

Prognostic significance of the recurrence pattern and risk factors for recurrence in patients with proximal gastric cancer who underwent curative gastrectomy

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Abstract Proximal gastric cancer has a high propensity of early recurrence after curative resection due to high incidence of lymph node involvement. In the present study, we aimed to investigate the pattern and time of recurrence and to evaluate the risk factors for recurrence of patients with proximal gastric cancer. Between 2005 and 2013, 99 patients with recurrent proximal gastric cancer who underwent radical gastrectomy were retrospectively analyzed. The prognostic significance of the pattern and the time of recurrence and the relationship between the pattern of recurrence and the other clinicopathological factors were evaluated. The median time to recurrence was 24 months; 45.5 % of patients relapsed within 2 years. Forty-three (43.4 %) patients indicated hematogenous recurrence and 41 (41.4 %) patients revealed peritoneal recurrence with the most predominant patterns. The median progression-free survival (PFS) time for patients with locoregional recurrence was significantly better than that of patients with peritoneal recurrences, hematogenous recurrences, and distant lymph nodes (32.2 vs. 18.9 vs. 18.2 vs. 9.7 months, $p=0.005$, respectively). Moreover, the median overall survival (OS) interval for patients with distant lymph nodes recurrence was significantly worse than that of patients with locoregional, peritoneal, and hematogenous recurrences (13.5 vs. 48.5 vs. 31.4 vs. 29.9 months, $p=0.006$, respectively). The presence of lymph node metastasis ($p=0.004$) and surgery type ($p=0.04$)

for PFS and the time of recurrence ($p=0.033$), lymph node metastasis ($p=0.03$), and surgery type ($p=0.04$) for OS were found to be independent prognostic factors by multivariate analysis. Logistic regression analysis indicated that the presence of lymph node metastasis and surgery type were independent risk factors for predicting the occurrence of early recurrence ($p=0.001$, OR 0.48 and $p=0.028$, OR 0.41, respectively). The median OS time of early recurrence patients was significantly shorter than that of patients with late recurrence (16.6 vs. 55.2 months, $p<0.001$). Furthermore, proximal gastrectomy, poorly differentiated histology, advanced pT stage, and lymph node metastasis were significantly associated with early recurrence. Our results showed that lymph node metastasis and surgery type were independent risk factors for prediction of early recurrence in proximal gastric cancer. Thus, total gastrectomy with regional lymph node dissection may be a suitable treatment option for proximal gastric cancer patients with tumors that have high risk features for recurrence.

Keywords Proximal gastric cancer · Recurrence pattern · Prognosis · Survival

Introduction

Despite a decrease in incidence and major advancements in the treatment of early gastric cancer, it remains the second most frequent cause of cancer death worldwide, and the survival time for advanced gastric cancer is still poor [1, 2]. Surgery is the only curative treatment, but it has a high rate of locoregional recurrence and distant metastases [3, 4]. There is no effective treatment for recurrence [5], and advanced gastric cancer has fatal outcomes and regarded as an incurable disease [6]. Therefore, identification of early recurrence may improve

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patients' survival because effective treatment strategies could be initiated while patients' performance status is still sufficient to receive effective treatments for metastatic gastric cancer [7].

The majority of recurrences after surgery of gastric cancer are diagnosed within 2 years. Therefore, some studies have indicated that 2 years should be defined as a cutoff value for early and late recurrences [8, 9]. In most patients, the patterns of recurrence are locoregional recurrence, peritoneal seeding, and hematogenous metastasis [10, 11]. In recent years, whereas proximal cancers have increased in developed countries, non-proximal tumors have continued to be predominant in Japan and other parts of the world [12–14].

Proximal gastric cancers have worse prognosis compared with those with gastric cancer located in the other parts of the stomach because the diagnosis is carried out in at advanced stage due to high incidence of lymph node metastasis and different anatomical characteristics [13, 14]. There have been few studies exploring the patterns of proximal gastric cancer in the literature [15, 16]. Recently, Li et al. found that there was a significant correlation between deeper invasion and a higher incidence of hematogenous metastases and peritoneal recurrence. They showed that the histological type, pT stage, and lymph node metastasis were independent risk factors for overall recurrence. In addition, negative lymph node counts were found to be another independent risk factor for early recurrence in their study [17]. In the current study, we aimed to investigate the pattern and time of recurrence of patients with proximal gastric cancer. Furthermore, the risk factors for recurrence and prognostic factors of recurrent patients were also analyzed.

