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Prognostic Factors in Advanced Gastric Cancer Patients With Suprapancreatic Lymph Node Metastasis

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Abstract

Background: There are few comprehensive studies on the prognosis of patients with suprapancreatic lymph node (LN) metastasis. In the present study, we evaluated prognostic factors in gastric cancer patients with suprapancreatic LN metastasis.

Methods: Between June 1982 and February 2004, 62 patients with suprapancreatic LN metastasis underwent radical gastrectomy and LN dissection at Oita University. Clinicopathologic factors of advanced gastric cancer with metastatic suprapancreatic LN were examined by univariate and multivariate analysis to identify prognostic factors.

Results: Five-year survival was associated with growth type (localized vs. infiltrative; P<0.01), depth of invasion (Muscularis propria or subserosa vs. exposed beyond the serosa or invasion to adjuvant organ; P<0.01), number of metastatic LNs (<7 vs. ≥ 7; P<0.01), and number of metastatic suprapancreatic LNs (1 vs. ≥ 2; P<0.01). By univariate analysis, localized growth type, an absence of serosal invasion, a metastatic LN count <7, and only 1 metastatic suprapancreatic LN were identified as good prognostic factors. By multivariate analysis, only 1 metastatic suprapancreatic LN was identified as independent prognostic factors. With analysis using the Kaplan-Meier method, there was a significant difference between these two factors.

Conclusions: Only one metastatic suprapancreatic LN was prognostic factors in advanced gastric cancer with suprapancreatic LN metastasis.

Keywords: Gastric cancer, Suprapancreatic LN metastasis, Prognosis

Introduction

Lymph node (LN) metastasis is one of the most important prognostic factors for patients after gastrectomy [1,2]. In Asian countries, gastrectomy with extended (D2) lymphadenectomy is performed as a standard procedure for advanced gastric cancer, whereas gastrectomy with perigastric (D1) lymphadenectomy is used in western countries. Whether gastrectomy with D2 lymphadenectomy improves the survival of patients with advanced gastric cancer remains controversial. The prognosis of gastric cancer patients with extended metastatic LNs is thought to be worse than that of patients without metastasis. The extended LNs of gastric cancer mainly consist of LNs along the common hepatic and splenic arteries [3].

Generally, the survival benefits of LN dissection and the incidence of complications are important for choosing the type of operation. Previously, we reported that patients with advanced gastric cancer with metastatic suprapancreatic LNs have poor prognoses [4]. The purpose of dissecting suprapancreatic LNs is to ensure complete clearance of local cancer cells to improve patient prognosis. However, LN dissection of the suprapancreas has not provided the expected survival benefit, and use of this operation has increased the incidence of complications [5]. Although many authors have identified the extent of LN metastasis as a key prognostic factor, there have been few comprehensive studies on the prognosis of patients with suprapancreatic LN metastasis.

Previously, we reported that patients with advanced gastric cancer with metastatic suprapancreatic LNs had poor prognoses, with a 5-year survival rate of 12.8% after gastrectomy [4]. A limited number of patients with suprapancreatic LN metastasis can expect long-term survival after D2 lymphadenectomy.

In the present study, we investigated prognostic factors in gastric cancer patients with suprapancreatic LN metastasis.

Patients and Methods

Our study population consisted of 455 patients with advanced gastric cancer who underwent radical gastrectomy and LN dissection at the First Department of Surgery, Oita University, Faculty of Medicine, between June 1982 and February 2004. There were 89 patients with suprapancreatic LN metastasis. We excluded cases with residual tumor, patients for which 5-year observation was impossible, and patients that died of other diseases, leaving a final group of 62 patients.

The age and sex of patients; the location, size, and histologic type of tumors; and the depth of wall invasion were obtained from operation and pathology records. The number of dissected LNs and the metastatic LNs was evaluated from pathological records. The pathologist evaluated lymph node metastasis at the maximum section of lymph node histologically. In this study, the patients with dissected LNs more than 15 are examined. These clinicopathologic findings were analyzed according to the Japanese classification for gastric cancer outlined by the Japanese Gastric Cancer Association, and we categorized lymph nodes No. 8, 9 and 11 as suprapancreatic LNs. The number of metastatic suprapancreatic LNs was examined.

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Patients were examined at post-operative follow-up visits every 3 months for the first 2 years, and every 6 months thereafter. Follow-up continued until death or for more than 5-years for surviving patients. Data were obtained from death certificates, and only patients who died of recurrent gastric cancer were included in the analysis of tumor-related death. We compared survival rates between patients with 5-year survival and those that died before 5 years using clinicopathologic factors. Patients with metastatic suprapancreatic LNs were divided into two groups: those with 1 metastatic suprapancreatic LN and those with ≥ 2. The 5-year survival rates of the two groups were compared. Moreover, factors identified univariate relationships with 5-year survival were analyzed using multivariate analysis.

