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Our Short- and Long-Term Results of Laparoscopic Gastrectomy in Locally Advanced Gastric Cancer

Lokal İleri Mide kanserinde Laparoskopik Gastrektomi Kısa ve Uzun Dönem Sonuçlarımız

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ABSTRACT

Objective: Gastric cancer is the fourth most common cause of death worldwide and the second most common cause of cancer-related deaths. Minimally invasive surgery now offers many advantages to both patients and surgeons all over the world. In our study, we presented our laparoscopic experiences in locally advanced gastric cancer (LAGC) surgery.

Method: Data of patients who underwent gastrectomy for LAGC in our clinic between January 2010 and January 2020 were retrospectively analyzed.

Results: Gastrectomy was performed on 288 patients with LAGC. Although laparoscopic surgery was conducted on 96 patients (33.3%), open surgery was performed on 192 (66.7%) patients. The mean operation time was 122.96 ± 44.06 (60-300) min. There was no statistically significant difference between the two groups in terms of anastomotic leakage (p = 0.724). The mean length of stay was 12.54 days in patients undergoing open surgery and 9.36 days in those undergoing laparoscopic surgery, with a statistically significant difference between the two groups (p < 0.001).

Conclusion: Although the learning curve is long and requires experience, we think that laparoscopic surgery is feasible in LAGC, as in early-stage gastric cancer.

Keywords: Gastric cancer, laparoscopy, gastrectomy

ÖZ

Amaç: Mide kanseri tüm dünyada en sık görülen dördüncü, kansere bağlı ölümlerin en sık ikinci nedenidir. Tüm dünyada artık minimal invaziv cerrahi hem hastalara hem de cerrahlara birçok avantaj sunmaktadır. Çalışmamızda lokal ileri mide kanseri (LİMİK) cerrahisinde laparoskopik deneyimlerimizi sunduk.

Yöntem: Ocak 2010 - Ocak 2020 tarihleri arasında kliniğimizde LİMİK nedeniyle gastrektomi yapılan hastaların verileri retrospektif olarak incelendi.

Bulgular: LİMİK nedeniyle 288 hastaya gastrektomi yapıldı. Hastaların 92'si (%31,9) kadın 196'sı (%68,1) erkekti. Hastaların 96'sına (%33,3) laparoskopik cerrahi yapılırken 192'sine (%66,7) ise açık cerrahi uygulanmıştır. Operasyon süresi ortalama 122,96 ± 44,06 (60-300) dakikaydı. Anastomoz kaçağı açısından iki grup arasında istatistiksel anlamlı fark bulunmamıştır (p=0,724). Yatış süresi bakımından açık cerrahide ortalama 12,54 gün iken laparoskopik cerrahide 9,36 gün olup iki grup arasında istatistiksel anlamlı fark gösterilmiştir (p<0,001).

Sonuç: Sonuç olarak öğrenme eğrisi uzun ve deneyim gerektirse de erken evre mide kanserinde olduğu gibi LİMİK'de laparoskopik cerrahinin uygulanabilir olduğunu düşünüyoruz.

Anahtar kelimeler: Mide kanseri, laparoskopi, gastrektomi

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INTRODUCTION

Gastric cancer is the fourth most common cause of death worldwide and the second most common cause of cancer-related deaths ^(1,2). Radical gastrectomy with lymphadenectomy is the main treatment in resectable gastric cancers ^(3,4). After Kitano et al. ⁽⁵⁾ introduced laparoscopy-assisted distal gastrectomy for early-stage gastric cancer in 1991, interest in laparoscopic gastric cancer surgery has grown considerably over the last two decades ⁽⁶⁾.

Compared with open surgery, laparoscopy is associated with advantages including shorter recovery times, less intraoperative blood loss, and lower postoperative morbidity rates ⁽⁷⁾. In recent meta-analyses of early-stage gastric cancer, similar oncological outcomes were obtained in short and long terms compared with open surgery ^(8,9). Although laparoscopic surgery has become the standard of care in early-stage gastric cancer surgery, there is an ongoing debate on the treatment of locally advanced gastric cancer (LAGC) ⁽⁷⁾. Recently, the number of studies showing the feasibility and safety of laparoscopic surgery in treating LAGC has increased ^(10,11).