Patients and methods

Between 2005 and 2013, a total of 99 patients with recurrent proximal gastric cancer who had undergone curative gastrectomy were included in the study. The primary tumor was staged according to the American Joint Committee on Cancer (AJCC) TNM staging classification for gastric cancer [18]. The clinicopathological findings were determined according to the Japanese Classification of Gastric Carcinoma (JCGC) [19]. D₁ lymph node dissection was defined as only the perigastric nodes directly attached along the lesser curvature, and greater curvatures of the stomach are removed (stations 1–6, N1 level). An incomplete N1 dissection was described as D₀ lymphadenectomy. D₂ dissection (N2 level) was defined as the removal of nodes along the left gastric artery (station 7), common hepatic artery (station 8), celiac trunk (station 9), splenic hilus, and splenic artery (stations 10 and 11). D₃ dissection included the dissection of lymph nodes at stations 12 through 14, along the hepatoduodenal ligament and the root of the mesentery (N3 level).

Proximal gastric cancer was described as adenocarcinoma of the proximal third of the stomach or gastroesophageal (GE)

junction. If the GE junction tumor extended >2 cm onto the stomach, it was accepted to be of gastric origin [20]. Tumors of the other part of stomach and diffusely involving the whole stomach were also excluded from study. Patients who had R₁ or R₂ resections and insufficient disease information were excluded from data analysis. Patient data were retrospectively obtained from patients' charts with respect to age, gender, resection type, tumor location, histopathology, tumor stage, tumor size, histological grade, lymph node involvement, depth of tumor invasion (pT stage), lymphatic and blood vessel invasion, resection margins, type of adjuvant chemotherapy and/or radiation therapy, responses to treatment, and survival after written informed consent had been obtained from patients or their relatives.

The patterns of recurrence were classified as locoregional, peritoneal, hematogenous, or distant lymph node metastases. Locoregional recurrences were defined as tumors within the gastric bed, regional gastric lymph nodes, and remnant stomach at the anastomosis or gastric stump. Peritoneal recurrences were defined as those cases with a positive cytology in the ascitic fluid, carcinomatosis, or ovarian metastasis. Hematogenous recurrences were described as visceral metastases. Distant lymph node metastases were also described as distant lymph nodes outside the regional basin. All recurrences were categorized as early and late. Early recurrence was defined as that recurring within 2 years, whereas late recurrence was defined as that recurring more than 2 years after resection.

Medical histories and physical examinations were performed every 3 months in the first postoperative year, every 6 months in the second postoperative year, and annually thereafter for at least 5 years during follow-up. Complete blood counts and biochemistry panels as well as tumor markers were examined every 3 months in the first and second years, and annually thereafter. Chest X-rays and abdominal CT scans were performed every 3 months in the first year, every 6 months in the second postoperative year and annually thereafter for 5 years. Gastroscopy was performed annually to control suspicious cancer in the gastric remnant.

A total of 87 patients (87.8 %) with lymph node metastasis or pT₃₋₄ received adjuvant chemoradiotherapy (CRT) within 4 weeks after surgery. Adjuvant CRT consisted of 5-fluorouracil 425 mg/m² per day, plus leucovorin 20 mg/m² per day for 5 days, followed by 4500 cGy of radiation at 180 cGy per day given 5 days per week for 5 weeks, with modified doses of fluorouracil and leucovorin on the first four and the last 3 days of radiotherapy. Adjuvant CRT was not given to the 12 of 99 patients without lymph node metastasis (12.2 %).