Cumulative survival rates were calculated by the Kaplan-Meier method, and survival curves were tested by the Log rank test. Statistically significant differences were analyzed by performing a χ^2 test, and independent prognostic factors were examined by Cox proportional hazards regression. Multivariate analysis was used for adjusting the hazard ratio and corresponding 95% confidence intervals. P<0.05 was considered statistically significant for all analyses.

All statistical analyses were performed using SPSS 11.0 statistics software package. This study was conducted according to the Ethical Guidelines for Clinical Studies of Oita University Faculty of Medicine.

Results

Among the 62 patients with metastatic suprapancreatic LNs, there were 14 patients that survived for 5 years or longer and 48 non-surviving patients. There was no significant difference in sex, age, operating procedure, or adjuvant chemotherapy between the two groups (Table 1).

The clinicopathologic features of the two groups are shown in Table 2. Five-year survival was associated with tumor growth type (localized vs. infiltrative; P<0.01), depth of invasion (Muscularis propria or subserosa vs. exposed beyond the serosa or invasion to adjuvant organ; P<0.01), number of metastatic LNs (<7 vs. ≥ 7; P<0.01), and number of metastatic suprapancreatic LNs (1 vs. ≥ 2; P<0.01). There was no significant difference in location, tumor size, histology, lymphatic invasion, and vascular invasion.

We divided the patients into those with one metastatic suprapancreatic LN and those with two or more metastatic suprapancreatic LNs. Figure 1 shows the survival curves with regard to the number of metastatic suprapancreatic LNs. The 5-year survival rate was significantly higher when the number of metastatic suprapancreatic LNs was only one.

Using multivariate analysis, we analyzed factors identified univariate relationships with survival such as growth type, depth of invasion, number of metastatic LNs, and number of metastatic suprapancreatic LNs.

	5year-survival		P value
	alive (n=14)	dead (n=48)	
age	61.4 ± 3.0	63.7 ± 1.5	0.481
Sex (male/female)	8/6	39/9	0.063
Operation procedure			0.102
DG	9 (64.3%)	19 (59.6%)	
TG	5 (35.7%)	29 (60.4%)	
chemotherapy			0.885
done	13 (92.9%)	44 (91.7%)	
none	1 (7.1%)	4 (8.3%)	

Table 1: Background of 5 year survival patients and not survival patients in advanced gastric cancer with metastatic suprapancreatic lymph nodes.
DG distal gastrectomy, TG total gastrectomy.

		5 year-survival		P value
		alive (n=14)	dead (n=48)	
Location	Lower two-thirds	10 (71.4%)	34 (70.8%)	0.965
	Upper one-third	4 (28.6%)	14 (29.2%)	
Tumor size	<10	13 (92.9%)	35 (72.9%)	0.116
	≥ 10	1 (7.1%)	13 (23.1%)	
Growth type	localized	8 (57.1%)	10 (20.8%)	<0.01
	infiltrative	6 (42.9%)	38 (79.2%)	
Depth of invasion	MP, SS	10 (71.4%)	13 (27.1%)	<0.01
	SE, SI	4 (28.6%)	35 (72.9%)	
Histology	well	7 (50%)	13 (27.1%)	0.11
	por	7 (50%)	35 (72.9%)	
Lymphatic invasion	present	14 (100%)	45 (93.8%)	0.337
	absent	0 (0%)	3 (6.2%)	
Vascular invasion	present	6 (35.7%)	28 (58.3%)	0.243
	absent	8 (57.1%)	19 (42.7%)	
Number of metastatic lymphnode	<7	9 (64.3%)	12 (25.0%)	<0.01
	≥ 7	5 (35.7%)	36 (75.0%)	
Number of metastatic suprapancreatic lymph node	1	12 (85.7%)	18 (37.5%)	<0.01
	≥ 2	2 (14.3%)	30 (62.5%)	

Table 2: Clinicopathologic feature of 5year survival patients and not survival patients in advanced gastric cancer with metastatic suprapancreatic lymph nodes. MP muscularis propria, SS subserosa, SE exposed beyond the serosa, SI invasion to adjuvant organ.

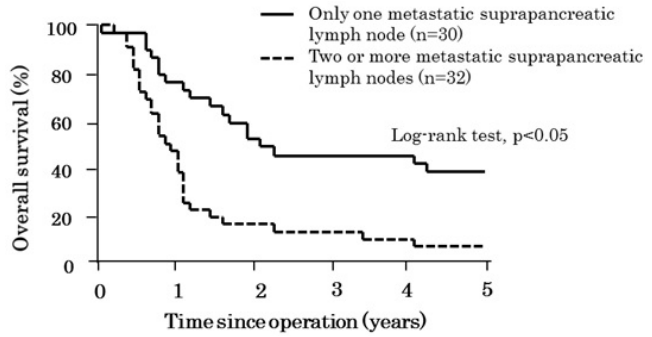

Figure 1: Kaplan-Meier survival analysis of advanced gastric cancer patients with only one metastatic lymph node and with two or more metastatic suprapancreatic lymph nodes (log-rank test).
The 5-year overall survival rate for patients with only one metastatic lymph node (LN) was 38.0% (n=30), and that for patients with two or more metastatic suprapancreatic LNs was 6.3% (n=32). The survival rate after gastrectomy for advanced gastric cancer was significantly higher in patients with only one metastatic suprapancreatic LN compared with those with two or more (P<0.05).

