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Clinicopathological analysis of patients with gastric cancer in 1200 cases

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INTRODUCTION

Gastric cancer is one of the most common fatal malignancies in the world. The prognosis is generally poor in advanced gastric cancer. The low survival is related to delayed diagnosis, metastasis and recurrence after operation. The aim of this paper was to find correlation between clinical factors and biologic behavior of gastric cancer in a series of 1200 patients undergoing surgical resection.

PATIENTS AND METHODS

Between November 1992 and December 1999, 1200 patients with stomach cancer confirmed by pathology underwent radical operations. The mean patient age at operation was 54.2 (range 22-89) years, 836 patients were male and 364 were female, with a mean postoperative hospitalization of 16.2 (range 6-127) days.

We analyzed the following clinicopathologic and surgical factors: age, sex, hemoglobin, operation manners, operation time, amount of transfusion during operation, postoperative hospital stay, postoperative complications, positive proximal margin, location of tumor, tumor size, differentiation, depth of tumor invasion, lymph nodes and lymphatic metastasis rate. Frequency of positive lymph nodes = numbers of metastatic lymph nodes / all lymph nodes excised × 100%.

Statistics

All data were analyzed by SPSS statistics program. The comparisons were made by Chi-square test, one-way ANOVA, linear and multivariate regression analysis, $P<0.05$ was considered as significant.

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RESULTS

Of these 1200 patients, 768 (64%) underwent distal gastrectomy, 72 (6%) proximal gastrectomy via abdomen and 264 (22%) via thorax, and 96 (8%) underwent total gastrectomy. Distal and total gastrectomy had more numbers of clearances of lymph nodes than the other operational approaches. The postoperative complications occurred in 96 patients (96/1200, 8%), including gastric retention in 22 (22/96, 23%), anastomotic leakage in 18 (18/96, 18.7%), infection of incision in 16 (16/96, 14.6%), disruption of wound in 8 (8/96, 8.3%), and thoracic cavity effusion in 8(8/96, 8.3%). The complication was most common in proximal gastrectomy via abdomen (16/96, 17% patients) (Table 1). The overall mortality was 0.4% (5/1200).

The diameter of the neoplasm was positively correlated with the depth of infiltration and lymphatic metastasis rate while hemoglobin was the opposite. One hundred and seventy-nine (14.9%) of 1200 were early gastric carcinoma (EGC) with metastasis of lymph nodes in 21 patients (21/179, 11.7%). The frequency of positive lymph nodes in these patients was 3%-4% less than in advanced gastric cancer (Table 2). In linear regression analysis, age and diameter of the tumor were negatively correlated with the preoperative hemoglobin ($P<0.001$). The diameter of the tumor was positively correlated with age and the frequency of positive lymph nodes ($P<0.01$).

The patients with tumor of bad differentiation were younger than the other groups, who had larger tumor diameter and higher frequency of positive lymph nodes. The degree of differentiation was not related with the depth of tumor invasion on the gastric wall (Table 3). The tumor diameter on the corpus and fundus was larger than the others, which had higher frequency of positive lymph nodes (Table 4). The proximal gastric cancer, bad differentiation and frequency >30% positive lymph nodes were more common in female than in male (Table 5).

Multiple analysis demonstrated that sex, location of tumor, tumor diameter, depth of tumor invasion and differentiation play an important role in the metastasis of lymph nodes (Table 6).

Table 1 Comparison of operation manner with numbers of lymph nodes, time for operation, amount of blood transfusion during operation, hospitalization days and complications ($\bar{x} \pm s_{\bar{x}}$)

Manners of operation	N (1200)	Numbers lymph nodes	Time for operation (hours)	Amount of blood transfusion (mL)	Hospitalization stays (days)	Complication (%)	Positive resection margin (%)
Distal gastrectomy	768	11.7 ± 0.3*	3.3 ± 0.04	426.5 ± 17.1*	16.9 ± 0.7	9.1	3.8
Proximal gastrectomy via abdomen	72	9.6 ± 0.4	4.0 ± 0.1*	629.5 ± 43.3*	18.3 ± 1.5	17*	8.2*
Proximal gastrectomy via thorax	264	8.2 ± 0.2	3.3 ± 0.03	771.5 ± 19.5	15.5 ± 0.6	1.6	8.7*
Total gastrectomy	96	13.8 ± 0.7*	4.6 ± 0.1*	768.2 ± 47.6	19.8 ± 1.7	12.9	9.3*
P		<0.0001	<0.0001	<0.0001	>0.05	<0.001	= 0.01

*Compared with other operative approaches.

