Original Article Outcome analysis of laporoscopic D1 and D2 dissection in patients 70 years and older with gastric cancer

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Abstract: Objective: Gastric cancer is a worldwide aggressive tumor with a bad prognosis. The purpose of this study was to retrospectively investigate operative findings of 53 patients aged over 70 with gastric cancer who underwent laporoscopic operations in our clinic. Material and methods: A retrospective review of all patients who underwent laporoscopic surgery for pathologically confirmed gastric cancer at our clinic between March 2008 and October 2010 was conducted. D1 resection (Level1 lymphadenectomy) was compared with D2 resection (Levels 1 and 2 lymphadenectomy). The two groups in which D1 and D2 Lymph node Dissection (LND) were applied were compared with respect to number of patients, sex, age, stage of disease, and score of American Society of Anesthesiologists (ASA). We analyzed surgical methods, the use of staplers, operative time, additional organ resections, hospital stay, postoperative complications and the need for re-operation, operative mortality, and the effects of prognostic factors on survival. Results: The patient group consisted of 31 (58%) males and 22 (42%) females. Of the patients, 28 (52%) underwent D1 and 25 (48%) D2 LND. There was a significant difference between the two groups with regard to length of surgery (p < 0.01). The length of operation, blood loss, and transfusion requirement in the D2 group were significantly more than those in the D1 group. There was no mortality in cases that underwent additional organ resection. The survival times of cases with a \leq 0.25 ratio of dissected number of lymph nodes to metastatic lymph nodes were significantly longer than those of other cases. The survival time of cases with perineural and vascular invasion was significantly shorter. The survival rates of Stage I patients was significantly higher than those of Stage III (p:0.002) and Stage IV (p:0.003) patients. Conclusions: Although extensive dissection had an increased morbidity, there was no significant statistical difference between the two procedures. Early complications should not be attributed only to the extent of LND. The important prognostic factors related to long-time survival are the stage of the tumor, perineural and perivascular invasion, and metastatic lymph nodes.

Keywords: Laparoscopic surgery, gastric cancer, older patients

Introduction

Gastric cancer is the fourth most frequent cancer in the world and is also the second cause of deaths related to cancer. In the United States of America in 2013, there were 21,600 newly diagnosed cancer cases and 10,990 deaths due to cancer [1]. Although surgery has been accepted as the golden standardin the therapy of gastric cancer, the optimal limits of this surgery is still a matter of dispute [2]. The disease is often characterized by regional nodal metastasis. The extension of lymph node dissection along with extended surgical dissection is also disputable. Some authors are of the opinion that extended dissection in gastric cancer increases morbidity and mortality, whereas others think the opposite [3]. Many western surgeons recommend and perform limited dissection (D1) [4]. In Japan, all surgeons perform D2 LND beside gastric resection as standard therapy [5]. Laparoscopic surgery is a minimally invasive operation and is proved to be an acceptable alternative to open surgery [6-9]. The first laparoscopic-assisted distal gastrectomy with a Billroth II gastrojejunostomy was performed by Goh et al. [10] in 1992, for the treatment of a complicated peptic ulcer. The first laparoscopic gastrectomy, with a Billroth II reconstruction, for cancer was performed by Kitano et al. [11] in 1992 and published in 1994.

The purpose of this study was to compare the postoperative morbidity and mortality rates of patients aged over 70 with gastric cancer who underwent laparoscopic D1 and D2 LND and to assess the factors affecting morbidity and mortality as well as survival.

Patients and methods

The data of 53 patients aged over 70 with gastric cancer hospitalized in the period between March 2008 and October 2010 were retrospectively evaluated. The study included only those patients who had undergone laporoscopic surgerv. Each patient's length of surgerv, blood loss, requirement for transfusion, and score of American Society of Anesthesiologists (ASA) were evaluated. Each patient's gender, tumor localization, comorbid conditions, and mortality were also noted. General complications (pneumonia, cardiac insufficiency, myocardial ischemia, acute renal failure, pulmonary embolus, cerebrovascular disorder) and surgical complications (pancreatic fistula, abdominal abscess, fluid collection, wound infection, ileus, anastomotic leakage) were also noted. The term "operative mortality" was used for death within the first month, and the term "postoperative morbidity" was used for postoperative complications that required longer hospitalization and/or additional treatment. We also studied the medical files and operational and histopathological reports of the patients in order to determine gender, symptoms during hospital referral, kind of surgery performed and additional resection of other organs, postoperative complications, tumor localization, macroscopy of the tumor, depth of the tumor invasion in the gastric wall, total number of lymph nodes resected, and number of metastatic lymph nodes. The impact of each of these parameters on survival time of the patients was assessed. With these parameters the patients were staged according to The Classification of Malignant Tumors (TNM). Subsequently, we assessed whether this classification system provided a stepwise relationship between the stage of the tumor and survival time or not.

