

Clinical epidemiology of gastric cancer in Hehuang valley of China: A 10-year epidemiological study of gastric cancer

Su Yan, Bin Li, Zhen-Zhong Bai, Jun-Qi Wu, Da-Wei Xie, Ying-Cai Ma, Xu-Xiang Ma, Jun-Hui Zhao, Xin-Jian Guo

Su Yan, Jun-Qi Wu, Da-Wei Xie, Department of Gastrointestinal Surgery (Surgical Oncology), Affiliated Hospital of Qinghai University, Xining 810001, Qinghai Province, China

Bin Li, Department of Public Health and Medical Statistics, School of Medicine of Qinghai University, Xining 810001, Qinghai Province, China

Zhen-Zhong Bai, Key Laboratory of High Altitude Medicine of Ministry of Education, Qinghai University, Xining 810001, Qinghai Province, China

Ying-Cai Ma, Department of Digestive Medicine, People's Hospital of Qinghai Province, Xining 810001, Qinghai Province, China

Xu-Xiang Ma, Department of Digestive Medicine, Affiliated Hospital of Qinghai University, Xining 810001, Qinghai Province, China

Jun-Hui Zhao, Department of Medical Oncology, Affiliated Hospital of Qinghai University, Xining 810001, Qinghai Province, China

Xin-Jian Guo, Consultation Centre of Clinical Pathology, Affiliated Hospital of Qinghai University, Xining 810001, Qinghai Province, China

Author contributions: Yan S was in charge of the research; Li B analyzed the clinical epidemiological data; Xie DW, Wu JQ, Ma YC, Ma XX and Zhao JH were in charge of collecting the clinical epidemiological information of the patients with gastric cancer in Hehuang valley; Bai ZZ and Guo XJ were equally involved in writing the manuscript.

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Correspondence to: Su Yan, MD, Associate Professor, Vice-Director, Department of Gastrointestinal Surgery (Surgical Oncology), Affiliated Hospital of Qinghai University, No. 29 Tongren Road, Chengxi District, Xining 810001, Qinghai Province, China. yansuqinghai@163.com

Telephone: +86-971-6230800 Fax: +86-971-6155740

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to provide a reference for treatment and prevention of regional gastric cancer.

METHODS: Between February 2003 and February 2013, the records of 2419 patients with gastric cancer were included in this study. The patient's characteristics, histological and pathological features, as well as the dietary habits of the patients, were investigated.

RESULTS: The clinical data showed that adenocarcinoma was the leading histological type of gastric cancer in this area. Characteristics of gastric cancer in different ethnic groups and age showed that the 60.55-65.50 years group showed the high incidence of gastric cancer in all ethnic groups. There were more male gastric cancer patients than female. Intestinal was the most common type of gastric cancer in the Hehuang valley. There was no significant difference in the proportion of sex in terms of *Helicobacter pylori* infection. The impact of dietary habits on gastric cancer showed that regular consumption of fried or grilled food, consumption of high-salt, high-fat and spicy food and drinking strong Boiled brick-tea were three important factors associated with gastric cancer in males and females.

CONCLUSION: Differences existed in race, sex, and age of patients according to the epidemiology of gastric cancer in the Hehuang valley. Moreover, dietary habits was also an important factor contributing to gastric cancer.

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Key words: Gastric cancer; Epidemiology; Dietary habits; Hehuang valley; Mortality

Core tip: Gastric cancer is an important public health burden in China (especially in northwest of China). The Hehuang valley part of the ancient Silk Road, is located in the northeast of the Qinghai-Tibetan Plateau. As an important population center on the Silk Road, a sys-

tematic clinical epidemiological study of gastric cancer is necessary. We conducted a clinical epidemiology study of gastric cancer in the Hehuang valley. Significant differences were observed for race, sex, and age of patients with gastric cancer in the Hehuang valley. Dietary habit was an important factor contributing to gastric cancer.

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INTRODUCTION

The incidence and mortality of gastric cancer have decreased significantly over the past several decades^[1]. However, gastric cancer remains a major public health issue as the fourth most common cancer and the second leading cause of cancer death worldwide^[2,3]. Gastric cancer has attracted much attention from epidemiologists over recent years, particularly in terms of risk factors^[1,4,5]. The different tumor types^[6], nationality^[7], food^[8] as well as geographic variation^[9] are all influencing factors. Detailed epidemiological analyses of their demographic trends and risk factors will help guide future cancer control strategies. Although gastric cancer is a worldwide problem, nearly two-thirds of stomach cancers occur in developing countries^[2], especially in South America and China^[10]. The high mortality^[11] and significant regional disparity in the distribution^[12] of gastric cancer remains an important public health burden in China.

