.7)	
CEA	1.97 (0.1–363.2)		1.8 (0.4–9.1)		0.885*
CA 19-9	8.0 (0.1–2157)		14.1 (1.2–700)		0.065*
Neoadjuvant chemotherapy	,				
Absent		110 (89.4)		11 (84.6)	0.598
Present		13 (10.6)		2 (15.4)	
Operation type					
lap.distal		(2 (58.5)		6 (46.2)	0.446
lap.total		43 (35)		5 (38.5)	
	200 (45 720)	8 (6.5)		2 (15.4)	0.004.
Operative Time, minute	300(45-720)		360 (20-480)		0.824*
Complication	100 (0-900)		100 (0-400)		0.934*
Aboont		02 (75 6)		11(04c)	0 467
Absent		93 (75.0)		11(04.0)	0.407
Complication Type		30 (24.4)		2 (15.4)	
Abcont		107 (97)		11 (94 6)	0 425
Chilous Leak			0 (0)	11 (04.0)	0.425
anastomosis look		1 (0.8)	1 (7	7	
naralytic ileus		6 (4 9)	n (n)		
duodenal leak		2 (1 6	0 (0) 0 (0)		
SSI		4 (4.9)	1 (7.	7	

Table 3. CONT.

	Surgical Margin Status			
	Negative surgical margin		Positive surgical margin	
	Median (min-max)	Count (%)	Median (min-max)	Coun
Post-operative hemoraji		1 (0.8)	0 ((J)
Length of stay (day)	8 (4–39)		10 (5–16)	
Tumor Size, cm	5.5 (0.1–19)		5.0 (1.7–9)	
T stage				
TI		29 (23.6)	0 (0	D)
T2		7 (5.7)	2 (15	5.4)
Т3		32 (26.0)	4 (30).8)
T4a		53 (43.1)	7 (53	3.8)
T4b		2 (1.6)	0 (0	D)
Tearly/late stage				
T1		28 (22.8)	0 (0))
T2-3-4		95 (77.2)	13 ((0)
Harvesting Total LAP	30 (15–85)		32 (15–58)	
Positive LAP	2 (0-44)		3 (0-17)	
N stage				
NO		31 (25.2)	2 (15	5.4)
N1		31 (25.2)	4 (30).8)
N2		12 (9.8)	3 (23	3.0)
N3a		28 (22.8)	2 (15	5.4)
N3b		21 (17.1)	2 (15	5.4)
Tumor location				
Distal		87 (70.7)	10 (7	6.9)
Proximal		36 (29.3)	3 (23	3.1)
TNM stage				
1a		20 (16.3)	0 (0	.0)

33
50
3: 5'

ASA: American Society of Anesthesiologists; HT: Hypertension; DM: Diabetes Mellitus; COPD: Chronic Obstructive Pulmonary Disease; CAD: Coronary Artery Disease; CEA: Carcinoembryonic antigen; CA19.9: Cancer antigen 19-9; SSI: surgical site infection; LVI: Lymphovascular Invasion; PNI: Perineural InvasionPearson Chi-square test; *Mann-Whitney U test results were considered significant at p<0.05.

with enough lymph node resection to leave a safe surgical margin. The determination of the surgical margin usually depends on the surgeon's palpation or the laparoscopy view. In proximal tumors, especially the gastroesophageal junction, surgical procedure shifts to the thorax to capture a negative surgical margin, which increases the diffi-

р

0.083* 0.841*

0.278

0.054

0.727* 0.882*

0.591

0.639

Count (%)

laparoscopic gastrectomy			
Variables	Median±SD, %	95% CI	р
Surgical margin			
Positive OS, month	51.00±18.56	40.14-51.86	0.977
Negative OS, month	46.00±2.99	14.62-87.38	
Total OS, month	47.00±3.16	40.81-53.19	
1-year SR			
Positive SM	69.2		0.426
Negative SM	78.9		
3-year SR			
Positive SM	46.2		0.990
Negative SM	46.3		
5-year SR			
Positive SM	30.8		0.225
Negative SM	17.1		

Table 4. Overall and 1-, 3-, and 5-year survival rates of patients with positive and negative surgical margins after laparoscopic gastrectomy

OS: Overall survival; SD: Standard deviation; CI: Confidence interval.