In our study, we have presented our experience in laparoscopic and open surgery in resectable LAGC in our clinic.

METHOD

Data of patients who underwent gastrectomy for LAGC in our clinic between January 2010 and January 2020 were retrospectively analyzed. The Ethics Committee of Ankara University Faculty of Medicine (İ1-48-21) granted the approval for the study. Patients who were younger than 18 years old, had distant metastasis, had a diagnosis other than adenocarcinoma, underwent surgery under emergency conditions, had positive peritoneal involvement, and had positive cytology were excluded from the study. The study included 288 LAGC patients. The demographic and clinicopathological data, postoperative complications, and overall survival of the patients were examined. The surgery and pathology reports, demographic characteristics, and overall survival of the patients were examined. Electronic radiological examination records of chest radiograms, computed tomography (CT), ultrasound, endoultrasound, magnetic resonance imaging, and positron emission tomography-CT were examined retrospectively. All data were retrieved through a retrospective review of patients' electronic files. The 8th edition of the Union for International Cancer Control TNM classification system was used for staging.

Statistical Analysis

SPSS 25.0 software was used for data analysis. For descriptive analysis, quantitative variables were presented as mean \pm standard deviation and median (minimum-maximum) and qualitative variables as the number of patients (percentage). The mean distributions of the quantitative data were tested using the Shapiro-Wilk test and histogram curves. For the quantitative variables, the difference between the categories of the qualitative variable with two categories was examined using the Mann-Whitney U test for those who provided normal distribution assumptions and the Student's t-test for those who did not provide. The chi-squared test was used to evaluate the relationship between two qualitative variables. The statistical significance level was accepted as 0.05.

RESULTS

Gastrectomy was performed in 288 patients with LAGC. Of the patients, 92 (31.9%) were women, and 196 (68.1%) were men. Although laparoscopic surgery was performed in 96 patients (33.3%), open surgery was performed on 192 (66.7%) patients. The mean age of the patients was 60.43 ± 13.48 (22-93) years. The tumor was in the antrum in 134 (46.5%) patients, corpus in 56 (19.4%), and cardia in 98 (34.0%). Subtotal and total gastrectomies were performed in 139 (48.3%) and 149 (51.7%) patients, respectively. The mean operation time was 122.96 ± 44.06 (60-300) min. Anastomotic leakage was observed in 17 (5.9%) patients after the operation, and of them, 4 (1.4%) were reoperated. The examination of the pathology specimens revealed positive surgical margins in 19 (6.6%) patients. The characteristics of the patients are presented in Table 1.

The average survival time was 21.47 ± 16.51 months. Factors affecting survival were assessed using the Kaplan-Meier test. Patients undergoing laparoscopic gastrectomy showed statistically significantly better survival than those undergoing open surgery ($p < 0.001$). Survival was not found to be statistically significantly related to the presence or absence of an anastomotic leak in patients ($p = 0.982$). Patients with positive surgical margins showed statistically significantly poorer survival ($p < 0.001$). When the relationship of survival to the general tumor stage and the T and N-stages was examined, it was statistically shown that survival became poorer as tumor stages advanced in the three groups, with p-values of <0.001 , 0.001, and 0.001, respectively. The survival analyses are shown in Table 2 and Figure 1-5.

Total and subtotal gastrectomies were performed, respectively, on 106 and 86 patients via open surgery and 33 and 63 patients via laparoscopy, with a statistically significant difference ($p = 0.001$). There was no statistically significant difference in the occurrence of anastomotic leaks between the two groups ($p = 0.724$). The mean lengths of stay were 12.54 and 9.36 days in patients undergoing open and laparoscopic surgery, respectively, with a statistically significant difference between the two groups ($p < 0.001$). The mean operative times were 108.54 and 151.82 min in the open and laparoscopic surgery groups, respectively, with a

statistically significant difference between the two groups ($p < 0.001$). The relationship between the operation type and other factors is shown in Table 3. The number of removed lymph nodes was 24.20 ± 9.35 in the laparoscopy group and 25.7 ± 10.59 in the open surgery group, without a statistically significant difference between the two groups ($p = 0.234$).