The Hehuang valley, one of the most important stations on the Tang-Tibet Road and the ancient Silk Road, is located in the northeast of the Qinghai-Tibetan Plateau. The Hehuang valley has convenient transportation and relatively low elevation^[13], and three-quarters of the population in Qinghai province are concentrated in this area. Native populations in Hehuang valley are Hui, Salar, Tu, Tibetan and Han. As an important population center on the ancient Silk Road, a systematic clinical epidemiological study of gastric cancer is necessary. Thus, in this study, a clinical epidemiology study of gastric cancer in the Hehuang valley was performed. We hope to understand the characteristics and trends of the clinical epidemiological data, and provide a reference for diagnosis and prevention of regional gastric cancer.

MATERIALS AND METHODS

Patients

Between February 2003 and February 2013, the records of 2419 patients with histologically demonstrated gastric cancer were reviewed at four departments: the Department of Gastrointestinal Surgery, Affiliated Hospital

of Qinghai University; the Department of Digestive Medicine, Affiliated Hospital of Qinghai University; the Department of Medical Oncology, Affiliated Hospital of Qinghai University; and the Department of Digestive Medicine, People's Hospital of Qinghai Province. The 10-year period was divided into two groups: previous 5-year group (Jan. 2003-Jan. 2008; $n = 985$) and past 5-year group (Feb. 2008-Feb. 2013; $n = 1394$). For each patient, the demographic information, clinical data and pathology reports were available in these Departments.

All the data could represent the epidemiology of gastric cancer in the Hehuang valley. Each patient provided informed consent, and the Ethics Committee of the People's Hospital of Qinghai Province and Affiliated Hospital of Qinghai University approved the study protocol.

Inclusion criteria and exclusion criteria

The inclusion criteria for the patients with gastric cancer were as follows: (1) primary gastric cancer confirmed by endoscopic biopsies or histological pathology after gastrectomy; (2) more than two generations dwelling in the Hehuang valley (including both of the Huangshui River basin and the Yellow River basin in the east of Qinghai province); and (3) gastric computed tomography (CT) scan with oral and IV contrast, detection of *Helicobacter pylori* (*H. pylori*), human epidermal growth factor receptor-2 (Her-2) expression, estrogen receptor (ER) and progesterone receptor (PR) in tumor tissue stained routinely by hematoxylin-eosin staining (HE) or by immunohistochemistry (IHC). The perineural infiltration, vessel invasion, lymph nodes metastasis, histological classification and grade should be confirmed by pathological examination. The exclusion criteria were: (1) dwelling outside of the Hehuang valley or less than two generations dwelling in the Hehuang Valley; and (2) missing clinicopathological data or deficient pathological information.

Diagnostic criteria

The stomach is anatomically divided into three portions; the upper (U), middle (M) and lower (L) portions. If more than one portion was involved, all involved portions were described as UML. All patients were subjected to gastric CT scan (PHILIPS Brilliance iCT; Enhanced scanning administration: Ultravist 300, 85 mL, 2.8 mL/s) with oral and IV contrast and barium-meal joint with gastroscopy (OLYMPUSCV-260) examination in the upper gastrointestinal tract to locate the tumor. The *in vivo* endoscopic optical biopsy with paraffin sections observation was used for gastric cancer diagnoses. As proposed by the Japanese Society of Gastroenterological Endoscopy^[14], the classification of early gastric cancer (EGC) was as follows: (1) type I: protruded type; (2) type IIa: superficial elevated type; type IIb: flat type; type IIc: superficial depressed type; and (3) type III: excavated type. The macroscopic classification of advanced gastric carcinoma was classified according to Borrmann^[15] as type I, type II, type III and type IV.

The classification of histological type was based on

Table 1 Demographic features of gastric cancer patients in Hehuang valley *n* (%)

		Previous 5 yr group (<i>n</i> = 985)	Past 5 yr group (<i>n</i> = 1394)	<i>P</i> value
Sex	Male	785 (79.7)	1083 (77.7)	0.241
	Female	200 (20.3)	311 (2.3)	
Age (yr)	18-44	190 (19.3)	390 (28)	0.000
	45-85	795 (80.7)	1004 (72)	
Family history	Positive	437 (44.4)	813 (58.3)	0.000
	Negative	548 (55.6)	581 (41.7)	
Nationality	Muslims	576 (58.5)	792 (56.8)	0.685
	Tibetan	18 (1.8)	24 (1.7)	
	Han	391 (39.7)	578 (41.5)	

The native Hui and Salar in Qinghai were also included in Muslims. The Hehuang valley, an agricultural area, is located in the eastern Qinghai Province, China.

the predominant pattern of the tumor (common types and special types), according to criteria of the World Health Organization (WHO)^[16]. The common types were classified as papillary adenocarcinoma, tubular adenocarcinoma (including well-differentiated types and moderately differentiated types), poorly differentiated adenocarcinoma (including undifferentiated carcinoma), signet-ring cell carcinoma and mucinous adenocarcinoma; the special types were classified as adenosquamous carcinoma, squamous cell carcinoma, carcinoid tumor and other tumors. Meanwhile, tumors were also classified as intestinal-type or diffuse-type, according to Lauren^[10].