Statistical analysis All data were analyzed with SPSS 17.0 (SPSS Inc., Chicago, IL, USA) software. The clinicopathological factors of the patients among recurrence groups were compared by means of the chi-squared test and Fisher's exact test. The survival analyses and curves were established with

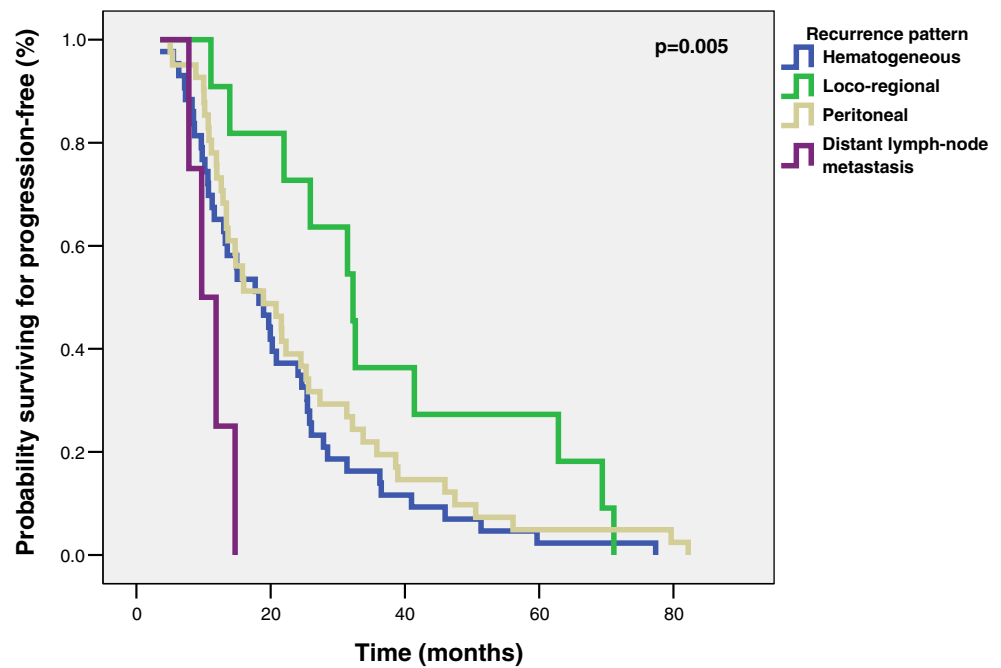
the Kaplan-Meier method and compared with the log-rank test. Progression-free survival (PFS) was defined as the time from curative surgery to recurrence or to the date of death or loss of follow-up. OS was described as the time from diagnosis to the date of the patient's death or loss of follow-up. Univariate and multivariate analyses were performed with the Cox proportional hazards model to evaluate the

importance of the recurrence type and other clinicopathological features as prognostic factors. To identify predictive factors related to recurrence, logistic regression analysis was used. Multivariate *p* values were used to characterize the independence of these factors. The 95 % confidence interval (CI) was used to quantify the relationship between survival time and each independent factor. All *p* values were two-sided

Table 1 Clinicopathological factors with respect to the recurrence patterns in patients with proximal gastric cancer who had curative gastrectomy

Factors	Locoregional recurrence <i>n</i> (%)	Peritoneal recurrence <i>n</i> (%)	Hematogenous recurrence <i>n</i> (%)	Distant lymph nodes <i>n</i> (%)	<i>p</i> values
All patients	11 (11.2)	41 (41.4)	43(43.4)	4 (4.0)	
Gender					0.49
Female	5 (45.5)	14 (34.1)	21 (48.8)	1 (25)	
Male	6 (54.5)	27 (65.9)	22 (51.2)	3 (75)	
Age (years)					0.038
≤60	10 (90.9)	27 (65.9)	22 (51.2)	1 (25)	
>60	1 (9.1)	14 (39.1)	21 (48.8)	3 (75)	
Surgery type					<0.001
Proximal	9 (81.8)	27 (65.9)	24 (83.7)	3 (75)	
Total	2 (18.2)	14 (39.1)	19 (16.3)	1 (25)	
Tumor size					0.20
≤5 cm	7 (53.8)	20 (51.2)	19 (44.2)	2 (50)	
>5 cm	6 (46.2)	21 (48.8)	24 (55.8)	2 (50)	
Tumor differentiation					0.15
Well differentiated	5 (45.5)	6 (14)	8 (17.3)	–	
Moderately differentiated	4 (36.4)	22 (53.5)	22 (51.9)	1 (25)	
Poorly differentiated	2 (18.2)	13 (32.5)	13 (30.8)	3 (75)	
pT stage					0.033
T1	1 (9.1)	4 (9.9)	4 (9.5)	–	
T2	1 (9.1)	9 (21.9)	10 (23.2)	2 (50)	
T3	6 (54.5)	19 (46.3)	23 (53.4)	1 (25)	
T4	3 (27.3)	9 (21.9)	6 (13.9)	1 (25)	
Lymph node metastasis					0.026
Absence	7 (63.6)	21 (51.2)	17 (39.5)	–	
Presence	4 (36.4)	20 (48.8)	26 (60.5)	4 (100)	
TNM stage					0.15
I	4 (36.4)	12 (23.3)	15 (25)	–	
II	4 (36.4)	15 (46.5)	10 (42.3)	4 (100)	
III	3 (27.2)	14 (30.2)	18 (32.7)	–	
Lymphatic vessel invasion					0.80
Absence	2 (18.2)	12 (29.3)	7 (16.3)	1 (25)	
Presence	9 (81.8)	29 (70.7)	36 (83.7)	3 (75)	
Blood vessel invasion					0.87
Absence	4 (20)	11 (30.3)	10 (32.7)	1 (25)	
Presence	7 (80)	30 (69.7)	33 (67.3)	3 (75)	
Adjuvant chemotherapy					0.54
Absence	1 (9.1)	3 (7.4)	7 (14.3)	1 (25)	
Presence	10 (90.9)	38 (92.6)	36 (83.7)	3 (75)	

