

Clinicopathological features and trend changes of gastric carcinoma in Southern China

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Abstract

AIM: To investigate the clinicopathological features of gastric carcinoma in southern China and disease trends changes over the last 18 years.

METHODS: We designed a retrospective study in the Department of Gastrointestinal Surgery, the first affiliated hospital, Sun Yat-sen University. A total of 2100 adult patients with definitely diagnosed, histologically proven gastric carcinomas treated with radical gastrectomy from 1994 to 2013 were examined retrospectively. In all cases patient age, gender, tumor location, Borrmann type, histopathological type and grade, and pTNM stage were identified and recorded. The information was obtained from hospital records. The data were analyzed with Stata12.0 software.

RESULTS: In this study, the mean age of patients was 57 years with a range from 19-89 years. A higher incidence was found in patients over 60 years of age. In the study population, 67.38% of patients were male and 32.62% were female. Women had a higher disease incidence than men in patients less than 40 years of age ($P < 0.001$). No obvious change of patient age and gender was observed in the last 18 years. The rates of disease by location were the following: antrum (44.57%), followed by fundus/ body (24.95%) and cardia/gastroesophageal junction (23.00%). The mean tumor diameter was 5.57 cm, and advanced gross type Borrmann III was most common. Most patients were at advanced stages when first diagnosed, and patients with early stage disease were relatively rare. More early stage patients were detected in recent years, especially after 2000 ($P < 0.001$). Gastric carcinoma has different features in young and old patients. The young patients had the following features: more frequently female, tumors in the antrum, larger tumor size, poorly differentiated carcinoma, high rate of metastasis to other sites and advanced stages ($P < 0.05$).

CONCLUSION: In southern China, gastric carcinoma was more frequent in old men and young women. Young and old patients should be treated differently for having different features.

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Key words: Gastric carcinoma; Retrospective study; Clinicopathological features; Southern China; Youth

Core tip: Gastric carcinoma is one of the most common malignant tumors in the digestive tract and is the second leading cause of cancer-related death. This study retrospectively examined 2100 adult patients from southern China. Gastric carcinomas were found frequently in old men and young women. No obvious changes of patient age and gender were observed in

the last 18 years. Although most patients were at advanced stages when first diagnosed, early detection rates have increased. The young and the old patients differed in gender composition, tumor size, predilection site, pathological type and prognosis. Therefore, these patients should be treated differently in the clinic.

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INTRODUCTION

Gastric carcinoma (GC) is one of the most common malignant tumors of the digestive tract and is the second leading cause of cancer related death^[1]. The geographical distribution of GC is characterized by wide international variations. More than 70% of cases occur in developing countries, and half of the world's cases occur in Eastern Asia^[2]. China has a high incidence of gastric cancer, and it accounts for over 40% of all new gastric cancer cases^[3]. This study retrospectively examined 2100 adult patients from southern China and enrolled in the first affiliated hospital, Sun Yet-sen University from 1994-2013. We have summarized the clinicopathological features of GC in Southern China and evaluated the changes over the last 18 years.

MATERIALS AND METHODS

Data collection

The data were collected from 2100 adult patients with definitely diagnosed, histologically proven gastric carcinomas treated at the Department of Gastrointestinal Surgery, the First Affiliated Hospital, Sun Yet-sen University between 1994 and 2013. The data included the following information: gender, age, tumor location, Borrmann type, pathological type (based on the WHO classification)^[4], and pTNM stage (based on the criterion of the American Joint Committee on Cancer, AJCC)^[5]. All information was obtained retrospectively from hospital records (including pathologic and operative reports).

Statistical analysis

The data were examined and confirmed by a controller after entering and were then analyzed by using Stata12.0 software. The χ^2 test, Fisher's exact test, ANOVA test and Student's *t*-test were used to analyze data. A *P* < 0.05 was considered statistically significant.