Moreover, gastric CT scan with oral and IV contrast detection of *H. pylori*, Her-2 expression, ER and PR in tumor tissue stained routinely by HE or IHC were performed. The perineural infiltration, vessel invasion, lymph nodes metastasis, histological classification and grade should be confirmed by pathological examination.

Dietary habits investigation

To reveal the influence of dietary habits on gastric cancer in the Hehuang valley, 2310 healthy residents were enrolled in this study as controls. The inclusion criteria for the normal controls were (1) more than two generations dwelling in the Hehuang valley (including both the Huangshui River basin and the Yellow River basin in Qinghai province); (2) no diagnosis or suspicion of gastrointestinal cancer; (3) no long-term exposure to carcinogens; and (4) no family history of neoplastic diseases.

Statistical analysis

The background data pertaining to patients were entered into an SPSS database. SPSS 17.0 was used for the statistical analysis. χ^2 tests and Mann-Whitney *U* tests were run to assess categorical covariates and continuous variables, respectively. We set the significance level $P \leq 0.05$.

RESULTS

Patients' data collection

A total of 785 male and 200 female patients were in-

cluded in the previous 5 years group; there were 190 patients distributed in the age range of 18-44 years, while 795 patients were in the age range of 45-85 years. Of 1394 patients (1083 male and 311 female) in past 5 years group, 390 patients were distributed in the age range of 18-44 years, while 1004 patients were in the age range of 45-85 years. The detail demographic information, including nationality and family history, are listed in Table 1.

Clinical data of gastric cancer in Hehuang valley

All patients were subjected to a barium-meal examination in the upper gastrointestinal tract to locate the tumor. The locations of the primary tumor in the previous (33.5%, in composition ratio) and past 5 years groups (27.0%) were both concentrated in the lower third portion of the stomach (Table 2). The result of Lauren classification in both previous (63.8%) and past 5 years groups (69.2%) indicated that intestinal was the major type of gastric cancer in the Hehuang valley. The proportion of early gastric cancer was significantly lower (in composition ratio) than that of advanced gastric cancer. Adenocarcinoma was the leading histological type of gastric cancer in the previous and past 5 years groups. The majority of histological type was moderate carcinoma (65.1% in the previous 5 years group and 73.9% in past 5 years group); compared with the previous 5 years group, the number of patients with moderate carcinoma had decreased in the past 5 years group.

Nearly half of the patients in the previous 5 years group had perineural invasion (49.1%) or vascular invasion (48.1%); however, there was a downward trend in the past 5 years group (39.5% and 38.5%). A low level of Her-2 expression was detected in both previous (7.5%) and past 5 years groups (6.3%). Moreover, compared with the previous 5 years group, there were a downward trend in *H. pylori* infection (43.8% vs 36.2%), ER expression (26.2% vs 4.6%), PR expression (24.4% vs 4%) and lymph node metastasis (90% vs 86.3%) in the past 5 years group. It was worth mentioning that huge downward trends existed for ER and PR expression. The detail characteristics of each element are listed in Table 2.

Characteristics of gastric cancer in different ethnic groups, ages and sexes

The patients in the 45-85 years age had a higher incidence of gastric cancer than those in 18-44 years age either in the past 5 years group (86.1% of Muslims, 83.3% of Tibetan and 84% of Han) or in the previous 5 years group (87.2% of Muslims, 83.3% of Tibetan and 83.9% of Han). The age distribution for most of the patients in the elderly group was between 60.55-65.50 years (data not shown), so the 60.55-65.50 years was the highest incidence age range for gastric cancer in Hehuang valley. The proportion of males among the gastric cancer patients was higher than that of females in the past 5 years group (81.4% of Muslims, 75% in Tibetan and 84% in Han) and the previous 5 years group (84.2% of Muslims, 88.9% in Tibetan and 80.8% in Han). There was no sig-

Table 2 Clinical data of patients in past and previous 5-year groups *n* (%)