Fig. 1 Progression-free survival curves according to the patterns of recurrences



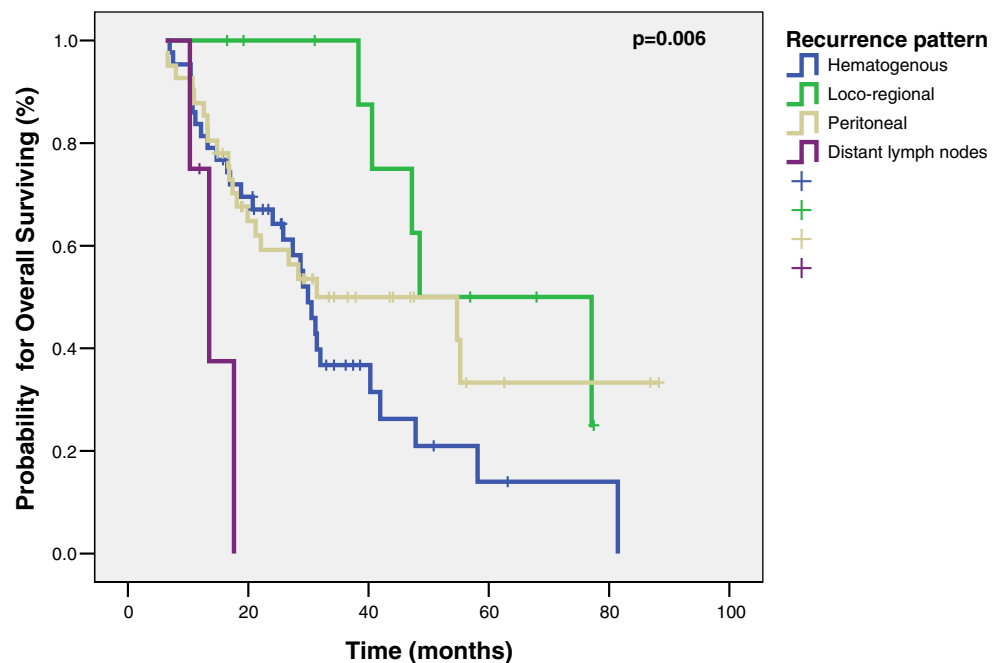
in tests and p values less than 0.05 were considered statistically significant.