Surgical method: The curative resection (RO resection) was accepted as the complete

removal of the cancer in the tumor bed both macroscopically and histopathologically. D1 and D2 lymphatic dissections were performed to the Guidelines of the Japanese Research Society for the Study of Gastric Cancer (JRSGC) [12]. D1 LND included the N1 lymph node group (right paracardial, left paracardial, lesser curvature, greater curvature, suprapyloric, and subpyloric) and D2 LND included the N1 lymph node group together with the N2 lymph node group according to the localization of the tumor (along the left gastric artery, common hepatic artery, celiac axis, splenic hilum, splenic artery, hepatoduodenal ligament). All patients underwent preoperative endoscopy and abdominal computed tomographic examination. In cases of proximal gastric cancer, Laporoscopic total gastrectomy (LTG), laparoscopy-assisted total gastrectomy (LATG) and usually Roux-en-Y esophagojejunostomy anastomosis were performed, whereas in cases of distal gastric cancer laporoscopic distal subtotal gastrotectomy (LDSG), Laparoscopy-assisted distal subtotal gastrectomy (LADSG) and usually Roux-en-Y gastrojejunostomy anastomosis were performed. The surgical interventions, which left no residual macroscopical tumor tissue behind, in the mentioned group of patients were evaluated as curative resection. Based on histopathological findings, the curative resection of less than 15 lymph nodes was evaluated as palliative resection.

Types of laparoscopic resections

Resections were performed either as laparoscopy-assisted, where the gastric transection and reconstruction were performed through minilaparotomy, or totally laparoscopic, where mobilization, resection, and reconstruction were performed intracorporeally.

Operative techniques

Laparoscopic distal subtotal gastrectomy: This procedure is performed for gastric cancer involving the gastric antrum or gastric body. The procedure is carried out under general anesthesia with endotracheal intubation. The patient lies on the table in the supine position, with legs apart and 20° head-up tilt. The surgeon operates in the "French" position with the camera assistant on his left. CO_2 pneumoperitoneum is induced after insertion of the first 10/12-mm cannula at the level of the umbili-

cus, five abdominal trocars are introduced. The entire stomach is mobilized including the gastric fundus by division of the short gastric vessels. The gastrohepatic and gastrocolic ligaments are divided for gastric mobilization. The right gastric and right gastroepiploic vessels are divided with the linear stapler. The first portion of the duodenum is divided using a 60-mm linear stapler. The site of proximal gastric resection depends on the site of the cancer and its extension. The vessels are carefully prepared and separately divided, the vein using harmonic scissors and the artery with an endostapler. A 50-cm transmesocolic Roux-en-Y loop is prepared and anastomosed side-to-side to the posterior wall of the gastric stump with a single or double application of endostapler (45- vs. 35-mm cartridge). A side-to-side jejunojejunal anastomosis at the foot of the Roux-en-Y loop is fashioned by further endostapler application. The surgical specimen is removed atraumatically through an enlarged trocar site that is protected with a plastic wound retractor and the specimen margin is identified.

Laparoscopic total gastrectomy: This procedure is performed for patients who have gastric cardia lesion with involvement of the gastric body and antrum. Five abdominal trocars are introduced. The entire stomach is mobilized including the gastric fundus by division of the short gastric vessels. The greater omentum was first dissected, using the ultrasonic activated scissors (Ultracision-Harmonic Scalpel; Ethicon Endo-Surgery Inc, Cincinnati, OH, United States), along the border of the transverse colon. The first portion of the duodenum is divided with a linear stapler. The distal esophagus is mobilized circumferentially for a segment of 5 to 6 cm into the mediastinum. The esophagus is divided with the ultrasonic scissor approximately 2 cm above the gastroesophageal junction. The anvil of the circular stapler is inserted into the esophageal stump and secured with a purse-string suture. The jejunum is divided at 30 cm distal to the ligament of Treitz. The length of the Roux limb is measured at 40 cm whereby a jejunojejunostomy is constructed. A 25-mm circular stapler is used to construct the esophago-jejunal anastomosis The surgical specimen is removed atraumatically through an enlarged trocar site that is protected with a plastic wound retractor and the specimen margin is identified.

Laparoscopic proximal gastrectomy: This procedure is performed for cancer of the gastric cardia without involvement of the esophagus. Five abdominal trocars are introduced. The entire stomach is mobilized including the gastric fundus by division of the short gastric vessels. The right gastroepiploic artery is maintained. The mid-aspect of the stomach is divided starting on the lesser curvature and completed on the greater curvature of the stomach. The distal esophagus is mobilized circumferentially for a segment of 5 to 6 cm into the mediastinum. The esophagus is divided with the ultrasonic scissor approximately 2 cm above the gastroesophageal junction. A gastrotomy is created in the distal gastric remnant. An esophagogastric anastomosis is performed using a 25-mm circular stapler. The remaining gastrotomy is sutured closed.

Statistical analysis

For the statistical analysis of the data obtained in the study, we used SPSS (Statistical Package for Social Sciences) for Windows 15.0. The differences between the groups as to gender and length of hospitalization were determined by using the Student's t test and differences in length of operations by using the Mann-Whitney U test. The nominal variables were evaluated with the chi-square test or Fisher's exact chisquared test. The value p < 0.05 was accepted as significant. The results of the survey were given as arithmetical mean and standard deviation. The survival rates of the patients were calculated by using Kaplan-Meier survival analysis. The log-rank test was used in the one-variable analysis made by comparing the prognostic factors with survival curves; and the significant or nearly significant factors in this analysis were evaluated further by using the Cox regression analysis.