	Past 5 yr group (<i>n</i> = 1394)	Previous 5 yr group (<i>n</i> = 985)	<i>P</i> value		Past 5 yr group (<i>n</i> = 1394)	Previous 5 yr group (<i>n</i> = 985)	<i>P</i> value
Tumor location			< 0.05	Perineural invasion			< 0.05
Upper (U)	467 (33.5)	266 (27.0)		Positive	685 (49.1)	389 (39.5)	
Middle (M)	142 (10.2)	94 (9.5)		Negative	709 (50.9)	596 (60.5)	
Lower (L)	705 (50.6)	530 (53.8)		Vascular invasion			< 0.05
UML	80 (5.7)	95 (9.6)		Positive	671 (48.1)	375 (38.1)	
Tumor classification				Negative	723 (51.9)	610 (61.9)	
Early stage ¹			> 0.05	Her-2 Expression			> 0.05
Type I	3 (0.2)	1 (0.1)		Positive	104 (7.5)	62 (6.3)	
Type II a	2 (0.1)	2 (0.2)		Negative	1290 (92.5)	923 (93.7)	
Type II b	5 (0.4)	5 (0.5)		<i>H. pylori</i> infection			< 0.05
Type II c	3 (2.0)	3 (0.3)		Positive	610 (43.8)	357 (36.2)	
Type III	8 (5.7)	4 (0.4)		Negative	784 (56.2)	628 (63.8)	
Advanced stage ²			< 0.05	ER Expression			< 0.05
Type I	201 (14.4)	199 (20.2)		Positive	365 (26.2)	45 (4.6)	
Type II	365 (26.2)	206 (20.9)		Negative	1029 (73.8)	940 (95.4)	
Type III	520 (37.3)	375 (38.1)		PR Expression			< 0.05
Type IV	288 (20.7)	190 (19.3)		Positive	340 (24.4)	39 (4.0)	
Pathological type			< 0.05	Negative	1054 (75.6)	946 (96.0)	
Adenocarcinoma	1335 (95.8)	902 (91.6)		Lymph node metastasis			< 0.05
Squamous cell carcinoma	38 (2.7)	16 (1.6)		Positive	1250 (90.0)	850 (86.3)	
Signet-ring cell carcinoma	9 (0.6)	14 (1.4)		Negative	144 (10.3)	135 (13.7)	
Other	12 (0.9)	53 (5.4)		Histological type			< 0.05
Histological type			< 0.05	Lauren classification			> 0.05
Well-differentiated type	264 (19.0)	157 (15.9)		Intestinal	890 (63.8)	682 (69.2)	
Moderately differentiated type	907 (65.1)	728 (73.9)		Nonintestinal	504 (36.2)	303 (30.8)	
Poorly/undifferentiated type	223 (16.0)	100 (10.2)					

¹Histological type was based on the criteria of World Health Organization; ²Advanced stage classification was in accordance with Borrmann type; Her-2: Human epidermal growth factor receptor-2; *H. pylori*: *Helicobacter pylori*; ER: Estrogen receptor; PR: Progesterone receptor. *P* < 0.05, the previous *vs* the past year group.

nificant difference in the distribution of age (*P* = 0.511) and sex (*P* = 0.281) among the three ethnic groups in the Hehuang valley. The majority of Tibetan patients were positive for *H. pylori* infection (79.2% in male and 66.7% in female). The result of Lauren classification indicated that intestinal was the most common type of gastric cancer in the Hehuang valley. The majority of tumors in patients were located in the lower part of stomach, either in the past 5 years group or in the previous 5 years group. The detail characteristics of each element are listed in Table 3.

The proportion of the majority histological type of gastric cancer (moderately differentiated type) in the youth group (74.7%) was higher than that in the elder group (66.8%); the incidence risk in males and females were similar (69% *vs* 67.7%). By contrast, the proportion of the majority pathological type of gastric cancer (adenocarcinoma) in the youth group (89.7%) was less than that in the elder group (95.4%); the incidence risks in males and females were 93.5% and 95.9%, respectively. In total, 16.4% of patients in the youth group showed Her-2 expression-positive status. However, the proportion of patients with Her-2 expression-positive status in the elder group was only 3.9%. Meanwhile, more females showed Her-2 expression than males (19.2% *vs* 3.6%). Compared with the youth group, the majority of patients in the elder

group were distributed in type I, type II and type III of the advanced stage. However, the majority of patients in the youth group were distributed in type III and type IV (Table 4). The numbers in the youth group with *H. pylori* infection-positive status (67.2%) were higher than in the elder group (32.1%). There was no significant difference in the proportion of sex in *H. pylori* infection (40.5% *vs* 41.4%).