RESULTS

Age and gender

This study evaluated 2100 cases with GC identified from 1994 to 2013. Within the study population, 67.38% of

Table 1 Age and sex *n* (%)

Age	Male	Female	Total	<i>P</i> value
Age Group				
≤ 40	91 (4.33)	122 (5.81)	213 (10.14)	
40-49	196 (9.33)	136 (6.48)	332 (15.81)	
50-59	412 (19.62)	181 (8.62)	593 (28.24)	
≥ 60	716 (34.10)	246 (11.71)	962 (45.81)	< 0.001
Number of periods				
1994-1999	278 (13.24)	106 (5.05)	384 (18.29)	
2000-2005	407 (19.38)	216 (10.29)	623 (29.67)	
2006-2013	730 (34.76)	363 (17.29)	1093 (52.05)	0.056
Total	1415 (67.38)	685 (32.62)	2100 (100)	
Mean ± SD age (yr)	58.69 ± 11.34	53.49 ± 13.73	57.00 ± 12.41	
Mean age of periods				
1994-1999	58.97 ± 10.87	53.99 ± 14.14	57.59 ± 12.05	
2000-2005	58.08 ± 11.84	51.78 ± 13.72	55.90 ± 12.87	
2006-2013	58.93 ± 11.23	54.36 ± 13.56	57.41 ± 12.24	

patients were male and 32.62% were female. The patient ages ranged from 19 to 89 years, and the mean age was 57.00 ± 12.41 years. The data indicated that 45.81% of cases were diagnosed in patients over 60 years of age, and 25.95% of cases occurred in patients under the age of 50. Women had a higher disease incidence than men in cases under 40 years old. There were significantly more male patients over age 40.

We also analyzed the changes in patient age and gender for GC over the last 18 years. The results indicated there was no change of mean age in the population or in the frequency of male and female patients. The incidence of female cases showed a trend of increasing frequency after 2000. However, this trend was not statistically significant. These data are listed in Table 1.

Morphologic features

Table 2 summarizes the morphological features of GC. The mean tumor diameter was 5.57 ± 3.43 cm. Tumors with diameters between 2.1 and 5 cm were most common, and accounted for nearly half of all cases. The tumor sites was most common in the antrum (44.57%), followed by fundus/body (24.95%) and cardia/gastroesophageal junction (23.00%) (GEJ). As for macroscopic type, Borrmann III was more common (59.62%) than Borrmann II. WHO pathologic classifications showed tubular/papillary adenocarcinoma was the most common histopathological type (79.57%). Most of the tumors were poorly differentiated.

pTNM stage

Tumor stages and the changes over the last 18 years are illustrated in Table 3. Most patients were at advanced stages (pTNM stage II, III and IV), when they were first diagnosed. Only a few tumors were detected at early stages (pTNM stage 0 and I). However, the detection rates of early patients substantially improved after 2000. The results are listed in Table 3.

Clinicopathological features of different ages

Table 4 shows that patients of different ages had differ-

Table 2 Morphologic features *n* (%)

Size (cm)	Mean ± SD	5.57 ± 3.43
	0-2.0	269 (12.81)
	2.1-5.0	969 (46.14)
	5.1-10	723 (34.43)
Location	> 10	139 (6.62)
	Cardia/EGJ	483 (23.00)
	Fundus/body	524 (24.95)
	Antrum	936 (44.57)
Borrmann type	Diffuse	75 (3.57)
	Remnant	74 (3.52)
	Multiple	8 (0.38)
	I	97 (4.62)
Pathologic type	II	510 (24.29)
	III	1252 (59.62)
	IV	241 (11.48)
	Tubular/papillary adenocarcinoma	1617 (79.57)
Differentiation	Mucinous carcinoma	127 (6.05)
	Signet cell carcinoma	255 (12.14)
	Neuroendocrine neoplasm	9 (0.43)
	Squamous carcinoma	32 (1.52)
	Others	6 (0.29)
Well	Well	87 (4.14)
	Moderate	613 (29.19)
	Poor	1400 (66.67)