Results

The patient group consisted of 31 (58%) males and 22 (42%) females. Of the patients, 28 (52%) underwent D1 and 25 (48%) D2 LND. The demographic and characteristic features of the patients are shown in **Table 1**. Our cases were divided into four groups according to the location of the tumor. The tumor was most frequently located in the antrum and corpus of the stomach. The distribution of the patients according to tumor stages is shown in **Table 2**.

		D1 group (n = 28)	D2 group (n = 25)	Total (n = 53)	P value
Male/Female		17/11	14/11	31/22	0.460
ASA score	ASA III and below	19	17	36	0.785
	ASA IV and upper	9	8	17	
Gastrectomy Type	Total gastrectomy	12	10	22	0.650
	Distal	14	14	28	
	Proximal	2	1	3	
Location	Cardia	2	1	3	0.495
	Corpus	11	8	19	
	Antrum	14	14	28	
	Linitis plastica	1	2	3	
Types of resections	Laparoscopy-assisted Gastrectomy	13	11		0.650
	Totally Laporoscopic Gastrectomy	15	14		
Distal pancreatectomy		2	3	5	0.651
Splenectomy		6	6	12	
Transvers colon resection		1	3	4	
Hepatic metastasectomy		1	2	3	
Blood loss (mL)		235.6 ± 125.0	400.6 ± 220.5	390.5 ± 253.8	< 0.01
The need for transfusion		22	48	72	< 0.01
The average exracting lymph node number		18.6 ± 5.4	33.5 ± 8.5	29.05 ± 11.4	< 0.01
Length of ICU stay (day)		1.2	2.6	2.2	< 0.01
Length of hospital stay (day)		11.8	12.7	14.6	0.82
Operation time (minute)		180 ± 14	218 ± 53	205.5 ± 25.8	< 0.01

Table 1. Patient demographics, tumor characteristics and surgical procedures associated with the
comprasion in terms of results

p < 0.05 was considered statistically significant.

Table 2. D1 and D2 dissection according to
the stages

Stages	D1 Dissection	D2 Dissection		
1A	5	6		
1B	8	4		
2	8	8		
ЗА	3	3		
3B	3	2		
4	1	2		

Detailed information related to operations is given in **Table 1**. Of the patients, 28 (52%) underwent subtotal gastrectomy. The length of surgery in the D1 group was 180 ± 14 minutes and in D2 group 218 ± 53 minutes. There was a significant difference between the two groups with regard to length of surgery (p < 0.01). The number of dissected lymph nodes and the total number of metastatic lymph nodes in the D2 group were significantly more than those in the D1 group (**Table 1**). The length of operation, blood loss, and transfusion requirement in the D2 group were significantly more than those in the D1 group (**Table 1**). Early postoperative complications are shown in **Table 3**. In 27 patients various postoperative complications developed. The morbidity was 50% and mortality 9%.

The histopathological examinations showed adenocarcinoma in 44 (83%), signet-ring cell carcinoma in 6 (11%), and mucinous adenocarcinoma in 3 (6%) patients. Additional organ resection was performed on 24 (45%) patients. Of these patients; 12 underwent laporoscopic splenectomy, 5 laporoscopic distal pancreatectomy, 4 laporoscopic colon resection, and 3 laporoscopic liver resection. In this respect, there was no statistically significant difference between the two groups. There was transverse colon invasion in all patients who underwent colon resection and infiltration in the left hepatic lobe in one patient who had liver resection by left lateral segmentectomy. On the other two patients with liver infiltration non-anatomical liver resection was performed. Out of 12 patients who underwent laporoscopic splenectomy, 6 were splenectomized due to iatrogenic reasons. In the D1 group, mortality occurred in 3 patients (due to pulmonary embolus, myocar-

	D1	D2	Р		
General Complications	Group (n	Group	-		
	= 28)	(n = 25)	value		
Pneumonia	1	1	0.285		
Heart failure	1	2			
Myocardial ischemia	1	1			
Acute renal failure	0	0			
Pulmonary embolism	1	0			
Cerebrovascular diseases	0	1			
Surgical Complications			0.651		
Pancreatic fistula	1	2			
Abdominal abscess	1	1			
Fluid collection	1	2			
Wound infection	2	1			
lleus	1	2			
Anostomosis leakage	1	1			
Mortality	3	2	0.877		
n < 0.05 was considered statistically significant					

Table 3. Complication rates in groups D1 and D2

p < 0.05 was considered statistically significant.

dial ischemia, and pneumonia, respectively). In the D2 group 2 patients died (due to cardiac insufficiency and pneumonia). There was no mortality in cases that underwent additional organ resection.

When the survival rates were determined with log-rank test according to lymphatic dissections, there was no significant difference between the 5-year survival rates (p:0.683).

When the survival rates were evaluated with log-rank test according to the ratio of dissected number of lymph nodes to metastatic lymph nodes, there was a significant difference between the 5-year survival rates (p:0.002). The survival times of cases with a \leq 0.25 ratio of dissected number of lymph nodes to metastatic lymph nodes were significantly longer than those of other cases. According to other ratios, there was no significant difference in survival time between the patients.

When the survival rates were determined by log-rank test according to the presence of perineural and vascular invasion, there was a significant difference between 5-year survival rates (p:0.002; p:0.006). The survival time of cases with perineural and vascular invasion was found to be significantly shorter. When the survival rates were evaluated according to tumor size, there was no statistically significant difference between the 5-year survival rates (p:0.135).