Impact of dietary habits on gastric cancer

To reveal the influence of dietary habits on gastric cancer in the Hehuang valley, 2310 healthy residents were enrolled in this study (Table 5). We conducted a survey for 10 dietary habits including smoking, drinking alcohol, rapid eating, irregular dinner-time, consumption of overnight food/preserved food/fried or grilled food/high-salt, high-fat and spicy food, drinking strong Boiled brick-tea and eating too hot or too cold food. The result showed that dietary habits such as smoking (*P* = 0.425), drinking alcohol (*P* = 0.963), irregular dinner-time (*P* = 0.600) and consumption of overnight food (*P* = 0.700) or preserved food (*P* = 0.750) had little effect on the incidence of gastric cancer in males and females. Compared with the healthy male residents, there were significant impact of rapid eating (*P* < 0.001) and eating too hot or too cold food (*P* < 0.001) on gastric cancer. Moreover, regu-

Table 3 Gastric cancer characteristics of different ethnic groups in the Hehuang valley *n* (%)

	Past 5 yr group			<i>P</i> value	Previous 5 yr group			<i>P</i> value
	Muslims (<i>n</i> = 792)	Tibetan (<i>n</i> = 24)	Han (<i>n</i> = 578)		Muslims (<i>n</i> = 576)	Tibetan (<i>n</i> = 18)	Han (<i>n</i> = 391)	
Age (yr)				0.511				0.268
20-44	110 (13.9)	4 (16.7)	93 (16.1)		72 (12.5)	3 (16.7)	63 (16.1)	
45-85	682 (86.1)	20 (83.3)	485 (84.0)		504 (87.2)	15 (83.3)	328 (83.9)	
Sex				0.281				0.310
Male	645 (81.4)	18 (75.0)	486 (84.0)		485 (84.2)	16 (88.9)	316 (80.8)	
Female	147 (18.6)	6 (25.0)	92 (20.0)		91 (15.8)	2 (11.1)	75 (19.2)	
<i>H. pylori</i> infection				0.002				< 0.001
Positive	340 (43.0)	19 (79.2)	251 (43.4)		182 (31.6)	12 (66.7)	163 (41.7)	
Negative	452 (57.1)	5 (20.8)	327 (56.6)		394 (68.4)	6 (33.3)	228 (58.3)	
Lauren classification				0.045				< 0.001
Intestinal	527 (66.5)	16 (66.7)	347 (60.0)		427 (74.1)	12 (66.7)	243 (62.1)	
Nonintestinal	265 (33.5)	8 (33.3)	231 (40.0)		149 (25.9)	6 (33.3)	148 (37.9)	
Tumor location				0.011				0.005
Upper (U)	260 (32.8)	15 (62.5)	192 (33.2)		143 (24.9)	2 (11.1)	121 (31.0)	
Middle (M)	86 (10.9)	3 (12.5)	53 (9.2)		45 (7.8)	1 (5.6)	48 (12.3)	
Lower (L)	414 (52.3)	4 (16.7)	287 (50.0)		336 (58.3)	11 (61.1)	183 (46.8)	
UML	32 (4.0)	2 (8.3)	46 (8.0)		52 (9.0)	4 (22.2)	39 (10.0)	

The native Hui and Salar in Qinghai were also included in Muslims; the Hehuang valley, an agricultural area, is located in the eastern Qinghai province, China; *P* < 0.05, the past 5 years group vs the previous 5 years group. *H. pylori*: *Helicobacter pylori*.

lar consumption of fried or grilled food, consumption of high-salt, high-fat and spicy food and drinking strong Boiled brick-tea were three important factors associated with gastric cancer in males and females.

DISCUSSION

In this study, a clinical epidemiological study of gastric cancer in Hehuang valley of Qinghai Province in China was performed. The clinical data showed that adenocarcinoma was the leading histological type of gastric cancer in this area. The majority histological type was moderate carcinoma. A huge downward trend was observed in ER and PR expression in the patients of the Hehuang valley. Characteristics of gastric cancer in different ethnic groups, age and sex showed that the 45-85 years group had the high incidence of gastric cancer among all ethnic groups. The proportion of male gastric cancer patients was higher than females. Lauren classification indicated that intestinal was the most common type of gastric cancer in the Hehuang valley. The majority of tumors in patients were located in the lower part of the stomach. There was no significant difference in the sex distribution for *H. pylori* infection. The impact of dietary habits on gastric cancer showed that regular consumption of fried or grilled food, consumption of high-salt, high-fat and spicy food and drinking strong Boiled brick-tea were three important factors associated with gastric cancer in males and females.

Pathological analysis of gastric cancer

A United States report showed that there has been a parallel five- or six-fold rise in adenocarcinoma^[17]. A rising incidence of adenocarcinoma has also been reported from Canada^[18], the United Kingdom^[19], Australia^[20] and the Netherlands^[21]. Pohl *et al*^[22] asked whether we are

reaching a peak of adenocarcinoma incidence? The results of our study in the Hehuang valley would suggest that we are. Compared with the previous 5 years, the proportion of patients with adenocarcinoma had decreased (95.8%-91.6%), even though adenocarcinoma was still the leading histological type of gastric cancer (Table 2). Moreover, there was a more equal male-to-female ratio in adenocarcinoma (Table 4). In the year 1965, Lauren^[10] indicated that the intestinal type is more common in males and older age groups. In the present study, the majority of gastric cancer in the elderly was intestinal (Table 4), which agreed with Lauren.