Table 3 pTNM stage and time periods

Stage	1994-1999	2000-2005	2006-2013	Total	<i>P</i> value
0	1	1	10	12 (0.57%)	
I a	10	56	105	171 (8.14%)	
I b	17	54	88	159 (7.57%)	
II a	35	89	133	257 (12.24%)	
II b	61	132	193	386 (18.38%)	
III a	90	75	134	299 (14.24%)	
III b	57	45	109	211 (10.05%)	
III c	24	9	85	118 (5.62%)	
IV	89	162	236	487 (23.19%)	
Total	384	623	1093	2100	< 0.001

ent clinicopathological features. With respect to gross features, patients older than 50 years of age had a smaller mean tumor size and fewer patients had tumors larger than 10 cm. The frequency of Borrmann IV (diffuse gastric cancer) tumors decreased significantly and the incidence of cardia/GEJ carcinoma increased significantly with age. Microscopically, signet ring cell carcinoma decreased significantly after 60 years of age. Increased age was associated with fewer poorly differentiated carcinomas and significantly more well-differentiated carcinomas. The proportion of pTNM stage IV and distant metastasis gradually declined with age. All of these results were statistically significant.

DISCUSSION

Gastric carcinoma is one of the most prevalent malignant tumors in China. According to the latest GLOBOCAN statistics on Chinese gastric cancer for 2008, the total incidence rate in Chinese patients has increased from 42% to 47% since 2002. Thus, gastric cancer now

accounts for approximately 1/5 of all cancer deaths^[6,7].

We investigated the clinicopathological features of GC in southern China. Consistent with previous research, this study showed GC was prevalent in men. The overall male:female ratio was 2.07:1. The average patient age is 57 years, and the highest morbidity occurs in patients over 60 years^[8,9]. A major cause of GC in middle-aged and older people may be the long-term repeated action of carcinogenic substances that cause cellular damage and malignant transformation. In addition, a declining immune system and a reduced ability to eliminate mutant cells may also be involved in disease development in the elderly. We analyzed the age changes of the past 18 years, but found no obvious differences of mean age. This result differs from reports in South Korea and Japan, which showed that GC patients are getting older and the proportion of elderly patients continues to increase^[10,11]. Additionally, the mean age of GC patients in China is younger than that reported in South Korea, Japan and the West.

In the study, women had a higher incidence of GC than men before 40 years of age, while GC in male patients was more frequent than in females after age 40. This result may be related with sex hormone levels. Both estrogen and androgen may be involved in disease pathogenesis. Studies have shown high estrogen receptor expression in many GC patients, including male patients^[12]. Estrogen levels are especially high in women with diffusely infiltrative GC and poorly differentiated adenocarcinoma^[13]. Previously published studies have shown the influences of estrogens on GC are controversial. Whether estrogen increases or decreases the risk of GC is still unclear^[14]. The androgen receptor was also found in GC, and it was an independent unfavorable prognostic factor^[15,16]. Independent of sex hormones, male incidence increases significantly after 40 years of age. This result may also be related to the use of cigarettes and alcohol, irregular life, heavy social pressure and other factors^[17]. Chung *et al*^[18] thought hormonal factors were more commonly associated with females, whereas environmental factors were more commonly associated with males in young GC patients. Although there was no significant difference over the last 18 years for incidence of disease by gender, there is a trend of increasing female incidence after 2000.

This research showed the mean tumor diameter was 5.57 cm. Most tumor diameters were between 2.1 and 5 cm. Only 12.81% tumors were less than 2.0 cm. Advanced gross type Borrmann III was the most common tumor type. Moreover, most patients were at advanced stage (pTNM stage II, III and IV) when first diagnosed, and cases of early stage disease (pTNM stage 0 and I) were relatively rare. According to our results, the mean tumor size is larger and the detection rates of early gastric carcinoma are lower in China than in Japan and South Korea^[10]. Fortunately, the detection rates of early tumors have increased, especially after 2000. This may be related to gradually increased use of gastroscopy in

Table 4 Clinicopathological features of different ages *n* (%)