The survival rates of Stage I patients was significantly higher than those of Stage III (p:0.002) and Stage IV (p:0.003) patients. When the survival rates were evaluated according tumor location, there was no statistically significant difference between 5-year survival rates (p:0.003). The survival time of cases with linitis plastica was shorter than 5 years. The results of Cox regression analysis showed that the stage of the tumor, location of the tumor, presence of perineural and perivascular invasion, and presence of metastatic lymph nodes were important prognostic factors in gastric cancer (**Table 4**).

Discussion

Gastric cancer is the fourth most frequent cancer in the world and is also the second cause of deaths related to cancer [1]. Among the risk factors for gastric cancer are wrong eating habits, secondary amines, food rich in nitrites and nitrates, smoking, and high-salt diets [13]. Most gastric cancers occur sporadically, whereas 8% to 10% of cases have an inherited familial component [14]. Many studies have reported the depth of tumor invasion, lymph node metastasis, far metastases, and curability as the main prognostic factors of gastric cancer [15-17]. Surgery is the most effective therapeutic method for gastric cancer. Curative resection is the resection of the whole stomach and all lymph nodes, including tumor-free margins in cases with no peritoneal and far organ metastases. The first laparoscopic-assisted distal gastrectomy with a Billroth II gastrojejunostomy as performed by Goh et al. [10] in 1992, for the treatment of a complicated peptic ulcer 34. The first laparoscopic gastrectomy, with a Billroth II reconstruction, for cancer was performed by Kitano et al. [11] in 1992 and published in 1994. Several prospective trials have demonstrated LG to be superior to open surgery because it results in less postoperative pain, faster recovery, and better cosmetic results [18-21]. The lymphatic dissections performed in gastric cancer are the following: DO resection, the incomplete resection of the N1 lymph node group; D1 resection, the complete resection of the N1 lymph node group; D2 resection, the resection of N1 and N2 groups plus bursa; D2.5 resection, D2 resection plus

		Mean ± SE	Р
ASA score	ASA III and less	36	0.432
	ASA IV and above	17	
Gastrectomy type	Total	44.12 ± 4.60	0.750
	Distal	58.2 ± 8.1	
	Proximal	45.0 ± 12.0	
Tumor size	< 5 cm	57.2 ± 6.3	0.135
	5-10 cm	47.2 ± 7.1	
	> 10 cm	42.8 ± 2.1	
Location	Cardia	45.0 ± 12.0	0.003
	Corpus	48.3 ± 7.2	
	Antrum	61.2 ± 8.3	
	Linitis plastica	11.8 ± 3.2	
Macroscopic type	Fungatif	45.1 ± 12.1	0.353
	Ülsero infiltrative	49.2 ± 7.3	
	Common infiltrative	13.8 ± 3.1	
	Polypoid	60.1 ± 7.1	
Depth of invasion	T1	60.2 ± 8.1	0.009
	T2	49.3 ± 6.2	
	T3	41.0 ± 12.3	
	T4	11.2 ± 3.1	
Additional organ resection	Yes	45.0 ± 8.6	0.237
Additional organ resection	No	48.2 ± 5.3	0.201
Intensive care unit stay (days)	3 day less	54.21 ± 3.80	0.375
intensive care unit stay (days)	3 day long	44.22 ± 4.80	0.575
LNR (The ratio of metastatic lymph	≤ 0.25	35.80 ± 5.09	0.002
nodes to resected lymphnodes)	0.26-0.50	27.23 ± 6.46	0.002
	> 0.50	27.23 ± 0.40 22.95 ± 4.92	
Lymphodonoctomy Typo			0 693
Lymphadenectomy Type	D1 resection	33.19 ± 3.23 32.54 ± 4.22	0.683
	D2 resection		0.000
Vascular invasion	Yes	26.74 ± 3.86	0.006
	No	47.58 ± 4.68	
Perineural invasion	Yes	26.12 ± 3.82	0.002
_	No	46.76 ± 4.58	
Stage	1A	56.70 ± 6.07	0.003
	1B	32.0 ± 7.1	
	2	39.90 ± 6.45	
	ЗА	26.90 ± 3.94	
	3B	14.0 ± 1.9	
	4	10.00 ± 6.94	
Post-operative chemotherapy	Yes	32.28 ± 1.22	0.450
	No	36.19 ± 2.60	
Post-operative radiotherapy	Yes	37.28 ± 1.32	0.365
	No	34.48 ± 6.85	
Types of resections	Laparoscopy-assisted Gastrectomy	39.80 ± 1.25	
	Totally Laporoscopic Gastrectomy	41.20 ± 4.60	

Table 4. General evaluation of survival

Log Rank tests were used.