Results

Forty-one patients (41.4 %) were female and 58 (58.6 %) were male, with a median age of 58 years (range 23 to 83 years). Thirty-one patients (31.4 %) were classified as stage I, 33

(33.3 %) as stage II, and 35 (35.3 %) as stage III. In 49 patients (49.4 %), the histology of the tumor was moderately differentiated; in 31 patients, tumors were poorly differentiated; and in the remaining 19 patients, tumors were well differentiated. The majority of patients had pT3 tumor ($n=49$, 49.4 %). The mean tumor size was 6.5 ± 2.9 cm (range 1–12 cm). Fifty-one (51 %) patients underwent D₁ lymph node dissection, while D₂ lymphadenectomy was performed in 41 patients (41 %). D₃ lymph node dissection was also carried out

Fig. 2 Overall survival curves with respect to recurrence patterns in patients with proximal gastric cancer



in only 8 patients (8 %). Moreover, the median number of dissected and metastatic lymph nodes were 19 (range 15–44) and 5 (range 0–23), respectively. Based on the presence of lymph node metastasis, 54 (54.5 %) patients were classified as node positive, and the remaining 45 patients (45.5 %) were node negative.

The median time to recurrence was 24 months (range 5–101 months) and 45.5 % of patients had relapsed within 2 years. According to the recurrence pattern, 43 (43.4 %) patients had hematogenous recurrence, and 41 (41.4 %) patients revealed peritoneal recurrence, which were the most predominant patterns. The liver was the most commonly involved organ within the hematogenous pattern. In peritoneal recurrence patients, the majority of patients (92.6 %) had recurrence at multiple peritoneal sites and three in the pelvic cavity and ovary. The remaining recurrence patterns were locoregional recurrence (11 patients, 11.2 %) and distant lymph nodes (4 patients, 4 %). Peritoneal and locoregional recurrences were significantly associated with younger age ($p=0.038$), and proximal resection was related to higher incidence of all recurrence patterns ($p<0.001$). Moreover, advanced pT stage (T3–T4) was significantly correlated with hematogenous, peritoneal, and locoregional recurrence patterns ($p=0.033$). Hematogenous recurrence and distant lymph node metastasis had more lymph node positivity ($p=0.026$). The relationship between clinicopathological factors and recurrence patterns is summarized in Table 1.

At the median follow-up of 27.5 months (range 6.5–88 months), the median PFS time for patients with

locoregional recurrence was significantly better than that of patients with peritoneal recurrences, hematogenous recurrences, and distant lymph nodes (32.2 vs. 18.9 vs. 18.2 vs. 9.7 months, $p=0.005$, respectively, Fig. 1). Moreover, the median OS interval for patients with distant lymph node recurrence was significantly worse than that of patients with locoregional, peritoneal, and hematogenous recurrences (13.5 vs. 48.5 vs. 31.4 vs. 29.9 months, $p=0.006$, respectively, Fig. 2).

The median OS time of early recurrence patients was significantly shorter than that of patients with late recurrence (16.6 vs. 55.2 months, $p<0.001$, Fig. 3). There were significant differences between the early and late recurrence groups with respect to age, surgery type, tumor differentiation, pT stage, presence of lymph node metastasis, TNM stage and blood vessel invasion. Patients with early recurrences had older age ($p=0.04$), poorly differentiated tumors ($p=0.04$), increased lymph node involvement ($p<0.011$), advanced pT stage ($p=0.025$), advanced-staged disease ($p<0.001$), and blood vessel invasion ($p=0.035$) compared with patients with late recurrences. Whereas proximal gastrectomy was commonly performed in the majority of patients with early recurrence, total gastrectomy was commonly done in patients with late recurrence ($p<0.001$). The relationship between the subgroups based on recurrences and clinicopathological factors is listed in Table 2. In both groups, the rate of patients who received adjuvant treatment was similar (93.2 % for early vs. 85.2 % for late, $p=0.33$). In addition, there was a significant difference between the early and late recurrence groups with

Fig. 3 The median overall survival time of early recurrence patients was significantly shorter than that of patients with late recurrence (16.6 vs. 55.2 months, $p<0.001$) for patients with proximal gastric cancer