		≤ 40 yr	40-49 yr	50-59 yr	≥ 60 yr	
Size (cm)	Mean ± SD	5.83 ± 4.03	5.96 ± 3.95	5.38 ± 3.27	5.49 ± 3.17	< 0.001
	0-2.0	34 (1.62)	44 (2.10)	80 (3.81)	111 (5.29)	
	2.1-5.0	88 (4.19)	140 (6.67)	290 (13.81)	451 (21.48)	
	5.1-10	69 (3.29)	119 (5.67)	183 (8.71)	352 (16.76)	
	> 10	22 (1.05)	29 (1.38)	40 (1.90)	48 (2.29)	0.013
Location	Cardia/GEJ	21 (1.00)	47 (2.24)	146 (6.95)	269 (12.81)	
	Fundus/body	77 (3.67)	101 (4.81)	148 (7.05)	198 (9.43)	
	Antrum	103 (4.9)	162 (7.71)	258 (12.29)	413 (19.67)	
	Diffuse	9 (0.43)	18 (0.86)	25 (1.19)	23 (1.10)	
	Remnant	2 (0.10)	3 (0.14)	15 (0.71)	54 (2.57)	
	Multiple	1 (0.05)	1 (0.05)	1 (0.05)	5 (0.24)	< 0.001
	Borrmann type	I	10 (0.48)	8 (0.38)	37 (1.76)	59 (2.81)
II	48 (2.29)	84 (4.00)	146 (6.95)	229 (10.90)		
III	116 (5.52)	179 (8.52)	335 (15.95)	605 (27.86)		
IV	39 (1.86)	61 (2.90)	75 (3.57)	89 (4.24)	< 0.001	
Pathologic type	Tubular or papillary adenocarcinoma	164 (7.81)	265 (12.62)	456 (21.71)	786 (37.43)	
	Mucinous carcinoma	9 (0.43)	12 (0.57)	36 (1.71)	70 (3.33)	
	Signet cell carcinoma	37 (1.76)	48 (2.29)	91 (4.33)	79 (3.76)	
	Neuroendocrine neoplasm	0 (0.00)	2 (0.10)	2 (0.10)	5 (0.24)	
	Squamous carcinoma	3 (0.14)	5 (0.24)	6 (0.29)	18 (0.86)	0.001
	Others	0 (0.00)	0 (0.00)	2 (0.10)	4 (0.19)	
Differentiation	Well	5 (0.24)	8 (0.38)	23 (1.10)	51 (2.43)	
	Moderate	15 (0.71)	66 (3.14)	169 (8.05)	363 (17.29)	
	Poor	193 (9.19)	258 (12.29)	401 (19.10)	548 (26.10)	< 0.001
pTNM stage	0	1 (0.05)	1 (0.05)	1 (0.05)	9 (0.43)	
	I a	21 (1.00)	27 (1.29)	48 (2.29)	75 (3.57)	
	I b	14 (0.67)	31 (1.48)	56 (2.67)	58 (2.76)	
	II a	25 (1.19)	33 (1.57)	82 (3.90)	117 (5.57)	
	II b	29 (1.38)	53 (2.52)	99 (4.71)	205 (9.76)	
	III a	29 (1.38)	35 (1.67)	80 (3.81)	155 (7.38)	
	III b	18 (0.86)	36 (1.71)	65 (3.10)	92 (4.38)	
	III c	11 (0.52)	23 (1.10)	29 (1.38)	55 (2.62)	
	IV	65 (3.10)	93 (4.43)	133 (6.33)	196 (9.33)	0.006
	Metastasis	M0	148 (7.05)	239 (11.38)	460 (21.90)	766 (36.48)
M1	65 (3.10)	93 (4.43)	133 (6.33)	196 (9.33)	0.002	

China, particularly in the east and south of China where there are better economic and health conditions. Earlier diagnosis leads to better effect of treatment for gastric carcinoma. However, there is no nationwide screening program for GC. Therefore, the early detection of GC relies on opportunistic screening^[19].

