

Clinical Characteristics of Gastric Cancer Among Chinese Patients Below 40 Years of Age

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Introduction: Gastric carcinoma is one of the major leading cause of cancer deaths worldwide. In many populations, however, there has been a dramatic decrease in its occurrence, though incidence varies significantly from country to country and within subpopulations. The poor prognosis of gastric cancer can be attributed to late presentation and diagnosis. Hence, early diagnosis of gastric cancer in young would enable improved prognosis and limit the evolution of disease. The aim of this study was to evaluate the clinical characters of gastric carcinoma in young Chinese patients aged below 40 years. METHODS: A retrospective study analysis was conducted at the Gastroenterology department of Union Hospital, Tongji Medical College of Huazhong University of Science and Technology, Wuhan, China for a period of 1 year from July 2009 to June 2010. A total of 130 patients younger than 40 years identified as consecutive gastric cancer cases from 2002 till 2009 and managed at the department were recruited. All participants were confirmed cases of malignancy and data was obtained from the clinical history files of the record room. Demographic details were included along with significant clinical information about carcinoma like preexisting benign gastric conditions, initial symptoms at diagnosis, radiological image examination, pathology, tumor marker, lymphatic invasion and metastasis stage. The study observed strict ethical consideration of Tongji Medical College and was approved by the ethical committee, and verbal informed consent was obtained from all the study participants to avoid ethical issues. All the data was analyzed by using SPSS version 18, and a P-value of 0.05 was considered significant.

RESULTS: Our study clearly reflected that majority of the cases had multifactorial etiology for gastric cancers. The incidence of gastric cancer was not predominantly involved to Helicobacter pylori, suggesting that environmental factor, diet or a genetic predisposition is becoming important risk factors for gastric cancer among the younger people in China.34.6% of our study participants had invasive carcinoma, and it was predominantly present at the gastric antrum. Most of the symptoms occurred during the middle age and affected both genders equally. Malena was strongly associated to women than men (P<0.01; 95% C.I., 15.047-16.962), and came out to be statistically significant. Also, our study ruled out that there was greater incidence of gastric malignancies among female gender (P<0.001). Immunohistochemical analysis showed that the minimum detectable concentration was slightly higher for CA 125 than for the other assays.

CONCLUSIONS: We concluded that pathophysiological process, such as environmental factors and dietary; may interact with genetic factors. The question of whet her age at acquisition of H. pylori infection has a bearing on the association with gastric cancer or ulcer disease is important in understanding the pathophysiology of disease process. A transmissible agent may not be significant in those cases and environmental factors or diet is becoming important risk factors as concluded by our study. Most stomach cancers (88%) are adenocarcinomas which may be further classified into poorly to moderately differentiated. The most common histological type ruled out in our study was poorly differentiated adenocarcinoma (68%). This and the signet ring cell cancers (26%) are the forms most closely corresponding to Lauren's diffuse type. The differentiated and tubular cancers resembling the intestinal tumors comprised 11%, while a few tumors could not be classified by Lauren's criteria. The adenocarcinomas are associated with a history of atrophic gastritis and are generally found in patient's age range between 25 to 35years.

KEYWORDS

Gastric Carcinoma, Clinical Characters, China.

Introduction

Gastric carcinoma is one of the most common malignancies worldwide. Although the incidence of gastric cancer has been declining steadily, gastric cancers remain the second most common malignancy in the world (1, 2) and contribute to significant cancer mortality, particularly in Asia (China, Japan, and Korea), parts of Europe and Latin America.

Multiple environmental factors, including *Helicobacter pylori* infection (3) and dietary factors (4), have been implicated in the initiation of gastric carcinogenesis. It occurs mainly in elderly patients, with a peak incidence over 60 years of age (5). Gastric cancer occurring in young patients, also designated as early onset gastric cancer (EOGC),accounts for less than 8%

of all cancers developing in the stomach (6). Controversial data have been reported in the literature regarding the clinicopathological features and prognosis of EOGC, and little is known about its profile in European populations (7). In other geographic regions like Japan (8), Taiwan (9), Korea (10), USA (11), Mexico (12) and South Africa (13), EOGCs occur predominantly in women and most of them are diffuse carcinomas according to Lauren's (14) classification. Regarding the prognosis of the disease, some studies suggested that younger patients have a poor prognosis (9, 13) due to delayed diagnosis and aggressive behavior, whereas other studies indicated that clinical outcome is mainly dependent on stage at diagnosis, regardless of the age of patients (7, 8, 11).