Figure 1. Kaplan–Meier survival estimates of the study population showing the overall survival rate of positive and negative surgical margins of the patients following laparoscopic gastrectomy.

culty of surgery and morbidity. According to the Japanese gastric cancer sixth edition guideline, the proximal surgical margin is recommended as 5 cm if the tumor has an aggressive and advanced pattern.^[5] However, according to western studies, overall survival was determined by tumor behavior rather than surgical margin.^[6,7]

Discussions on the effect of surgical margin positivity on survival and locoregional recurrences in gastric cancer continue in the literature. Keun et al. showed that positive surgical margin decreased the disease free survival and overall survival.^[3] In that study, it was mentioned that locoregional recurrences were more common in patients with negative surgical margins. In another study, it was reported that recurrences were not generally within positive surgical margins, whereas peritoneal or distant recurrences were more frequent.^[8,9] Zhao et al. showed that a positive resection margin was associated with tumor aggressive behavior.^[9] According to that study, serosal and lymphovascular invasion were independent risk factors for positive surgical margins.^[9] Lee et al. showed that surgical margin positivity had no effect on local recurrence or survival.^[10] In their study, they recommend intraoperative frozen-section examination and state that no further resection is necessary when a negative margin is reached. Cho et al. reported that positivity of surgical margins affected overall survival in early-stage tumors, and that positivity of surgical margins did not contribute to overall survival in node positive tumors.^[11] Because overall survival in lymph node positive group was determined by locoregionally advanced disease, not by surgical margin positivity.^[11] The recent study Juez et al. reported that positive surgical margin was sign of advanced and more aggressive disease.^[7]

Although studies generally draw attention to the proximal surgical margin, in our patient cohort, we had a higher

Table 5. Analysis of continuous variables and categorical dates by tumor localization					
	Proximal		Distal		р
	Median (min-max)	Count (%)	Median (min-max)	Count (%)	
Age, years	64 (36–80)		61 (26–91)		0.113*
Gender					
Male		30 (76.9)		57 (58.8)	0.046
Female		9 (23.1)		40 (41.2)	
BMI, kg/m ²	24.2 (15.8–42)		25.06 (18.2–45)		0.038*
ASA					
1		2 (5.1)		14 (14.4)	0.421
2		27 (69.2)		61 (62.9)	
3		10 (25.6)		21 (21.6)	
4		0 (0)		1 (1.0)	
НТ					
Absent		27 (69.2)		72 (74.2)	0.554
Present		12 (30.8)		25 (25.8)	
DM					
Absent		33 (84.6)		86 (88.7)	0.519
Present		6 (15.4)		11 (11.3)	
COPD					
Absent		37 (94.9)		90 (92.8)	0.658
Present		2 (5.1)		7 (7.2)	
CAD					
Absent		38 (97.4)		88 (90.7)	0.175
Present		1 (2.6)		9 (9.3)	
CEA	2.93 (0.1–167)		1.55 (0.1-363.2)		0.018*
CA 19-9	16.7 (0.1-293)		7.2 (0.1–2157)		0.012*
Operation type					
Distal Gastree	ctomy	0 (0)		78 (80.4)	<0.001
Total Gastrect	tomy	39 (100)		9 (9.3)	
Near Total Ga	strectomy	0 (0)		10 (10.3)	
Operative Time,	360 (180–600)		300 (120-720)	· · ·	<0.001*
minute	`		· · · ·		
Perioperative	200 (120–900)		100 (0-800)		<0.001*
bleeding, mL	`				
Complication					
Absent		28 (71.8)		76 (78.4)	0.562
Present		11 (28.2)		21 (21.6)	
Complication typ	e	. ,		· · ·	
Absent		33 (84.6)		85 (87.6)	0.431
Lymphatic Lea	ak	0 (0)		0 (0)	
Anastomosis	leak	0 (0)		2 (2.1)	
Paralytic ileus	6	2 (5.1)		4 (4.1)	
Duodenal stu	mp leak	0 (0)		2 (2.1)	
SSI		4 (10.3)		3 (3.1)	

