

Clinicpathological Features of Gastric Cancer in Young Patients

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Abstract

The incidence of gastric cancer (GC) in young patients has showed a stable or even slightly increasing trend in recent years all over the world. Little is known about the clinicpathological features of young patients with GC in Ningxia region, located in the northwest part of China. To define the clinicpathological features of GC in young patients in this region, 117 patients with GC, who were admitted to the Department of Medical Oncology, General Hospital of Ningxia Medical University, Ningxia, China, were enrolled in a retrospective database between 2000 and 2005. The data from 55 patients aged less than 35 years old were compared with those from 62 controls aged between 36 and 70. It was found that in young group, the percentages of females, the tumors in the lower third of the stomach, tumor size larger than 4 cm, macroscopic type Borrmann III tumors, poorly differentiated histology, the 7th T stage T3 + T4, the distribution of tumor-nodes-metastasis (TNM) stage IV, surgical exploratory laparoscopy, and anemia symptoms were significantly higher than those in the control group ($P < 0.05$). The 5-year survival in the young group was lower than that in the control group (21.8% vs. 48.4%, $P < 0.05$). It was obvious that the clinicpathological features of GC in young patients were different from those in the control group. Focusing on early diagnostic rate and choosing a suitable operative treatment should be critical to improve prognosis of young patients with GC in Ningxia region of China.

Keywords

Young People, Gastric Cancer, Clinicpathological Features

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1. Introduction

The incidence of gastric cancer (GC) has been gradually declining in the worldwide in the last decades; however it remains the fifth highest in cancer incidence and the third leading cause of cancer death [1]. The incidence of GC has varied widely according to geographic region and is particularly common in eastern Asia [2]. In China, GC is the third cause of death among all cancers, with an age-standardized incidence of 15.85 and 12.54 cases per 100,000 person-years for men and women, respectively [3]. Ningxia region, located in the northwest part of China, has a very high incidence of GC. Although GC is considered to be a disease of elderly patients with a mean age of approximately 50 to 60 years old, the incidence of GC in young patients less than 35 years old shows a stable or even slightly increasing trend [3] [4]. There were some reports supporting that the clinicopathological features of GC in young patients differed from those in elderly patients [5] [6]. For example, Nakamura *et al.* showed a poorer prognosis in young patients than that in elderly patients [7]. However, other reports showed that survival outcomes, which depended on whether the patients underwent a curative resection, were similar in young and elderly patients [8] [9]. Up to now, however, it is still controversial as to whether GC in young patients differs from that in older patients. In this study, we compared the clinicopathological features and the prognosis of GC between young patients and elderly controls in Ningxia region of China.

2. Materials and Methods

2.1. Patients

In this study, one hundred and seventeen GC patients were enrolled, who were admitted to the Department of Medical Oncology, General Hospital of Ningxia Medical University, Ningxia of China from 2000 to 2005. Among 117 GC patients, fifty five patients defined as less than 35 years old were classified as the young group and 62 patients aged over 35 years old were classified as the control group. We compared the clinicopathological features between the young group and the control group. The features compared included gender (female or male), presentation symptoms (abdominal pain, hematemesis and melena, emaciation, indigestion, anemia), tumor size (≤ 4 cm or > 4 cm), tumor location (upper 1/3, middle 1/3, lower 1/3, \geq two thirds), degree of differentiation (well + moderately differentiated or poorly differentiated + signet-ring cell differentiation), the 7th Union for International Cancer Control (UICC) T stage (T1, T2, T3, and T4), lymph node metastasis (N0, N1, N2, and N3), the 7th UICC tumor-nodes-metastasis (TNM) stage (I, II, III and IV), adjuvant chemotherapy (yes or no), and surgical radicalism (curative resection, palliative resection, and exploratory laparoscopy). Clinical data were retrieved from the patients' operative and pathological reports, and follow-up data were obtained by phone, letter, and the outpatient clinical database. Staging was performed according to the UICC TNM Staging Classification for Carcinoma of the Stomach (Seventh Edition, 2010). The written informed consent had been obtained from all subjects, and this study was approved by the Ethical Committee of Ningxia Medical University of China.

2.2. Statistical Analysis

Clinicopathological parameters were analyzed by chi-square test and fisher's exact test. All statistical analyses were performed by Statistical Package of Social Sciences 13.0 software. *P* value below 0.05 was considered to be statistically significant. Disease-specific survival was calculated by the method of Kaplan-Meier. Kaplan-Meier analysis with log-rank testing was used for multivariate analysis.