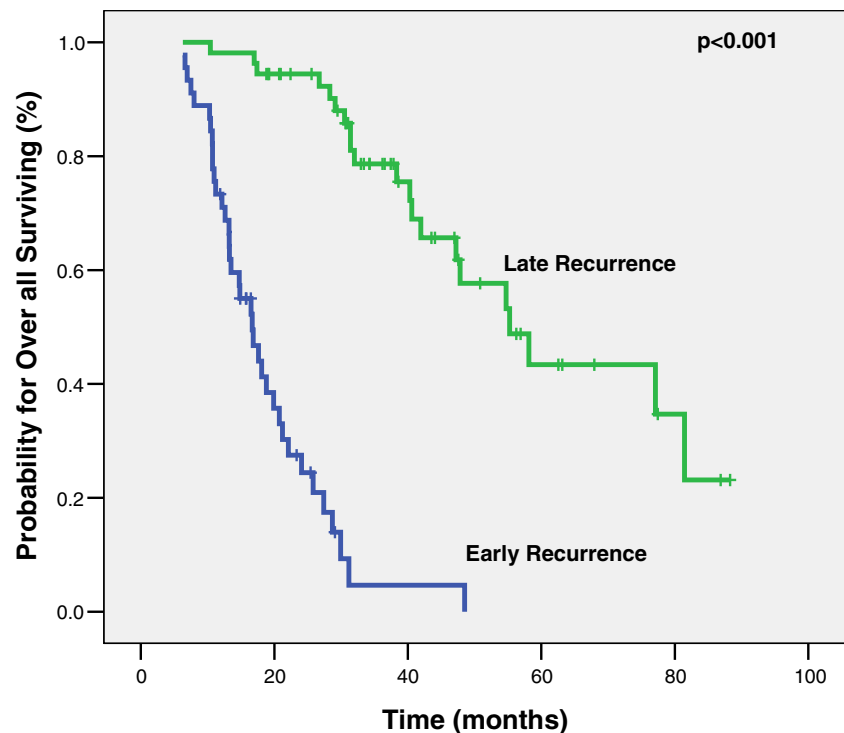


Table 2 Clinicopathological factors according to the recurrence times in patients with proximal gastric cancer who had curative gastrectomy

Factors	Early recurrence <i>n</i> (%)	Late recurrence <i>n</i> (%)	<i>p</i> values
All patients	45 (45.5)	54 (54.5)	
Gender			0.84
Female	18 (40)	23 (42.6)	
Male	27 (60)	31 (57.4)	
Age (years)			0.04
≤60	22 (48.9)	38 (70.4)	
>60	23 (51.1)	16 (29.6)	
Surgery type			<0.001
Proximal	28 (62.2)	17 (31.5)	
Total	17 (37.8)	37 (68.5)	
Tumor size			0.99
≤5 cm	21 (53.8)	28 (51.2)	
>5 cm	24 (46.2)	26 (48.8)	
Tumor differentiation			0.04
Well differentiated	4 (8.8)	15 (27.8)	
Moderately differentiated	25 (55.6)	24 (44.4)	
Poorly differentiated	16 (35.6)	15 (27.8)	
pT stage			0.025
T1	1 (2.2)	8 (14.8)	
T2	7 (15.6)	15 (27.8)	
T3	24 (53.3)	25 (46.3)	
T4	13 (28.9)	6 (11.1)	
Lymph node metastasis			<0.001
N0	6 (13.3)	39 (72.2)	
N1	14 (31.1)	10 (18.5)	
N2	15 (33.3)	5 (9.3)	
N3	10 (22.2)	–	
TNM stage			<0.001
I	4 (9.0)	27 (50.0)	
II	13 (28.8)	20 (37.0)	
III	28 (62.2)	7 (13.0)	
Lymphatic vessel invasion			0.05
Absence	7 (15.6)	15 (32.6)	
Presence	38 (84.4)	29 (67.4)	
Blood vessel invasion			0.035
Absence	8 (17.8)	18 (33.3)	
Presence	37 (82.2)	36 (66.7)	
Adjuvant chemotherapy			0.33
Absence	4 (6.8)	8 (14.8)	
Presence	41 (93.2)	46 (85.2)	

respect to the pattern of recurrence ($p=0.017$, Table 2). Patients with distant lymph node metastasis had early relapse, whereas locoregional recurrence tended to be late.

In the univariate analysis of factors associated with PFS, there were significant differences with respect to tumor

differentiation ($p=0.04$), surgery type ($p=0.010$), lymph node metastasis ($p<0.001$), TNM stage ($p=0.0013$), and pattern of recurrence ($p=0.005$). The univariate analysis for all recurrent gastric cancer patients showed that surgery type, presence of lymph node metastasis, TNM stage, pattern of recurrence ($p=0.006$), and time of recurrence (<24 vs. >24 months, $p<0.001$) were significant prognostic factors for OS (Table 3).