resection of upper para- aortic and hepatoduodenal lymph node groups; D3 resection, resection of the N3 lymph node group; and D4 resection, the resection of all para-aortic lymph nodes [22]. There is still an uncertainty about the oncological efficacy of laparoscopic manipulation in serosa-positive disease, all efforts must be made to prevent preoperative and intraoperative understaging to apply conventional open measures of preventing peritoneal seedling in advanced disease [23, 24]. Hwang et al. [25] reported their experience of LAG for AGC. They compared LAG (n = 45) with ODG (n= 83) performed between 2004 and 2007 in a non-randomized fashion. These authors found no difference in the mean number of nodes harvested in either group and felt that extended lymphadenectomy for AGC is possible and safe. Kawamura et al. [26] in yet another non-randomized trial comparing LDG (n = 53) and ODG (n = 67) over a two year period examined the safety and accuracy of D2 dissection for AGC. They concluded that D2 dissection could be performed safely and accurately without undue complications provided the surgical team was skilled in minimally invasive surgical techniques. Dulucg et al. [27] reported similar lymphadenectomy between groups, and resection margins were negative in all patients who underwent laparoscopic gastrectomy. In addition, Huscher et al. [28] randomized patients to laparoscopic-assisted and open radical subtotal gastrectomy for distal gastric cancer and found that the mean number of resected lymph nodes as well as the 5-year overall and diseasefree survival rates were similar between groups. Some authors are of the opinion that extended dissection in gastric cancer increases morbidity and mortality, whereas others think the opposite [3]. Kitano and colleagues, in a multicenter retrospective study of 1,294 LGs in 16 institutions, reported that the morbidity and mortality rates were 14.8% and 0%, respectively, and 5-year disease-free survival rate was 99.8% for stage IA disease, 98.7% for stage IB disease, and 85.7% for stage II disease with a median follow-up of 36 months [29]. Dao-Jun Gang et al. [30] studied 125 gastric cancer patients with a mean age of 60 years who underwent total gastrectomy in the period between 2003 and 2008 and found a significant relationship between operative morbidity and factors of age, gender, extension of resection, and preoperative comorbidity. Orsenigo et al. [31], in their

study covering the period between 1990 and 2005, divided 1118 patients wih gastric cancer into two groups (aged over and under 75 years) and reported that postoperative morbidity was more frequent in the older age group but with no significant difference. On the contrary, Persianiet et al. [32], with multivariant analysis of their study, showed that age \geq 64 years was a predictive factor for all morbidities. Saidi and Piso [33] reported that chronological age as well as biological age and comorbidity had an impact on the selection of resection type. Gil-Renda et al. [34] set forth that curative resection performed on aged patients could provide long- term survival with an acceptable rate of mortality. In our study, the rates of morbidity and mortality in aged cases of D2 LND and D1 LND were similar. D2 LND prolongs the operation time. The type of gastric resection, additional organ resection, and stage of tumor were not found to have an impact on morbidity and mortality. There are studies reporting that additional organ resections, like splenectomy and/ or pancreatectomy, lead to increased morbidity and mortality and have no contribution to survival rates [35, 36]. Also many studies have shown additional organ resection (particularly splenectomy) and Stage IV as independent predictive factors for complications [30, 32, 37, 38]. In our study, 24 patients underwent additional organ resection, and 2 out of 12 patients splenectomized showed morbidity; in other patients no mortality/morbidity developed. The morbidity rates increased with extended dissection, but this increase was statistically insignificant. Additional organ resection in elderly patients did not have an important effect on survival rates (Table 4). Know et al. [39] grouped the ratio of dissected lymph nodes to metastatic lymph nodes as 0%, 1-25%, 26-50%, and 50% and found the related 5-year survival rates as 83%, 66%, 30%, and 23%, respectively. Many studies have shown that the prognosis of gastric carcinoma worsens as this ratio increases. A study reported that among patients who underwent D1 and D2 dissection, this ratio had prognostic significance in groups where \leq 15 and \geq 16 lymph nodes were extirpated [40]. In the German Gastric Cancer Study, Siewert et al. [41] analyzed the 10-year prognosis of 1654 patients who had undergone curative gastrectomy and concluded that the state of lymph nodes, invasion depth of the tumor, postoperative complications, presence of far metastases,

and tumor size had an impact on prognosis. The ratio of metastatic lymph nodes to resected lymph nodes is also an important prognostic factor. Kim et al. [42] grouped 9262 patients according to ratio groups of 0, 0.1, 0.3, 0.5, and above 0.5 and showed that survival rates declined as the ratio increased. Likewise, Ding et al. [43] reported that in patients with ratios of 0, 1%-20%, and above 20%, the survival rates were 91.2%, 70.6%, and 12%, respectively. With the publication of Dutch's study covering 15 years [44], the western world showed the positive contribution of extended lymph node dissection to a life without morbidity as well as to survival rates. Lee et al. [45] compared 384 node-negative gastric cancer patients with 305 node-positive patients and determined that lymphovascular invasion and depth of invasion were independent prognostic factors affecting survival. The location of the tumor is another prognostic factor [46]. Gastric cancer is often located in the antrum. In our study, in 41.9% of the cases the tumor was located in the gastric antrum. The proximal tumors have worse prognosis than distal tumors because they are larger in size, show increasing frequency, cause deeper invasion, and more frequently lead to lymph node metastasis [47]. We found the average survival to be 44-45 months in patients with proximal gastric cancer who underwent proximal subtotal and total gastrectomy and 58 months in patients with distal tumor who had distal subtotal gastrectomy.

It has been shown that increase in the size of gastric tumor is related to bad prognosis and early recurrence of the tumor [48, 49]. In our study, although tumors sized 10 cm and over were characterized by short survival, the tumor size was not an independent prognostic factor. When evaluated with log-rank test, there was no significant relationship between the tumor size and 5-year survival rates.