DISCUSSION

The Japanese gastric cancer treatment guidelines recommend gastrectomy and D2 dissection for curative treatment of LAGC ⁽¹⁾. The D2 lymph node dissection

Table 1. Patient characteristics

Variables			Laparoscopic	Open	P value
Age (years)	Mean ± SD	60.43 ± 13.48	58.4	62.46	0.284
Survival	Mean ± SD	21.47 ± 16.51	26.4	16.54	<0.001
Sex, n (%)	Male	196 (68.1)	50	146	0.56
	Female	92 (31.9)	46	46	0.62
Location, n (%)	Antrum	134 (46.5)	44	90	
	Corpus	56 (19.4)	18	38	
	Cardia	98 (34.0)	34	64	
Operation, n (%)	Laparoscopy	96 (33.3)			
	Open	192 (66.7)			
Blood transfusion, n (%)	Yes	68 (23.6)	30	38	0.14
	No	220 (76.4)	66	134	
Mortality, n (%)	No	103 (35.9)	33	70	0.11
	Yes	184 (64.1)	63	121	
Operation type, n (%)	Total gastrectomy	139 (48.3)	33	106	0.001
	Subtotal gastrectomy	149 (51.7)	63	86	
Operation time	Mean ± SD	122.96 ± 44.06	151.82 ± 51.91	108.54 ± 30.91	<0.001
Oral intake	Mean ± SD	3.23 ± 1.59	2.4	4.06	0.82
Total lymph node, n (%)	Mean ± SD	25.2 ± 10.20	24.2	25.7	0.234
Metastatic lymph node, n (%)	Mean ± SD	7.27 ± 8.11	8	6.54	0.63
Anastomotic leak, n (%)	No	271 (94.1)	91	180	
	Yes	17 (5.9)	5	12	0.724
Reoperation, n (%)	No	284 (98.6)	95	189	
	Yes	4 (1.4)	1	3	0.44
Surgical margin, n (%)	Negative	269 (93.4)	90	179	
	Positive	19 (6.6)	6	13	0.26
T-stage, n (%)	3	134 (46.7)	55	79	0.2
	4	153 (53.3)	40	113	0.21
N-stage, n (%)	0	59 (20.5)	19	39	0.13
	1	54 (18.8)	20	36	0.22
	2	64 (22.2)	21	42	0.2
	3	111 (38.5)	36	75	0.2

SD: Standard deviation

leads to better oncological outcomes, but it is associated with technical difficulties and increased postoperative morbidity (12). Many randomized controlled studies have shown the superiority of laparoscopic surgery over open surgery in early gastric cancer (13,14). However, there is still an ongoing debate about the role of laparoscopy in

treating LAGC because of the concerns that laparoscopic instruments may traumatize large tumors and metastatic lymph nodes, causing peritoneal transplanted and port site metastasis, and that prolonged operation times may deteriorate immune defense systems and facilitate

Table 2. Kaplan-Meier survival analysis			
		Lifetime	P value
		Mean ± SD	
General		31.23 ± 1.78	-
Operation	Open	26.15 ± 1.82	<0.001
	Laparoscopy	45.82 ± 4.03	
Stage	2	50.20 ± 3.58	<0.001
	3	22.20 ± 1.42	
Surgical margin	Negative	32.85 ± 1.86	<0.001
	Positive	7.68 ± 1.29	
T-stage	3	43.59 ± 2.84	<0.001
	4	19.90 ± 1.48	
N-stage	0	52.60 ± 4.30	<0.001
	1	31.60 ± 3.62	
	2	30.18 ± 2.94	
	3	18.40 ± 1.52	