We observed a tendency for the location of the primary tumor to move up in the stomach, even if the lower 1/3 of the stomach was still the most common site of gastric cancer in the Hehuang valley. The proportion of upper 1/3 gastric cancer is increasing, and the proportion of squamous carcinoma/adenosquamous carcinoma has undergone a sharp increase. This was also accordance with the situation in Europe^[23]. In Europe, Barrett's esophagus is associated with this disease. Whereas in the Hehuang valley, the increase of upper 1/3 gastric cancer might be related to chronic gastritis, habits of food-intake and the high level of *H. pylori* infection.

Lymph node metastasis is the main way for solid tumors to metastasize; it is an essential factor for clinical, pathological staging and prognosis of cancer^[24]. Tumor metastasis is a sign of deterioration. In this study, 90% patients in previous 5 years group showed lymph node metastasis (Table 2). The ratio was still very high in the past 5 years group. This indicated that the treatment of gastric cancer in the Hehuang valley would be more difficult. Meanwhile, the statuses of other factors such as Her-2, ER and PR were mostly negative. In 1994, the International Agency for Research on Cancer classified *H. pylori* as carcinogenic to humans^[25]. Countries with

Table 4 Clinical data of patients of different ages and genders *n* (%)

	Gastric cancer in youth (<i>n</i> = 580)	Gastric cancer in the elderly (<i>n</i> = 1799)	<i>P</i> value	Male (<i>n</i> = 1868)	Female (<i>n</i> = 511)	<i>P</i> value
Histological type			< 0.001			< 0.001
Well-differentiated type	22 (3.8)	399 (22.2)		298 (16.0)	123 (24.0)	
Moderately differentiated type	433 (74.7)	1202 (66.8)		1289 (69.0)	346 (67.7)	
Poorly/undifferentiated type	125 (21.6)	198 (11.0)		281 (15.0)	42 (8.2)	
Pathological type			< 0.001			0.050
Adenocarcinoma	520 (89.7)	1717 (95.4)		1747 (93.5)	490 (95.9)	
Squamous cell carcinoma	29 (5.0)	25 (1.4)		42 (2.2)	12 (2.3)	
Signet-ring cell carcinoma	17 (2.9)	6 (0.3)		19 (1.0)	4 (0.79)	
Other	14 (2.4)	51 (2.8)		60 (3.2)	5 (0.98)	
Her-2 Expression			< 0.001			< 0.001
Positive	95 (16.4)	71 (3.9)		68 (3.6)	98 (19.2)	
Negative	485 (83.6)	1728 (96.1)		1800 (96.4)	413 (80.8)	
Early stage ¹			0.681			0.026
Type II a	0 (0.0)	4 (0.2)		4 (0.2)	0 (0.0)	
Type II b	0 (0.0)	4 (0.2)		3 (0.2)	1 (0.2)	
Type II c	0 (0.0)	9 (0.5)		7 (0.4)	2 (0.4)	
Type III	1 (0.2)	5 (0.3)		4 (0.2)	2 (0.4)	
Type III	2 (0.3)	10 (0.6)		5 (0.3)	7 (1.3)	
Advanced stage ²			< 0.001			< 0.001
Type I	44 (7.6)	356 (19.8)		255 (13.7)	145 (28.4)	
Type II	60 (10.3)	511 (28.4)		484 (25.9)	87 (17.0)	
Type III	317 (23.6)	578 (32.1)		679 (36.3)	216 (42.3)	
Type IV	156 (26.9)	322 (17.9)		427 (22.9)	51 (10.0)	
<i>H. pylori</i> infection			< 0.001			0.816
Positive	390 (67.2)	577 (32.1)		757 (40.5)	210 (41.1)	
Negative	190 (32.8)	1222 (67.9)		1111 (59.5)	301 (59.0)	
Lauren classification			< 0.001			
Intestinal	124 (21.4)	1448 (80.5)		-	-	
Nonintestinal	456 (78.6)	351 (19.5)		-	-	

¹Early stage classification was in accordance with the Japanese Society of Gastroenterological Endoscopy; ²Advanced stage classification was in accordance with Borrmann type. Gastric cancer in youths refers to patients between 18 and 45 years old; Gastric cancer in the elderly refers patients between 45 and 85 years old. Her-2: Human epidermal growth factor receptor-2; *H. pylori*: *Helicobacter pylori*.

high gastric cancer rates typically have a high prevalence of *H. pylori* infection^[26]. Compared with the previous 5 years group, the proportion of gastric cancer patients with *H. pylori* infection had decreased in the past 5 years group (Table 2). Webb and Forman^[27] indicated that *H. pylori* infection might disappear with the development of atrophic gastritis, which is present in many gastric cancer patients. This might explain the reason why there was a decrease in *H. pylori* infection in the Hehuang valley.