0 (0)

1 (1.0)

Post-operative Hemorrhage

Table 5. CONT.					
	Pro	oximal	Distal		р
_	Median (min-max)	Count (%)	Median (min-max)	Count (%)	
Lenght of stay (day) Tumor Size (cm)	8 (4–12) 6 (0.1–19)		8 (4–39) 5.3 (0.1–13)		0.765* 0.226*
T1 T2 T3 T4a T4b		4 (10.3) 2 (5.1 7 (17.9) 26 (66.2) 0 (0)		25 (25.8) 7 (7.2) 29 (29.9) 34 (35.1) 2 (2.1)	0.009
T early/late stage T1 T2-3-4		4 (10.3) 35 (89.7)		24 (24.7) 73 (75.3)	0.059
Harvesting Total LAP Positive LAP N stage	33 (15-84) 6 (0-44)	· · ·	29 (15-85) 2 (0-42)		0.526* 0.102*
N0 N1 N2 N3a N3b		9 (23.1) 8 (20.5) 3 (7.7) 8 (20.5) 11 (28.2)		24 (24.7) 27 (27.8) 12 (12.4) 22 (22.7) 12 (12.4)	0.256
INM stage 1a 1b 2a 2b 3a 3b 3c IVI		4 (10.3) 1 (2.6) 3 (7.7) 2 (5.1) 11 (28.2) 7 (17.9) 11 (28.2)		16 (16.5) 8 (8.2) 7 (7.2) 18 (18.6) 18 (18.6) 16 (16.5) 14 (14.4)	0.111
Absent Present		7 (17.9) 32 (82.1)		25 (25.8) 72 (74.2)	0.458
Absent Present		11 (28.2) 28 (71.8)		45 (46.4) 52 (53.6)	0.054
Neoadjuvant Absent Present		30 (76.9) 9 (23.1)		91 (93.8) 6 (6.2)	0.004
Positive Negative		3 (7.7) 36 (92.3)		10 (10.3) 87 (89.7)	0.639
Surgical Margin diameter (cm)	2 (0–10)		2.3 (0-6)		0.084*

ASA: American society of anesthesiologists; HT: Hypertension; DM: Diabetes mellitus; COPD: Chronic obstructive pulmonary disease; CAD: Coronary artery disease; CEA: Carcinoembryonic antigen; CA19.9: Cancer antigen 19-9; SSI: Surgical site infection; LVI: Lymphovascular Invasion; PNI: Perineural Invasion. Pearson Chi-square test; * Mann–Whitney U test results were considered significant at P<0.05. number of distal surgical margin positivity in tumors with an antrum location. One of the reasons for this high positivity rate may be the fact that antral tumors do not require a frozen section due to the easier surgical technique and the fear that too much descent below the pylorus may cause duodenal stump leakage. The second reason is that the tumors had an advanced stage and were located near the antropyloric junction. Kumar et al. found a high rate of positivity in the distal surgical margins in tumors located close to the pylorus and in tumors with locally advanced stage.^[12]

The main limitation of the present study is that it is retrospective. Since it is a retrospective study, the data of the patients cannot be collected adequately. Second, there was a loss of data due to the delay in the control examinations of the patients during the pandemic process. The third limitation is the post-operative exclusion of patients with <15 lymph nodes. The reason for this was to eliminate the difference between the groups as the number of lymph nodes would determine the adjuvant chemotherapy treatment of the patients and this would affect evaluation of long-term survival.

Conclusion

While most studies emphasized surgical margin positivity in proximal tumors, the rate of distal surgical margin positivity was found to be higher in this study. In conclusion, no correlation was found between surgical margin positivity and overall survival in gastric cancer patients who had laparoscopic resections.

Disclosures

Ethichs Committee Approval: The study was approved by the ethics comity of Inonu University (Approval No: 2023/703).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – C.A., K.S.; Design – K.S.; Supervision – C.A.; Data collection and/or processing – H.C., Y.S.A., C.C., Ö.G., F.K.; Analysis and/ or interpretation – C.C., H.K.; Literature search – F.K., F.A.; Writing – K.S.; Critical review – C.A., K.S.

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