SD: Standard deviation

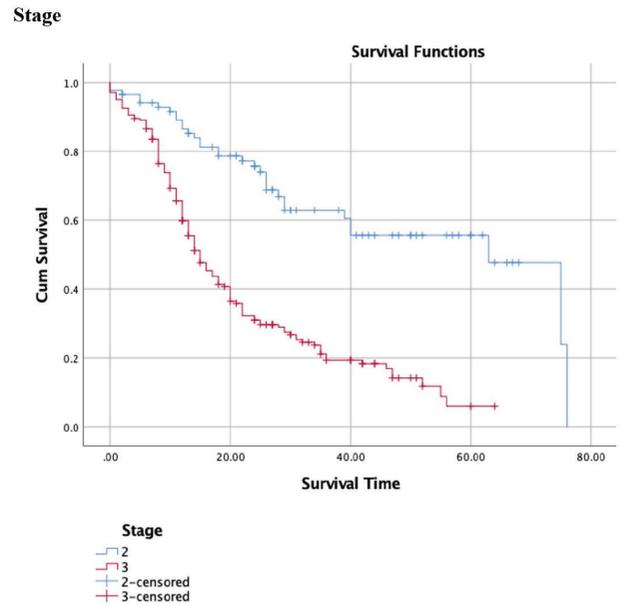


Figure 2. The relationship between stage and survival

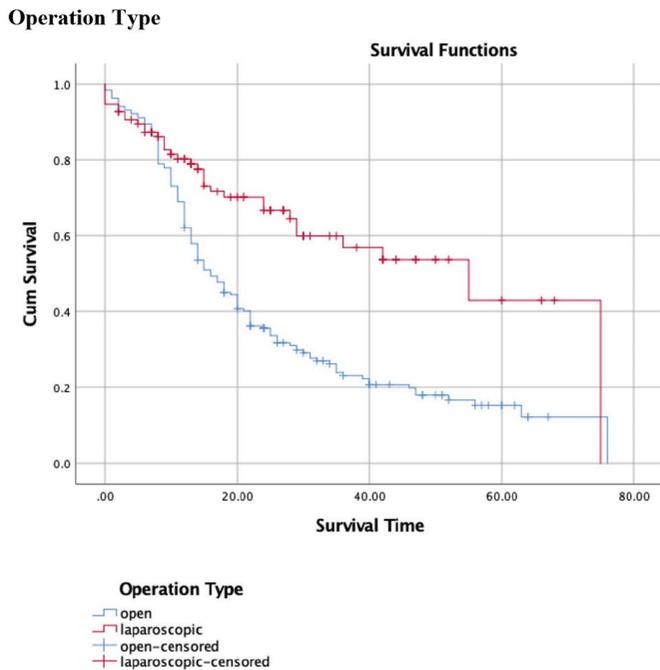


Figure 1. The relationship between operation type and survival

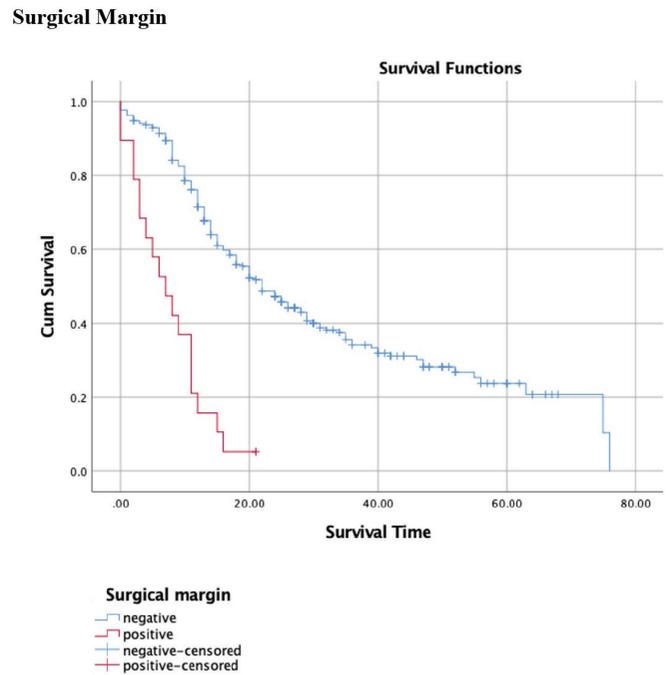


Figure 3. The relationship between surgical margin and survival

Table 3. The relationship between the operation type and factors

Variable		Open	Laparoscopy	
Survival	Mean ± SD	26.15 ± 1.82	45.82 ± 4.03	<0.001
Operation time	Mean ± SD	108.54 ± 30.91	151.82 ± 51.91	<0.001
T-stage, n (%)	T3	79	55	0.007
	T4	113	40	