Table 3 shows the independent prognostic factors. The analysis revealed that the factor associated with 5-year survival of patients with suprapancreatic LN metastasis was only one metastatic suprapancreatic LN.

Discussion

The results of the present study indicated that the number of metastatic suprapancreatic LNs independently influenced the prognosis of patients with gastric cancer with suprapancreatic LN metastasis. Therefore, patients with the potential for long-term survival are those that present with only one metastatic suprapancreatic LN are treated by curative radical gastrectomy.

	Hazard ratio (95% CI)	P value
Only one metastatic suprapancreatic lymph node	3.12 (1.72-5.87)	<0.01

Table 3: Results of multivariate analyses of the well prognostic factors for 5-year survival. CI, confidence interval.

Seven or more metastatic LNs were reported to be an independent prognostic indicator for node-positive gastric cancer [6]. We reported that patients with advanced gastric cancer with metastatic suprapancreatic LNs had a large number of total metastatic LNs and poor prognoses [4]. The present study showed that patients with only one metastatic suprapancreatic LN can expect long-term survival, regardless of the number of perigastric metastatic LNs. The survival benefit effect of D2 dissection may be observed in only these cases. For cases with suprapancreatic LN metastasis, post-operative adjuvant chemotherapy may be more effective for prolonging survival after gastrectomy because these cases look systematic disease.

The lymph fluid from the stomach flows to the LN along the celiac artery and aorta via the following three routes [7]:

(1) the route along the left gastric artery (No. 7 LN) from the No. 3 LN

(2) the route along the common hepatic artery directly from the pyloric part of the stomach; and

(3) the route along the splenic artery from the No. 4d LN.

Adachi et al. showed that the prognosis of patients with 2 or more metastatic LNs around the celiac artery was extremely poor [8]. Sasako et al. showed that para-aortic nodal dissection does not improve the survival rate in gastric cancer patients [9]. These data suggested that LNs along the celiac artery are key nodes in identifying whether the cancer is localized or systemic.

Whether gastrectomy with D2 lymphadenectomy improves the survival of patients with advanced gastric cancer compared with gastrectomy with D1 lymphadenectomy is controversial. The Dutch trial and British Medical Research Council trial failed to show a survival benefit of gastrectomy with D2 lymphadenectomy but instead showed that this procedure increased the rate of complications, such as pancreatic juice leakage [5,10-15]. In contrast, as a long-term result (15 years) of the randomized nationwide Dutch D1/D2 trial, it was shown that disease-free survival rates in patients undergoing D2 lymphadenectomy improved [16]. In addition, a randomized trial in Taiwan demonstrated an improved survival of 6% after D2/3 lymphadenectomy compared with that after D1 lymphadenectomy [17]. This study suggested that D2 lymphadenectomy is effective for patients with only one metastatic suprapancreatic LN. In our previous study on advanced gastric cancer, we found that 12.8% of advanced gastric cancer patients had suprapancreatic metastatic LNs [4]. Furthermore, among this group, 22.6% of patients with metastatic suprapancreatic LNs had only one metastatic LN. These data suggested that patients with advanced gastric cancer acquired a survival benefit with D2 LN dissection.

In this retrospective study, there were three main limitations. First, only 62 patients in total were included in the analysis. This low number of patients was because the number of advanced gastric cancer patients was only 12.8%. To our interesting, the prognosis of female patients seems to be better than male (p=0.06). There are possibilities that male patients have more advanced gastric cancer and/or that the frequency of metastatic suprapancreatic LN is high in male patients. To clarify the effect of the gender on the prognosis in patients with metastatic suprapancreatic lymph node, multicenter study including large number of patients is required. Second, in this retrospective study, we could not analyze the effect of chemotherapy and recurrence patterns after gastrectomy because of insufficient data from clinical records. Finally, in the present study, the quantity of metastatic cancer cells in each LN was not evaluated, and micro-metastasis and extra-nodal metastasis were not examined. Thus there was limitation of this study; we identified only one metastatic suprapancreatic LN as a good prognostic factor in advanced gastric cancer patients with suprapancreatic LN metastasis. To confirm this result, prospective multicenter study including large number of patients to observe the patient with suprapancreatic LN metastasis after surgery is necessary.

In conclusion, only one metastatic suprapancreatic LN was identified as good prognostic factors in advanced gastric cancer patients with metastatic suprapancreatic LNs. These patients can expect long-term survival by undergoing D2 lymphadenectomy. In the future, we may be able to use D2 lymphadenectomy more effectively by developing a system for the pre-operative identification and diagnosis of LN metastasis.

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