3. Results

In this analysis, 117 patients were enrolled, including 55 patients less than 35 years old (young group) and 62 patients aged over 35 years old (control group). The mean ages of the young group and the control group were about 32.94 years old (range, 17 to 35 years old) and 52 years old (range, 36 to 70 years old), respectively. The demographic results were shown in **Table 1**. There was a significant difference in the proportion of females between two groups (52.73% vs. 20.97%, $P < 0.001$). In the young patients group, the gender ratio (female to male) was higher than that in the control group (1.12:1 vs. 0.27:1, $P < 0.05$). Significant differences could also be seen between the young group and control group in the tumor location, tumor size, macroscopic type, histological type, TNM stage, and surgical radicalism with all *P* values being below 0.05. For the young patients, the percentage of the tumor in the lower third of the stomach in the young group was much higher than that in the control group (56.36% vs. 32.26%, $P < 0.05$). It was more common to see a tumor with larger size in young patients than the older patients (85.45% vs. 59.68%, $P = 0.004$). With respect to macroscopic type, the most common

Table 1. Clinicopathological features of gastric cancer in the young (≤ 35 years old) and control (>35 years old) groups.

Variables	Young Group	Control Group	P
Age (Mean)	32.94	52.00	
Gender			<0.001
Female, n (%)	29 (52.73)	13 (20.97)	
Male, n (%)	26 (47.27)	49 (79.03)	
Female:Male	1.12:1	0.27:1	
Tumor Location, n (%)			0.001
Upper 1/3	2 (3.64)	18 (29.03)	
Middle 1/3	15 (27.27)	19 (30.65)	
Lower 1/3	31 (56.36)	20 (32.26)	
\geq Two Thirds	7 (12.73)	5 (8.06)	
Tumor Size, n (%)			0.004
≤ 4 cm	8 (14.55)	25 (40.32)	
>4 cm	47 (85.45)	37 (59.68)	
Macroscopic Type, n (%)			0.001
Borrmann I	2 (3.64)	17 (27.42)	
Borrmann II	18 (32.73)	24 (38.71)	
Borrmann III	32 (58.18)	20 (32.26)	
Borrmann IV	3 (5.45)	1 (1.61)	
Histological Type, n (%)			0.039
Poorly Differentiated	45 (81.82)	39 (62.90)	
Well-Differentiated	10 (18.18)	23 (37.10)	
The 7 th T Stage (UICC), n (%)			0.025
T1 + T2	10 (18.18)	24 (38.71)	
T3 + T4	45 (81.82)	38 (61.29)	
Lymph Node Involvement, n (%)			0.063
N0	8 (14.55)	21 (33.87)	
N1	10 (18.18)	13 (20.97)	
N2	32 (58.18)	23 (37.10)	
N3	5 (9.09)	5 (8.06)	
TNM Stage, n (%)			<0.001
I	4 (7.27)	11 (17.74)	
II	5 (9.09)	14 (22.58)	
III	9 (16.36)	27 (43.55)	
IV	37 (67.27)	10 (16.13)	
Surgical Radicalism, n (%)			<0.001
Curative Resection	31 (56.36)	46 (74.19)	
Palliative Resection	5 (9.09)	13 (20.97)	
Exploratory Laparoscopy	19 (34.55)	3 (4.84)	
Adjuvant Chemotherapy, n (%)			0.063
Yes	27 (49.10)	42 (67.74)	
No	28 (50.90)	20 (32.26)	

type of GC in young patients was Borrmann type III (58.18%), while Borrmann type I was rarely found (3.64%). According to the histological type, the percentage of the poorly differentiated in young group was 81.82%, which was higher than that in the control group (61.29%) ($P = 0.039$). It was also found that T stage (T3 + T4) in the young group was higher than that in the control group (81.82% vs. 61.29%, $P = 0.025$). No difference was found in lymph node metastasis between the two groups, $P = 0.063$. The distribution of tumor-nodes-metastasis (TNM) stage IV in young patients group was significantly higher than that in the control group (67.27% vs. 16.13%, $P < 0.05$). The rate of radical resection was 56.36% and the rate of palliative resection was 9.09%. The exploratory laparoscopy was more frequently performed in young patients than that in the control group (34.55% vs. 4.84%, $P < 0.05$).

During the study period, we did not have a standardized protocol for postoperative chemotherapy or radiotherapy. Adjuvant therapy was suggested to all patients with T3 - T4 classification or lymph node metastasis. Among the young patients, 27 (49.1%) patients completed the adjuvant chemotherapy. The median cycle of chemotherapy was four. Adjuvant chemotherapy was performed with a 5-fluorouracil based combination regimen. There was no difference in the adjuvant therapy between two groups. No patients received adjuvant radiotherapy.

The exact data of presentation symptoms with GC in two groups were summarized in **Table 2**. For the young patients, the most common presenting symptom was abdominal pain (63.4%), followed by anemia (34.54%) and indigestion (21.82%).

At the last follow-up, there were 12 (21.82%) patients alive and 40 (72.73%) who died from disease in the young group. Median survival was 24 months and 49 months in young and elder groups, respectively. The 5-year survival rates were significantly different between the young patients and elderly groups (21.8% vs. 48.4%, $P < 0.05$) (**Figure 1**).

Table 2. Presentation symptoms with gastric cancer in two groups.