Operation type, n (%)	Total	106	33	0.001
	Subtotal	86	63	

SD: Standard deviation

T Stage

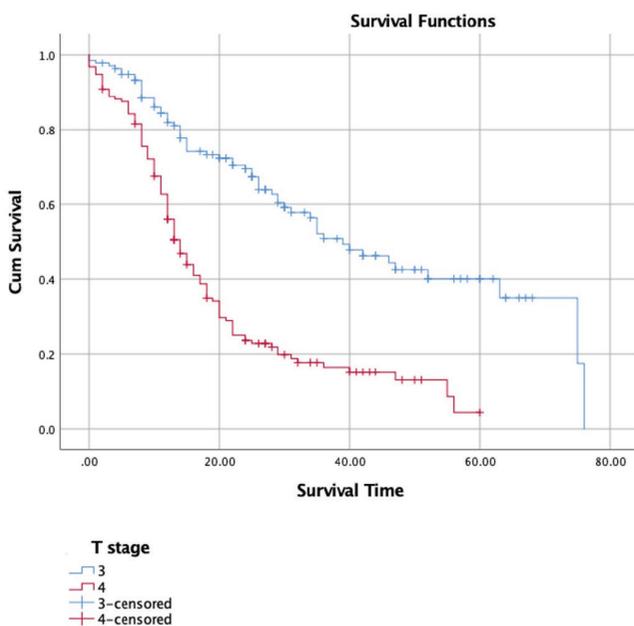


Figure 4. The relationship between T-stage and survival

N Stage

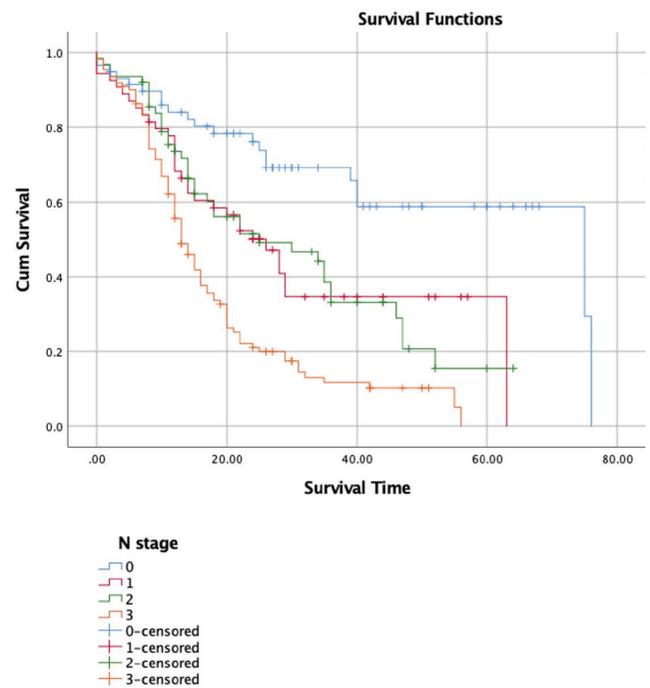


Figure 5. The relationship between N-stage and survival

tumor progression ^(15,16). In the literature, there has been an increasing number of studies showing the feasibility and safety of laparoscopic surgery in LAGC ^(10,11). We prefer performing laparoscopic surgery routinely in our clinic in the absence of contraindications.