Age, sex, and race associated with gastric cancer

A previous study indicated that the incidence of gastric cancer rises progressively with age, meanwhile cases in patients younger than 30 years are very rare^[28]. The number of gastric cancer patients in the elder group (48-85 years old) in our study was three times that in the youth (18-45 years old) group (Table 4), which correlates with the results of the previous study. However, near 25% of patients were distributed in the youth group in our study. A study with a large-size sample in South Korea^[29] has evaluated the epidemiological features of young age gastric cancer. Therefore, the younger trend of gastric cancer may be happening not only in the Hehuang valley of China, but also worldwide. This should be a cause for concern.

Gastric cancer has a higher male-to-female ratio: reaching nearly 6:1 in the United States^[30]. The high ratio also existed in the Hehuang valley: the 10 years observation of gastric cancer showed that the male-to-female ratio was 3.6:1 (Table 4). The moderately differentiated type was the major histological type of gastric cancer in male patients.

In England, the incidence of gastric cancer is related to ethnic groups^[31]. There are significant variations in the overall incidence of gastric cancer between different ethnic groups living in the same region. The ethnic distribution of gastric cancer is different, with a preponderance in Whites over Blacks in the United States and non-Maoris over Maoris in New Zealand^[30]. In the present study, the race with highest incidence of gastric cancer was Muslim, followed by Han (Table 3). However, there was no significant difference in the distribution of age ($P = 0.511$) and sex ($P = 0.281$) among three ethnic groups in the Hehuang valley.

Dietary factors associated with gastric cancer

Diet has a great influence on the human body. Continuous use of high doses of salt result in early atrophic gastritis and increase the later risk of stomach cancer^[32]. Recently, a meta-analysis of prospective studies of ha-

Table 5 Comparison of dietary habits in gastric cancer patients and healthy residents in Hehuang valley *n* (%)

	Male		<i>P</i> value	Odds ratio (95%CI)	Female		<i>P</i> value	Odds ratio (95%CI)
	Gastric cancer patients (<i>n</i> = 1868)	Healthy residents (<i>n</i> = 1810)			Gastric cancer patients (<i>n</i> = 511)	Healthy residents (<i>n</i> = 500)		
Smoking	326 (17.5)	298 (16.5)	0.425	1.73 (0.903-1.274)	2 (0.4)	3 (0.6)	0.636	0.651 (0.108-3.912)
Drinking alcohol	475 (25.4)	460 (25.4)	0.963	1.004 (0.865-1.164)	5 (1.0)	6 (1.2)	0.734	0.814 (0.247-2.683)
Rapid eating	1492 (79.9)	320 (17.7)	< 0.001	18.476 (15.659-21.801)	12 (2.3)	10 (2.0)	0.704	1.178 (0.504-2.753)
Irregular dinner-time	285 (15.3)	237 (13.1)	0.600	1.195 (0.992-1.439)	15 (3.0)	17 (3.4)	0.673	0.859 (0.424-1.740)
Regular consumption of overnight food	153 (8.2)	142 (7.8)	0.700	1.048 (0.826-1.330)	36 (7.0)	28 (5.6)	0.345	1.278 (0.767-2.128)
Regular consumption of preserved food	269 (14.4)	254 (14.0)	0.750	1.031 (0.856-1.240)	164 (32.1)	105 (21.0)	< 0.001	1.778 (1.338-2.363)
Regular consumption of fried or grilled food	1320 (70.7)	410 (22.7)	< 0.001	8.225 (7.090-9.541)	350 (68.5)	62 (12.4)	< 0.001	15.358 (11.097-21.253)
Consumption of high-salt, high-fat and spicy food	1437 (76.9)	35 (1.9)	< 0.001	169.807 (118.983-240.290)	368 (72.0)	122 (24.4)	< 0.001	7.973 (0.602-10.560)
Drinking strong boiled brick-tea ¹	1395 (74.7)	260 (14.4)	< 0.001	17.582 (14.867-20.793)	375 (73.4)	120 (24.0)	< 0.001	8.732 (6.573-11.598)
Eating too hot or too cold food	1205 (64.5)	45 (2.5)	< 0.001	71.286 (52.249-97.260)	45 (8.8)	32 (0.6)	0.149	1.412 (0.882-2.262)

¹Boiled brick-tea is a pressed dark tea popular in Northwestern China.