Duraker et al. [50] in their retrospective study on 354 patients who were curatively resected, reported that the incidence of perineural invasion had an important effect on survival. By using the log-rank test, we found a significant relationship between the presence of perineural invasion and 5-year survival rates (p:0.001). In cases with perineural invasion, the survival time is significantly shorter. In a randomized study where a group of patients

treated with only surgery was compared with a group treated with surgery plus adjuvant chemotherapy, the group that received adjuvant chemotherapy showed better 3-year survival rates, less local recurrence, and no increase in toxic effects in 10-year follow-ups [51, 52]. Because of high rates of local relapse and recurrence and low rates of survival in gastric cancer cases treated with only surgery, it is crucial to administer a combined therapy of surgery and chemotherapy. The appropriate systemic therapy for each patient is determined according to the surgical margin, stage of the tumor, extent of lymph node dissection, and metastatic or advanced morbidity [53]. Highdose radiation is required for the radiotherapy of gastric cancer, a situation which limits the therapy. Hermans et al. [54] have stated that radiotherapy should be made in cases of relapse in patients formerly resected or in cases where resection is not possible. Another study reported that radiotherapy increases the survival rates in gastric cancer patients who are in stages ranging from IB to IV according to the American Joint Committee on Cancer stage; who have undergone partial gastrectomy, total gastrectomy, or en-bloc gastrectomy plus resection of other organs; nodepositive and have > 15 lymph nodes dissected [55]. In our study, when evaluated by log-rank test, we found no significant relationship between postoperative radiotherapy and 5-year survival rates (p:0.365). In conclusion, among patients aged over 70 years with gastric cancer, the morbidity and mortality rates in patients who underwent D2 LND were similar to those in patients who had D1 LND. D2 LND prolongs the operative time. Early complications should not be attributed only to the extent of LND. Important prognostic factors related to long-time survival are the stage of the tumor, perineural and perivascular invasion, and metastatic lymph nodes. We are of the opinion that determination of these prognostic factors will contribute to the planning of appropriate therapy.

Disclosure of conflict of interest

None.

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References

- Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. CA Cancer J Clin 2013; 63: 11-30.
- [2] Allum WH, Griffin SM, Watson A, Colin-Jones D. Guidelines for the management of oesophageal and gastric cancer. Gut 2002; 50: 1-23.
- [3] Sano T, Katai H, Sasako M, Maruyama K. One thousand consecutive gastrectomies without operative mortality. Br J Surg 2002; 89: 123.
- [4] NHS Executive: Guidance on Commissioning Cancer Services: Improving outcomes in upper gastro-intestinal cancers, 2001.
- [5] Sasako M, Kodera Y, Yamamoto S, Sano T, Nashimoto A, Kurita A. Identification of risk factorsfor the development of complications following extended and süper extended lymphadenectomies for gastric cancer. Br J Surg 2005; 92: 1103-9.
- [6] Schulze S, Thorup J. Pulmonary function, pain and fatigue after laparoscopic cholecystectomy. Eur J Surg 1993; 159: 361-364.
- [7] Iwanaka T, Arkovitz MS, Arya G, Ziegler MM. Evaluation of operative stres and peritoneal macrophage function in minimally invasive operations. J Am Coll Surg 1997; 184: 357-363.
- [8] Gupta A, Watson DI. Effect of laparoscopy on immune function. Br J Surg 2001; 88: 1296-1306.
- [9] Carter JJ, Whelan RL. The immunologic consequences of laparoscopy in oncology. Surg Oncol Clin North Am 2001; 10: 655-677.
- [10] Goh P, Tekant Y, Kum CK, Isaac J, Shang NS. Totally intra-abdominal laparoscopic Billroth II gastrectomy. Surg Endosc 1992; 6: 160.
- [11] Kitano S, Iso Y, Moriyama M, Sugimachi K. Laparoscopy-assisted Billroth I gastrectomy. Surg Laparosc Endosc 1994; 4: 146-148.
- [12] Kajitani T. The general rules for gastric cancer study in surgery and pathology. Part I. Clinical classification. Jpn J Surg 1981; 11: 127-145.
- [13] Gore R. Gastric cancer. Clinical and pathologic features. Radiol Clin North Am 1997; 35: 295-310.
- [14] Lavecchia C, Negri E, Fraceschi S. Family history and the risk of stomach and colorectal cancer. Cancer 1992; 70: 50-5.
- [15] Kim JP, Lee JH, Kim SJ, Yu HJ, Yank HK. Clinicopathologic characteristics and prognostic factors in 10783 patients with gastric cancer. Gastric Cancer 1998; 1: 125-33.
- [16] Harrison JP, Fielding JW. prognostic factors for gastric cancer, influencing clinical practice. World J Surg 1995; 19: 496-500.
- [17] Nakamura K, Ueyama T, Yan T, Xvan ZX, Ambe K, Adachi Y. Pathology and prognosis of gastric carcinoma. Finding in 1000 patients who underwent primary gastrectomy. Cancer 1992; 70: 1030-7.
- [18] Mochiki E, NakabayashiT, Kamimura H, Haga N, Asao T, Kuwano H. Gastrointestinal recov-

ery and outcome after laparoscopy-assisted versus conventional open distal gastrectomy for early gastric cancer. World J Surg 2002; 26: 1145-1149.