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The poor prognosis of gastric cancer can largely be attributed to late presentation and diagnosis. In contrast to the West, Japan has introduced systematic mass screening programs which have led to increased detection rates of gastric cancers confined to the mucosa or submucosa (so called early gastric cancers) (15).

Unlike the low survival rates usually associated with gastric cancer, patients with early gastric cancers have 5-year survival rates in excess of 90% independent of their histological subtype. Hence, this would suggest that if all gastric cancers could be detected early, it would enable improved prognosis. Aside from mass screening programs which have large cost implications and may be impractical, another approach would be to identify individuals at high risk for developing gastric cancer. The major risk factor for intestinal gastric cancer identified so far is Helicobacter pylori infection (16, 17). However, whether H. pylori eradication is an effective cancer prevention measure has not yet been proven (17). In contrast to these sporadic occurrences of gastric cancers, a small percentage of gastric cancers (1-3%) arise as a result of clearly identified inherited gastric cancer predisposition syndromes (18). The existence of a familial gastric cancer has been known about since the 1800s, when multiple cases of gastric cancers were observed in the Bonaparte family (19). Gastric cancers can be classified in terms of their anatomical sites as well as histopathological subtypes. The two major histopathological subtypes are the intestinal and the diffuse or linitis-plastica type. The diffuse types are common in endemic areas, tend to have a poorer prognosis and their etio-pathology is less well understood. A subset of these diffuse type gastric cancers is hereditary and recently, linkage analysis has implicated E-cadherin (CDH1) mutations in an estimated 25% of them (20). This subset of gastric cancer has been termed hereditary diffuse gastric cancer (HDGC).In this study we investigated the clinical characters of gastric carcinoma in young Chinese population aged younger than 40 years using available data and scientific methods. The basic aim was to rule out the specific pattern of disease with disease burden, and try to make possible causation factors

Material and methods Selection of the Patients

A retrospective database study was conducted at the Gastroenterology department of Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China. They study period was about 1 year from July 2009 to June 2010. A systematic review of the database of 130 patients, younger than 40 years of age, with defined pathological diagnosis of gastric cancer that were managed at this institution between 2002 and 2009 was performed. All the patients were cases of primary advanced gastric carcinoma.

Data Recording

Data was collected from patient history sheets at the record room of the hospital and was analyzed to identify the influence of various factors on the etiology for young patients with gastric carcinoma. A total of 130 patients record were available for the study. Patient with diagnosis of gastric cancer were evaluated in term of age, sex, race and symptoms.

Clinical manifestations, image examination, pathological, and operative records of these patients were reviewed to identify patients with pattern of gastric cancer. The age, sex, course of disease, tumor location, symptoms, image examination, pathology, tumor mark, lymphatic invasion and metastasis stage were evaluated by reviewing medical charts and pathologic records. The implication of the Helicobacter pylori and genetic predisposition were also evaluated.

Data Analysis

Potential factors related to gastric carcinoma and some outcome variables were adjusted. Chi-square test was used to calculate the trends of various factors influencing gastric carcinomas. The categorical variables were described by using logistic regression so as to compare the data and analyze the incidence of the gastric cancer among the studied population. Different groups were compared by multinomial logistic regression and were expressed in terms of confidence intervals (CI) 95% and P-values. A P-value of 0.05 was considered significant. All the data were analyzed using SPSS version18.0 and PASWStatistics18 (SPSS Inc. Chicago, Illinois. U.S.).

Results

The mean age of the patients was 30.51 years. Of all patients, 81 (62.3%) were female and 49 (37.7%) were male. Patients were categorized by age range of 5 years. We estimated the number of people who needed to be screened for gastric cancer is more important for those aged between 26-30 years and 31-35 years old with cumulative percentage of 23.8% and 56.95% respectively (table 1).