bitual salt intake and risk of gastric cancer showed that dietary salt intake was directly associated with risk of gastric cancer^[33]. In our study, there was a significant relationship ($P < 0.001$) between consumption of high-salt and gastric cancer in males and females (Table 5). Not only high-salt intake, but also high-fat and spicy foods were related to the incidence of gastric cancer. Unfortunately, quantitative data are lacking in our research. Tea is a specialty drink of China. Some studies have shown that tea consumption reduces the risk of gastric cancer^[34,35]; however, others disagree^[36,37]. Boiled brick-tea, a popular fermented Chinese dark tea, is a common drink in the Hehuang valley. Our study showed that drinking strong Boiled brick-tea was significantly ($P < 0.01$) associated with gastric cancer (Table 5). Fungal growth during the production process is the key step^[38], so the factor associated with cancer might be the Fungi. The relationship between tea consumption and cancer still needs further investigation. Moreover, some incorrect diet patterns, like eating too hot or too cold food and rapid eating in males, also lead to an increased incidence of gastric cancer (Table 5). These incorrect eating habits might related to the work pressure and male-dominated responsibility for their families. Therefore, advocating a scientific and reasonable diet would be very useful to reduce the incidence of gastric cancer. There were some limitations in this study, such as no investigation of the mortality rate and socioeconomic status of patients with gastric cancer. Thus, a further study on gastric cancer is necessary.

In conclusion, gastric cancers exhibit unique epidemiological features, characterized by marked dietary habits and differences based on race, sex, and age. The results in this study will help our understanding of the characteristics and trends of the clinical epidemiological data in the Hehuang valley, and provide a reference for the diagnosis

and prevention of regional gastric cancer.

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COMMENTS

Background

Gastric cancer is the second most common cause of death in all types of malignant tumors according to data released by the Ministry of Health. The incidence and mortality of gastric cancer vary geographically, with the highest rates in China, although a trend of declining incidence has been observed. Numerous epidemiological studies have been conducted in China to identify environmental lifestyle factors that contribute to the development of gastric cancer. Hehuang valley, one of the high-risk area of gastric cancer in China, is an important population center on the ancient Silk Road, and a systematic clinical epidemiological study of gastric cancer is necessary. In this study, a clinical epidemiological study of gastric cancer in Hehuang valley was performed.

Research frontiers

Hehuang valley, one of the most important stations on the Tang-Tibet Road and the ancient Silk Road, is located in the northeast of the Qinghai-Tibetan Plateau. The Hehuang valley has convenient transportation and relatively low elevation, and three-quarters of the population of Qinghai province are concentrated in this area. The authors investigated the clinical epidemiology of gastric cancer in Hehuang valley of China, and provided a reference for treatment and prevention of regional gastric cancer.

Innovations and breakthroughs

Differences were existed in races, sex, and age of patients according to the epidemiology of gastric cancer in Hehuang valley. Moreover, dietary habit was also an important factors contributing to gastric cancer.

Applications

Gastric cancers exhibit unique epidemiological features, characterized by marked dietary habits and differences based on race, sex, and age. The results in this study help to understand the characteristics and trends of the clinical epidemiological data in the Hehuang valley, and provide a reference for diagnosis

and prevention of regional gastric cancer.

Terminology

Hehuang valley is a fertile triangle zone carved out by the Yellow River and Huangshui River, and it is located between the Daban and Jishi Mountains, in the northeast of the Qinghai-Tibetan Plateau. Hehuang valley is also the transitional zone of the Qinghai-Tibetan Plateau and the Huangtu Plateau in the northwest of China where it is the main agricultural region. Furthermore, it includes thirteen administrative counties along the Yellow River and the Huangshui River in Qinghai province. It has a typical plateau climate, such as low pressure, hypoxia and cold in Hehuang valley through the year and its average height above sea level is 2000-3000 m. Native people dwelling in Hehuang valley comprise Hui, Salar, Tu, Tibetan and Han nationalities. Certain studies have shown that the regions along the Silk Road are high-risk areas of gastric cancer, and the Hehuang valley is one of the most important stations on the Tang-Tibetan Road and the ancient Silk Road.

Peer review

In this study, the authors conducted a clinical-epidemiology study of gastric cancer in Hehuang valley of Qinghai Province in China. They included 2379 cases of gastric cancer from the past 10 years. They analyzed the following criteria: histopathological classification of gastric cancer, tumor location according to the anatomy of the stomach, age, sex, ethnic origin and dietary factors. The epidemiology of gastric cancer in Hehuang valley shows differences in its prevalence according to race, sex, and age of patients. Dietary habits were also important factors contributing to gastric cancer. The report represents a contribution to the study of the epidemiology of gastric cancer worldwide, especially in Asia.

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