Symptoms	Young Group		Control Group		P
	n	%	n	%	
Abdominal Pain	35	63.60%	37	59.67%	0.803
Hematemesis Melena	11	20.00%	16	25.80%	0.600
Emaciation	9	16.40%	14	22.58%	0.541
Indigestion	12	21.82%	38	61.29%	<0.001
Anemia	19	34.54%	10	16.13%	0.037

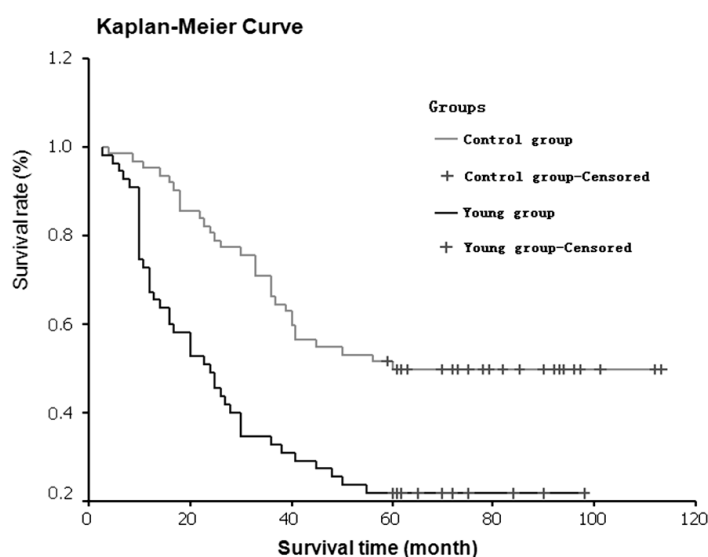


Figure 1. Survival curves for patients with gastric cancer in the young and control groups. Kaplan-Meier method was performed to analyze disease-specific survival difference between two groups. There was a significant difference in the survival between two groups, $P < 0.05$.

4. Discussion

In spite of the gradually declining incidence of GC in the worldwide in recent thirty years, the incidence of GC in young patients shows a stable or even slightly increasing trend [10]. Some reported the proportion of patients with GC under the age of 40 years old varied between 2% and 9% [4] [5]. Some claimed the incidence in young patients with gastric adenocarcinoma ranged from 4.4% to 16.2% when cut-off point was set at 40 years old [9] [11]. In our series, the young age group was defined as patients under 35 years old because intestinal metaplasia, an aging process due to acid reflux affecting the gastric mucosa, was thought to begin at around the age of 30 - 35 [12] [13]. We focused on young patients under 35 years old to determine the clinicopathological features of GC in the comparisons between young patients and elderly patients.

Many reports showed a higher incidence of GC in females among young patients than among older patients [6] [14]-[16]. For example, Qiu *et al.*, who investigated 294 young patients with gastric carcinoma, reported that the female-to-male ratio was 1.39:1 [6] and Kim *et al.* reported a female predominance of about 1.17 fold of male in young patients [16]. In this study, we also found a female/male ratio of 1.12:1 in young patients as opposed to 0.27:1 in control group. Although the reasons for the high incidence of female patients in the young group are still under-covered, it was proposed that the differences may due to the female hormones such as estrogens [17] or at least due in part to the higher expression of estrogen receptors and intracytoplasmic estradiol in young patients with GC [18].

Surgery is the only potential curative modality for localized GC. Curative resection offered the only chance of long term survival. It was reported that the young patients with curatively resected GC had a better survival rate than the young patients with non-resected GC (median survival = 70.6 months *vs.* 9.1 months, $P < 0.001$) [16]. However, tumor staging was a crucial factor in determining whether and how to perform surgery. Some investigators have reported low radical surgery resection and extremely poor survival in young patients, apparently reflecting the advanced stage at which these carcinomas were diagnosed. Our results showed that the percentages of poorly differentiated were significantly higher in the young group than in the control group. We also noticed that there was a trend to more cases with the TNM stage IV in the group of young patients than that in control patients. Therefore, it seemed quite reasonable that the proportion of curative resection (56.36%) in the young group was lower than that in the control group (74.19%) and the overall survival curves for the young and control groups were quite different in our study.

5. Conclusion

All in all, in our series, we found that the clinicopathological features of GC differed between young and elderly patients. The prognosis of the youth group was worse than that of older patients. There might be some explanations for the differences: first, the number of early stage of GC took up low proportion and advanced stage of GC accounted for the majority, which delayed the diagnosis; second, the rate of radical surgery resection was low; third, the number of poor differentiation of pathology was high. These partly reflected the characteristics of GC in young people in this region. In conclusion, focusing on early diagnostic rate and choosing a suitable operative treatment should be critical to improve prognosis of young patients with GC in Ningxia region of China. One limitation of the current study is the relatively small sample size, potentially limiting its statistical power. These findings, while significant, warrant validation in a larger study of GC patients.

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