Table 2 Comparison of depth of infiltration with age, diameter, hemoglobin, and lymphatic metastasis rate ($\bar{x} \pm s_{\bar{x}}$)

Depth of invasion	N (1200)	Age (yrs)	Diameter (cm)	Hemoglobin(g/L)	Lymphatic metastasis rate (%)
pT1(m)	114	51.6 ± 1.2	2.3 ± 0.4	12.1 ± 0.3	3.2 ± 0.8
pT1(ms)	65	55.7 ± 1.5*	2.5 ± 0.7	11.3 ± 0.4*	4.1 ± 1.3
pT2	91	56.8 ± 1.4*	3.1 ± 0.3	11.2 ± 0.1*	9.8 ± 1.6*
pT3	95	57.1 ± 1.2*	4.2 ± 0.6*	11.4 ± 0.2*	20.4 ± 2.9*
pT4	835	56.9 ± 0.3*	5.6 ± 0.1*	11.2 ± 0.1*	37.1 ± 1.2*
P		<0.003	<0.0001	<0.001	<0.0001

*Compared with pT1(m).

Table 3 Comparison of differentiation with age, diameter, hemoglobin and lymphatic metastasis rate ($\bar{x} \pm s_{\bar{x}}$)

Differentiation	N (1200)	Age (yrs)	Diameter (cm)	Hemoglobin (g/L)	Lymphatic metastasis rate (%)
I	37	61.4 ± 1.4	3.5 ± 0.2	10.7 ± 0.4	10.3 ± 3.2*
II	161	57.9 ± 0.8	4.1 ± 0.3	11.1 ± 0.1	26.1 ± 2.5
III	329	58.6 ± 0.7	4.2 ± 0.2	11.2 ± 0.3	22.7 ± 1.4
IV	673	53.2 ± 0.3*	4.9 ± 0.3*	11.8 ± 0.1*	33.6 ± 1.2*
P		<0.0001	=0.004	=0.01	<0.0001

*Compared with other groups.

Table 4 Comparison of tumor site with age, diameter, hemoglobin and positive lymph node rate ($\bar{x} \pm s_{\bar{x}}$)

Location of tumor	N (1200)	Age (yrs)	Diameter (cm)	Hemoglobin (g/L)	Lymphatic metastasis rate (%)
Pylorus	27	54.3 ± 2.9	3.9 ± 0.7	12.6 ± 0.7	13.9 ± 3.2
Antrum	379	56.6 ± 0.5*	4.6 ± 0.2	11.5 ± 0.3	26.3 ± 1.4
Incisura	372	54.2 ± 0.4	3.3 ± 0.4	12.5 ± 0.1	22.5 ± 1.3
Corpus	91	55.2 ± 1.2	6.4 ± 0.5*	12.2 ± 0.4	38.3 ± 4.2*
Fundus	331	59.8 ± 0.6*	5.6 ± 0.2*	12.8 ± 0.2	35.1 ± 1.9*
P		<0.0001	<0.0001	>0.005	<0.001

*Compared with other locations.

Table 5 Comparison of sex with tumor location, differentiation, depth of invasion and positive lymph node rate ($\bar{x} \pm s_{\bar{x}}$)

Sex	Location (%)			Differentiation (%)			Depth of invasion (%)			Frequency of metastatic lymph node (%)	
	Proximal	Middle	Distal	Well	Middle	Bad	pT1	pT2	pT3	<30	>30
Male (836)	31	2	40	18	30	52	14	8	78	64	36
Female (364)	40	3	25	13	21	66	15	7	78	56	44
P		<0.001			<0.001			>0.05			=0.01