Park et al. compared laparoscopic and open surgery in LAGC in 204 patients and found that the mean operative times were 257 ± 86.7 and 183.0 ± 52.5 min, respectively, with a statistically significant difference between the two groups (p < 0.001) ⁽¹⁷⁾. Another study compared open and laparoscopic surgery and reported a mean operative time of 389 min for laparoscopic surgery ⁽¹⁸⁾. In our study, the mean operative

time in laparoscopic surgery was 151.82 ± 51.91 min, which was shorter than in the literature. We think that this is because of our low laparoscopic total gastrectomy cases and increased experience over the years.

The main concern in LAGC surgery is the risk of failing to perform an efficient D2 dissection in laparoscopic surgery. Despite reports of the low number of dissected lymph nodes in the early stages of transition to laparoscopic surgery than open surgery ^(5,19), it has been shown that the numbers of removed lymph nodes have become similar across open and laparoscopic surgery along with the increasing surgeons' experiences and technological advancements ^(20,21). In our

study, there was no difference between the two groups ($p = 0.234$). Additionally, because laparoscopy allows for a comfortable viewing angle and easier accessibility using flexible instruments, we think that laparoscopy provides comfort to the surgeon, especially in dissecting lymph node stations such as 8p and 12p, as classified under the Japanese Gastric Cancer Association criteria.

In general, laparoscopic surgery has advantages such as shorter hospital stay, early onset of oral intake, and less use of blood products⁽²²⁾. In our study, the length of hospital stay was shorter in the laparoscopic group than in the open surgery group, and the difference between the two groups was statistically significant ($p < 0.001$). Between the two groups, we did not find a statistically significant difference in the occurrence of anastomotic leaks, which could lead to a prolonged hospital stay and increased mortality and morbidity ($p = 0.724$). Although we know that bowel movements begin earlier in laparoscopic surgery, we prefer to switch to oral feeding in 3.23 days on average in the early postoperative period after laparoscopic and open surgery in our clinical practice.

A few studies are reporting the long-term results of laparoscopic and open surgery in the treatment of LAGC. Qiu et al.⁽²³⁾ did not find a difference in the 3-year overall survival between the two groups. Choi et al.⁽²⁴⁾ did not report any statistically significant difference in long-term disease-free survival and overall survival. In their meta-analysis, Quan et al.⁽²⁵⁾ did not detect a difference in the disease-free and overall survival between the two groups. Similar to our study, we reported a better mean survival time of 21.47 ± 16.51 months and better survival after laparoscopic surgery, with statistical significance ($p < 0.001$). We attribute this difference to the higher number of patients in the open surgery group and the higher number of patients who did not receive adjuvant therapy or who were lost to follow-up in the open surgery group. Meanwhile, we found that the T and N-stages and surgical margin positivity were the factors affecting survival.

Study Limitations

The limitations of our study include the retrospective design, significant difference in the number of patients between the two groups, assessment of electronically retrieved data only, inadequate data to find out whether the patients who were lost to follow-up received adjuvant therapy or not, missing data to analyze neoadjuvant therapy outcomes, and lack of evaluation of the factors that could act on mortality and morbidity in laparoscopic and open surgery including

obesity, comorbid diseases, benign causes, and abdominal surgery history.

CONCLUSION

In conclusion, despite the long and experience-requiring learning curve in laparoscopic surgery, we prefer laparoscopic surgery for treating LAGC, similar to our clinical practice in early gastric cancers, especially because of comfortable accessibility to difficult-to-reach locations, early postoperative recovery, and less postoperative pain.

Ethics Committee Approval: The Ethics Committee of Ankara University Faculty of Medicine (İ1-48-21) granted the approval for the study.

Informed Consent: Retrospective study.

Conflict of Interest: No conflict of interest was declared by the authors.

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