- [19] Reyes CD, Weber KJ, Gagner M, Divino CM. Laparoscopic vs open gastrectomy. A retrospective review. Surg Endosc 2001; 15: 928-931.
- [20] Kitano S, Shiraishi N, Fujii K, Yasuda K, Inomata M, Adachi Y. A randomized controlled trial comparing open vs laparoscopy-assisted distal gastrectomy for the treatment of early gastric cancer: an interim report. Surgery 2002; 131 Suppl: S306-S311.
- [21] Adachi Y, Shiraishi N, Shiromizu A, Bandoh T, Aramaki M, Kitano S. Laparoscopy-assisted Billroth I gastrectomy compared with conventional open gastrectomy. Arch Surg 2000; 135: 806-810.
- [22] Coburn NG. Lymph nodes and gastric cancer. J Surg Oncol 2009; 99: 199-06.
- [23] Volz J, Koster S, Spacek Z, Paweletz N. The influence of pneumoperitoneum used in laparoscopic surgery on an intraabdominal tumor growth. Cancer 1999; 86: 770-774.
- [24] Lee YJ, Ha WS, Park ST, Choi SK, Hong SC. Port-site recurrence after laparoscopyassisted gastrectomy: report of, the first case. J Laparoendosc Adv Surg Tech A 2007; 17: 455-457.
- [25] Hwang SI, Kim HO, Yoo CH, Shin JH, Son BH. Laparoscopic-assisted distal gastrectomy versus open distal gastrectomy for advanced gastric cancer. Surg Endosc 2009; 23: 1252-1258.
- [26] Kawamura H, Homma S, Yokota R, Yokota K, Watarai H, Hagiwara M, Sato M, Noguchi K, Ueki S, Kondo Y. Inspection of safety and accuracy of D2 lymph node dissection in laparoscopy-assisted distal gastrectomy. World J Surg 2008; 32: 2366-2370.
- [27] Dulucq JL, Wintringer P, Stabilini C, Solinas L, Perissat J, Mahajna A. Laparoscopic and open gastric resections for malignant lesions: a prospective comparative study. Surg Endosc 2005; 19: 933-8.
- [28] Huscher CG, Mingoli A, Sgarzini G, Sansonetti A, Di Paola M, Recher A, Ponzano C. Laparoscopic versus open subtotal gastrectomy for distal gastric cancer: five-year results of a randomized prospective trial. Ann Surg 2005; 241: 232-7.
- [29] Kitano S, Shiraishi N, Uyama I, Sugihara K, Tanigawa N; Japanese Laparoscopic Surgery Study Group. A multicenter study on oncologic outcome of laparoscopic gastrectomy for early cancer in Japan. Ann Surg 2007; 245: 68-72.
- [30] Gong DJ, Miao CF, Bao Q, Jiang M, Zhang LF, Tong XT,Chen L. Risk factors for operative morbidity and mortality in gastric cancer patients undergoing total gastrectomy. World J Gastroenterol 2008; 14: 6560-3.

- [31] Orsenigo E, Tomajer V, DiPalo S, Carlucci M, Vignali A, Tamburini A, Staudacher C. Impact of age on postoperative outcomes in 1118 gastric cancer patients undergoing surgical treatment. Gastric Cancer 2007; 10: 39-44.
- [32] Persiani R, Antonacci V, Biondi A, Rausei S, La Greca A, Zoccali M, Ciccoritti L, D'Ugo D. Determinants of surgical morbidity in gastric cancer treatment. J Am Coll Surg 2008; 207: 13-9.
- [33] Saidi RF, Bell JL, Dudrick PS. Surgical resection for gastric cancer in elderly patients: is there a difference in outcome? J Surg Res 2004; 118: 15-20.
- [34] Gil-Rendo A, Hernández-Lizoain JL, Martínez-Regueira F, Sierra Martínez A, RotellarSastre F, Cervera Delgado M, Valentí Azcarate V, Pastor Idoate C, Alvarez-Cienfuegos J. Risk factors related to operative morbidity in patients undergoing gastrectomy for gastric cancer. Clin Transl Oncol 2006; 8: 354-61.
- [35] Griffith JP, Sue-Ling HM, Martin I, Dixon MF, McMahon MJ, Axon AT, Johnston D. Preservation of the spleen improves survival after radical surgery for gastric cancer. Gut 1995; 36: 684-90.
- [36] Hartgrink HH, Van de Velde CJ, Putter H, Bonenkamp JJ, Kranenbarg EK, Songun I, Welvaart K, van Krieken JH, Meijer S, Plukker JT, van Elk PJ, Obertop H, Gouma DJ, van Lanschot JJ, Taat CW, de Graaf PW, von Meyenfeldt MF, Tilanus H, Sasako M. Extended Lymph Node Dissection for Gastric Cancer: Who May Benefit ? Final Resultsof the Randomized Dutch Gastric Cancer Group Trial. J Clin Oncol 2004; 22: 2069-77.
- [37] McCulloch P, Ward J, Tekkis PP; ASCOT Group of Surgeons; British Oesophago-Gastric Cancer Group. Mortality and morbidity in gastrooesophageal cancer surgery: initial results of ASCOT multicenter prospective cohort study. BMJ 2003; 327: 1192-7.
- [38] Park DJ, Lee HJ, Kim HH, Yang HK, Lee KU, Choe KJ. Predictors of operative morbidity and mortality in gastric cancer surgery. Br J Surg 2005; 92: 1099-102.
- [39] Know SJ, Kim GS. Prognostic significance of lymph node metastasis in advanced carcinoma of the stomach. Br J Surg 1996; 83: 1600-3.
- [40] Marchet A, Mocellin S, Ambrosi A, Morgagni P, Garcea D, Marrelli D, Roviello F, de Manzoni G, Minicozzi A, Natalini G, De Santis F, Baiocchi L, Coniglio A, Nitti D; Italian Research Group for Gastric Cancer (IRGGC). The ratio between metastatic and examined lymphnodes (N ratio) is an independent prognostic factor in gastric cancer regardless of the type of lymphadenectomy: Results from an Italian multicentric study in 1853 patients. Ann Surg 2007; 245: 543-552.