A multivariate analysis showed that only the presence of lymph node metastasis ($p=0.004$) and surgery type ($p=0.04$) were independent prognostic indicators for PFS. For OS, time of recurrence ($p=0.033$), presence of lymph node metastasis ($p=0.03$), and surgery type ($p=0.04$) were independent prognostic factors (Table 3). In the logistic regression analysis, the presence of lymph node metastasis and surgery type were independent risk factors for predicting the occurrence of both overall and early recurrence ($p=0.001$, OR 0.48 and $p=0.028$, OR 0.41, respectively, Table 4).

Discussion

Proximal gastric cancer is known to have unique clinicopathological features and is generally associated with higher incidence of recurrence compared with cancers of the other parts of stomach [21, 22]. Therefore, the determination of risk factors for recurrence and the pattern of recurrence may improve patient outcomes because effective treatment strategies may be initiated postoperatively, and eligible follow-up strategies may be produced to diagnose early recurrence. However, there are few papers which address prognostic factors for recurrence and the pattern of recurrence for proximal gastric cancer in the literature [15, 16].

Recurrences are usually detected within 24 months of surgery in gastric cancer [8–10]. Likewise, Li et al. reported that 85.9 % of patients with proximal gastric cancer were recurred in 2 years [17]. In our study, early recurrence was detected in 45.5 % patients with proximal gastric cancer. This may be due to high number of patients with lymph node negativity ($n=45$). Patients with early recurrences had older age, poorly differentiated tumor, increased lymph node involvement, advanced pT stage, advanced stage disease, and blood vessel invasion compared with patients with late recurrences. In addition, proximal gastrectomy was significantly related to early recurrence. The median OS time of early recurrent patients was significantly shorter than that of patients with late recurrence, and the prognostic importance of time of recurrence was proved by both univariate and multivariate analysis for OS. Our results were thus different from those of Li et al. [17].

Kim et al. reported that hematogenous and locoregional recurrence were the most recurrent types for proximal gastrectomy, whereas hematogenous spread was the dominant pattern after total gastrectomy. In addition, they showed that patients with proximal gastrectomy had a much higher recurrence rate

Table 3 Univariate and multivariate analysis of patients with proximal gastric cancer for overall survival (OS) according to clinicopathological factors

Factors	Median OS time (months)	Univariate <i>p</i> values	Multivariate <i>p</i> values	HR (95 % CI)
Gender		0.70		
Male	31.4			
Female	40.3			
Age (year)		0.086		
≤60	41.9			
>60	27.4			
Surgery type		0.001	0.04	0.68 (0.29–1.10)
Proximal	19.9			
Total	34.5			
Tumor size		0.97		
≤5 cm	30.9			
>5 cm	27.6			
Tumor differentiation		0.46		
Well differentiated	40.5			
Moderately differentiated	32.0			
Poorly differentiated	24.0			
pT stage		0.85		
T1	NR			
T2	32.0			
T3	31.1			
T4	27.4			
Lymph node metastasis		<0.001	0.03	2.53 (0.98–5.49)
Absence	48.5			
Presence	19.9			
TNM stage		0.004	0.32	0.77 (0.45–1.29)
I	40.5			
II	31.1			
III	18.8			
Lymphatic vessel invasion		0.28		
Absence	41.9			
Presence	31.4			
Blood vessel invasion		0.15		
Absence	55.2			
Presence	31.1			
Adjuvant treatment		0.91		
Absence	31.4			
Presence	38.4			
Recurrence pattern		0.006	0.22	1.28 (0.85–1.92)
Locoregional	48.5			
Peritoneal	31.4			
Hematogenous	29.9			
Distant lymph node metastasis	13.5			
The time of recurrence		<0.001	0.033	0.49 (0.31–0.96)
Early	16.6			
Late	55.2			

HR hazards ratio, CI confidence interval, NR not reached

than patients with total gastrectomy. The authors concluded that this might be related to inadequate extensive lymph node

dissection for proximal gastrectomy [23]. Therefore, Li et al. in their study including 135 recurrent proximal gastric cancer