Table 6 Multi-factors analysis of lymphatic metastasis in gastric patients

Related factors	Regression coefficient	Standard error	Standard regression coefficient	*P*
Constant	-24.3	7.1		0.001
Age	-0.006144	0.079	-0.22	0.438
Sex	-6.489	2.027	-0.092	0.001
Tumor location	2.326	0.780	0.087	0.003
Diameter of tumor	2.368	0.459	0.165	0.0001
Depth of invasion	7.043	0.786	0.285	0.0001
Differentiation	3.687	1.146	0.094	0.001

DISCUSSION

Gastric cancer remains one of most common causes of death. Although the etiology of gastric cancer is still unclear, but studies have shown that many factors are associated with the development, metastasis of gastric cancer, and recurrence after operation[1-9]. Recent studies suggest that infection with *Helicobacter pylori* may play an important role in the development of gastric cancer[10-15]. It has been proposed that *Helicobacter pylori* infection may produce acute and chronic gastritis, intestinal metaplasia, dysplasia, and eventually resulting in gastric cancer. Some abnormal expression[16-18] in gene is involved in carcinogenesis of gastric cancer such as matrix metalloproteinases gene, *p*53 gene and dinucleotide repeat sequence gene. Abnormal contents of some trace elements may also be one of the risk factors in gastric cancer[19,20].

Early gastric cancer (EGC) has been considered to be a form of gastric malignancy with a relatively good long-term prognosis compared to that of advanced gastric cancer because of rare metastasis in lymph nodes[21-26]. In Japan, EGC is diagnosed in 30%-50%, due to partly at least the extensive use of endoscopy and mass screening programs[27-29]. In this study, the proportion of EGC diagnosed in all patients is 14.9%, similar to the proportion in the United States and Europe[30,31]. In recent years, endoscopic treatment has become increasingly popular as an alternative to surgical treatment of patients with EGA in hope of offering superior quality of life (QOL)[32]. However, because of presence of metastasis in 10%-20% and skip metastasis of lymph nodes, whether the rationale for a standard resection with systematic lymphadenectomy is necessary is still a controversial issue[33-37].

Different operative approaches were carried out according to the different locations of the tumor. In our study, the number of lymph nodes excised were the largest in total gastrectomy, followed by distal gastrectomy which may be related to the resection of all or most parts of omentum. The number of lymph nodes excised in proximal gastrectomy via a transabdomen was similar to via transthorax. There was shorter time for operation and lower frequency of complication in proximal gastrectomy via transthorax while lower blood transfusion in proximal gastrectomy via transabdomen. The postoperative hospitalization stay and the positive resection margin was same between them. The complications varied among different operations: gastric retention was common in distal gastrectomy while thorax effusion and infection of lung were mainly found in total gastrectomy.

Although the overall incidence of gastric cancer has remained stable in the West, there is well-documented shift from distal to proximal lesion. The clinical relevance of this shift is that the overall prognosis for patients with proximal gastric cancer is worse than for those with distal tumor. This difference in survival may be attributed to a variety of factors, ranging from an increased biologic aggressiveness of proximal tumors to an advanced stage of presentation[38,39]. In study, a higher frequency of positive lymph nodes was found in gastric cancer located on corpus and the fundus which may be associated with the larger diameter of the tumor in corpus and the fundus. In tumors with larger diameters there were worse differentiation, deeper infiltration, and higher frequency of positive lymph nodes. Apparently, the prognosis will be worse in these patients. The present results also show that the more proximal lesions, bad differentiation, and the higher >30% frequency of positive lymph nodes can be found in female than in male.

The numbers of metastatic lymph nodes play an important role in the long-term outcome after curative resection[40-43]. Thus it is suggested that extended lymphadenectomy should be performed in advanced gastric cancer[44-47]. Our multivariate analysis indicated that among six clinicopathologic variables (age, sex, location of tumor, tumor diameter, depth of invasion and differentiation), the depth of invasion was the most important factor influencing metastasis of lymph node.

In conclusion, this retrospective study has shown that clinicopathological characters in gastric cancer varied with sex, location, and diameter of the tumor. The depth of invasion plays a very important role in metastasis of lymph node. The prognosis in female with gastric cancer may be worse than in man. Because metastasis of lymph nodes may occur even in patients with EGC, radical gastrectomy witi lymphadenectomy may be necessary in all stages of gastric cancer.

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