- [41] Siewert JR, Böttcher K, Stein JH, Roder DJ. Relevant prognostic factors in gastric cancer: ten years result of the German Gastric Cancer Study. Ann Surg 1998; 228: 449-461.
- [42] Kim JP. Surgical results in gastric cancer. Semin Surg Oncol 1999; 17: 132-8.
- [43] Ding YB, Chen GY, Xia JG, Zang XW, Yang HY, Yang L, Liu YX. Correlation of tumor- positive ratio and number of perigastric lymph nodes with prognosis of patients with surgically-removed gastric carcinoma. Word J Gastroenterol 2004; 10: 182-5.
- [44] Songun I, Putter H, Kranenbarg EM, Sasako M, van de Velde CJ. Surgical treatment of gastric cancer: 15-year follow-up results of the randomised nationwide Dutch D1D2 trial. Lancet Oncol 2010; 11: 439-49.
- [45] Lee CC, Wu CW, Lo SS, Chen JH, Li AF, Hsieh MC, Shen KH, Lui WY. Survival predictors in patients with node-negative gastric carcinoma. J Gastroenterol Hepatol 2007; 22: 1014-8.
- [46] Kim TH, Han SU, Cho YK. Perigastric lymph node status can be a simple prognostic parameter in patients with gastric cancer. Hepatogastroenterology 2000; 47: 1485-8.
- [47] Talamanti MS, Kim SP, Yao KA, Wayne JD, Feinglass J, Bennett CC, Rao S. Surgical outcomes of patients with gastric carcinoma: the importance of primary tumor location and microvessel invasion. Surgery 2003; 134: 720-7.
- [48] Sánchez-Bueno F, Garcia-Marcilla JA, Perez-Flores D, Pérez-Abad JM, Vicente R,Aranda F, Ramirez P, Parrilla P. Prognostic factors in a series of 297 patients with gastric adenocarcinoma undergoing surgical resection. Br J Surg 1998; 85: 255-60.
- [49] Adachi Y, Shiraishi N, Suematsu T, Shiromizu A, Yamaguchi K, Kitano S. Most important lymph node information in gastric cancer: multivariate prognostic study. Ann Surg Oncol 2000; 7: 503-7.
- [50] Duraker M, Sişman S, Can G. The significance of perineural invasion as a prognostic factor in patients with gastric carcinoma. Surg Today 2003; 33: 95-100.
- [51] Macdonald JS, Smalley SR, Benedetti J, Hundahl SA, Estes NC, Stemmermann GN, Haller DG, Ajani JA, Gunderson LL, Jessup JM, Martenson JA. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. N Engl J Med 2001; 345: 725-730.
- [52] Smalley SR, Benedetti JK, Haller DG, Hundahl SA, Estes NC, Ajani JA, Gunderson LL, Goldman B, Martenson JA, Jessup JM, Stemmermann GN, Blanke CD, Macdonald JS. Updated analysis of SWOG-directed intergroup study 0116: a phase III trial of adjuvant radiochemotherapy versus observation after curative gas-

tric cancer resection. J Clin Oncol 2012; 30: 2327-33.

- [53] Ajani JA, Bentrem DJ, Besh S, D'Amico TA, Das P, Denlinger C, Fakih MG, Fuchs CS, Gerdes H, Glasgow RE, Hayman JA, Hofstetter WL, Ilson DH, Keswani RN, Kleinberg LR, Korn WM, Lockhart AC, Meredith K, Mulcahy MF, Orringer MB, Posey JA, Sasson AR, Scott WJ, Strong VE, Varghese TK Jr, Warren G, Washington MK, Willett C, Wright CD, McMillian NR, Sundar H; National Comprehensive Cancer Network. Gastric cancer, version 2.2013: featured updates to the NCCN Guidelines. J Natl Compr Canc Netw 2013; 11: 531-46.
- [54] Hermans J, Bonenkamp JJ, Boon MC, Bunt AM, Ohyama S, Sasako M, Van de Velde CJ. Adjuvant therapy after curative resection for gastric cancer: meta-analysis of randomized trials. J Clin Oncol 1993; 11: 1441-7.

[55] Shridhar R, Dombi GW, Weber J, Hoffe SE, Meredith K, Konski A. Adjuvant radiation therapy increases overall survival in node-positive gastric cancer patients with aggressive surgical resection and lymph node dissection: a SEER database analysis. Am J Clin Oncol 2012; 35: 216-21.