In our research, GC predominantly occurred in the gastric antrum, followed by body and cardia, which is similar with most statistics. Recently, scholars found the incidence of proximal GC was increasing. The Chinese and European/American literature report the incidence of distal GC was significantly declining and cardia/GEJ carcinoma was significantly increasing^[20,21]. In the United States, male cardia carcinoma incidence is increasing annually, and it is becoming one of the fastest growing tumors. The incidence of this tumor type accounts for nearly half of GCs. Smoking, drinking, obesity, and esophageal reflux are risk factors of cardia carcinoma. Additionally, cardia carcinoma is related to diet, especially reduced cereal fiber intake and high protein, fat and salt consumption. These dietary problems may increase the incidence of cardia carcinoma. Increasing cereal fiber intake can reduce the risk of cardia carcinoma. In addition, the eradication of *Helicobacter pylori* (*H. pylori*) reduces distal GC and relatively increases the incidence of

cardia carcinoma^[22]. Reports from Turkey, Iran and Korea demonstrated the antrum is the most common site of GC^[10,23,24]. The incidence of cardia has not increased and this result may be related to the local environment, habits and customs. In southern China the people have a bland diet, and less smoking and drinking are popular.

We found young patients differed from the older patients not only in the sex ratio but also in the morphologic features and clinical stages. In the young, the tumors were larger and the proportion of Borrmann IV (diffuse gastric cancer) was higher than in the older patients. The incidence of cardia/GEJ carcinoma increased significantly with age. Microscopically, poorly differentiated and signet ring type carcinoma decreased significantly after 60 years of age. Clinically, the proportion of pTNM stage IV and distant metastasis gradually declined with age. The above data suggest that GC in young adults has more aggressive infiltration ability, higher malignancy, faster progress, and worse prognosis than GC in older patients.

Although the predominant tumor site is the antrum in China, we found the risk of occurrence of cardia/GEJ carcinoma significantly increased in patients more than 50 years old. The following may be the possible reasons: (1) the degeneration of esophageal smooth

muscle in older people, the lower esophageal sphincter muscle tension, disorders of nervous regulation mechanism are commonly seen simultaneously, which causes gastroesophageal reflux and repeated reflux results in inflammatory injury, repair and hyperplasia, and finally cancerous changes of the membrane of cardia area; (2) the fundic glands atrophy, the junction of fundus and body moves up in the old, which results in weakening of the mucosal barrier; and (3) as the patients age, the gastric mucosa epithelium degenerates and intestinal metaplasia develops to the fundus from the antrum^[25]. The difference of predilection site between the young and the old may mainly relate to the above, but the specific mechanism is still unclear.

In southern China, GC is predominant in old men and young women and is mostly located at the gastric antrum. Although most patients have advanced stage disease at diagnosis, more patients are being detected at early stages. The detection and treatment of early GC needs further improvement. Patients of different ages have different clinicopathological features. Young and old patients differ in the gender composition, predilection site, pathological type and disease prognosis. Thus, these diseases should be treated differently in clinical settings.

COMMENTS

Background

Despite the decreasing global incidence, gastric carcinoma remains one of the most common forms of malignancy around the world. The geographical distribution of gastric carcinoma is characterized by wide international variations. According to WHO data, more than 70% of cases occur in developing countries and half of the world's cases occur in Eastern Asia. China has highest rates of morbidity and mortality of gastric cancer.

Research frontiers

The available data in the literature regarding gastric carcinoma in Southern China are limited. Therefore, the aim was to investigate the clinicopathological features of gastric carcinoma in Southern China and changes in trends over the last 18 years.

Innovations and breakthroughs

In the present study, the authors found in Southern China gastric carcinoma had a predilection in old men and young women. There were no changes in patient age and gender observed over the last 18 years. Most patients were diagnosed at advanced stages and early stage patients were relatively rare. More patients with early disease have been diagnosed since 2000.

Applications

The study results suggest early detection rates of gastric carcinoma are increasing, but still lag behind developed countries and need further improvement. The young and the old patients had different clinicopathologic features and should be treated differently in the clinic.

Terminology

Southern China is one of the seven major Chinese geographical divisions and is located in China's southernmost region. Southern China includes the provinces of Guangdong, Guangxi, Hainan, Hong Kong and Macao.

Peer review

This paper retrospectively studied 2100 adult gastric cancer patients from southern China from 1994-2013. This is a well-written article with interesting data.

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