Table 4 Logistic regression analysis of the predictive factors for recurrence in patients with proximal gastric carcinoma

Factors	<i>p</i>	OR	95 % CI
Surgery type	0.028	0.41	0.19–0.90
Lymph node metastasis	0.001	0.48	0.27–1.15
TNM stage	0.34	0.51	0.13–2.02

OR odds ratio, CI confidence interval

patients recommended that proximal gastrectomy should not be performed to be rational surgical approach in patients with advanced pT stage [17]. In our study, hematogenous recurrence and peritoneal recurrence were the predominant patterns of recurrence. We detected a significant relationship with respect to surgery type. Proximal gastrectomy was significantly associated with locoregional and peritoneal recurrence patterns, which was compatible with previous reports [17, 21, 24, 25] but was not consistent with the study of Kim et al. [23].

In a study performed by Li et al., the authors demonstrated that tumor differentiation, pT stage, lymph node metastasis, and count of negative lymph nodes were risk factors for overall and early recurrence for patients with proximal gastric cancer. In the multivariate analysis, tumor differentiation, pT stage, and negative lymph node count were remained to be independent predictive factors for recurrence in their study [17]. In the present study, the univariate analysis determined that tumor differentiation, surgery type, lymph node metastasis, TNM stage, and the pattern and time of recurrence for OS were significant prognostic factors. Subsequently, a multivariate analysis showed that only the presence of lymph node metastasis and surgery type were independent prognostic indicators for PFS. For OS, the time of recurrence, the presence of lymph node metastasis, and surgery type were independent prognostic factors. In the logistic regression analysis, the presence of lymph node metastasis and surgery type were independent risk factors for predicting the occurrence of both overall and early recurrences. Thus, our results were comparable with previous reports [17, 23] with regard to lymph node metastasis and tumor differentiation. However, our results were different from their study with regard to the pattern of recurrence, surgery type, and the time of recurrence and TNM stage.

In contrast to the above reports [17, 21, 23–25], we analyzed survival according to the pattern of recurrence. The median PFS time for patients with locoregional recurrence was significantly better than that of patients with the other recurrence patterns. Moreover, the median OS interval for patients with distant lymph node recurrence was significantly worse than that of patients with locoregional, peritoneal, and hematogenous recurrences in the current study. This may be related to the significant relationship between the pattern of recurrence and age, surgery type, and pT stage. Li et al. also

reported that the pT stage, negative lymph node count, and surgery type were associated with the recurrence pattern. Furthermore, pT stage was also related with higher incidence of hematogenous metastases and peritoneal recurrence [17]. Our results were thus compatible with their study.

Proximal gastrectomy, poorly differentiated histology, advanced pT stage (T3/T4), and the presence of lymph node metastasis were found to provide additional information in postoperative surveillance for early recurrence after curative surgery for patients with proximal gastric cancer according to our results. Consequently, these factors may be related to a more aggressive nature of tumor biology. Therefore, it may be recommended that patients with these factors should closely be followed up for recurrence after postoperative adjuvant treatment.

The short follow-up intervals and a relatively small sample size were important limitations of our study, which might have influenced the results. The other limitation was the retrospective nature of this study. Although our results should be confirmed by prospective studies with larger sample sizes which will analyze different follow-up protocols for proximal gastric cancer, we believe that these results contribute to the knowledge of proximal gastric cancer because distinct prognostic factors were detected for both early and late recurrence groups and analyzed survivals according to the recurrence pattern differently from previous studies.

In conclusion, our study demonstrated that the presence of lymph node metastasis and surgery type were independent risk factors for predicting the occurrence of early recurrence in patients with proximal gastric cancer. Moreover, proximal gastrectomy, poorly differentiated histology, advanced pT stage and lymph node metastasis were found to be related to early recurrence. Therefore, total gastrectomy with extensive lymph node dissection was thought to be a more suitable treatment approach for proximal gastric cancer patients who had tumors characterized by advanced pT stage, poorly differentiated histology, and lymph node metastasis. These factors may provide additional information to explore the biological aggressiveness of proximal gastric cancer as a beneficial prognostic marker, which is important in predicting recurrence during follow-up and may guide to develop more appropriate and aggressive adjuvant therapies.

Conflict of interest None

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