Table 1: Total number and percentage of patients screened for gastric cancer by Age and Sex

| Age (years) | Female | Male | Total | Percent |
|-------------|--------|------|-------|---------|
| Age(years) | | | | |
| ≤20 | 4 | 4 | 8 | 6.2% |
| 21-25 | 8 | 2 | 10 | 7.7% |
| 26-30 | 22 | 9 | 31 | 23.8% |
| 31-35 | 42 | 32 | 74 | 56.9% |
| 36-40 | 5 | 2 | 7 | 5.4% |
| Total | 81 | 49 | 130 | 100% |

Table 2: Incidence of Helicobacter pylori among young Chinese patients

| | He | elicobacter Pylori | |
|-------------|----------|--------------------|-------|
| Age (years) | Negative | Positive | Total |
| ≤20 | 8 | 0 | 8 |
| 21-25 | 10 | 0 | 10 |
| 26-30 | 30 | 1 | 31 |
| 31-35 | 73 | 1 | 74 |
| 35-40 | 7 | 0 | 7 |
| Sex | | | |
| Male | 49 | 0 | 49 |
| Female | 79 | 2 | 81 |

The results in the table (2) show that the incidence of gastric cancer among the patients was not predominantly involved to Helicobacter pylori. Only two cases out of 130 patients were tested positive, suggesting that environmental factors, diet or a genetic predisposition is becoming important risk factors for gastric cancer among the younger people in China.

Table 3: Family history in the gastric cancer in young Chi-

| Age (years) | Total | Yes | Percent | |
|-------------|-------|-----|---------|--|
| ≤20 | 8 | 0 | 0.0% | |
| 21-25 | 10 | 0 | 0.0% | |
| 26-30 | 31 | 2 | 0.6% | |
| 31-35 | 74 | 7 | 0.9% | |
| 35-40 | 7 | 0 | 0.0% | |
| Sex | | | | |
| Female | 81 | 5 | 0.6% | |
| Male | 49 | 4 | 0.8% | |

<u>Table 4</u>: The distribution of gastric carcinoma in screened patients by age group and sex

 $\underline{\textbf{Table 4}}\text{: The distribution of gastric carcinoma in screened patients by age group and sex}$

| | | | Age | | | | | Sex | | |
|-------------------------|-----|-------|-------|-------|-------|-----------|------|--------|---------|----------|
| | ≤20 | 21-25 | 26-30 | 31-35 | 36-40 | Total | Male | Female | Ratio | P-value |
| Location | | | | | | | | | | |
| Cardia | 0 | 1 | 4 | 4 | 0 | 9(6.9%) | 1 | 8 | 0.125/1 | P =.665 |
| Gastric, fundus | 2 | 0 | 1 | 2 | 0 | 5(3.8%) | 2 | 3 | 0.667/1 | P =.993 |
| Gastric body | 3 | 4 | 8 | 21 | 3 | 39(30.0%) | 15 | 24 | 0.662/1 | P =.899 |
| Gastric body, G. antrum | 0 | 0 | 0 | 5 | 0 | 5(3.8%) | 3 | 2 | 1.5/1 | P =.605 |
| Gastric antrum | 1 | 4 | 11 | 27 | 2 | 45(34.6%) | 18 | 27 | 0.667/1 | P = .917 |
| Gastic angle, antrum | 0 | 0 | 1 | 0 | 0 | 1(.8%) | 0 | 1 | 0/1 | P =.995 |
| Gastric angle | 0 | 0 | 3 | 7 | 1 | 11(8.5%) | 3 | 8 | 0.375/1 | P =.660 |
| Gastric remnants | 0 | 0 | 1 | 1 | 0 | 2(1.5%) | 1 | 1 | 1/1 | P=.768 |
| NS | 1 | 1 | 2 | 7 | 1 | 12(9.2%) | 5 | 7 | 0.714/1 | P =.882 |
| Total | 8 | 10 | 31 | 74 | 7 | 130(100%) | 49 | 81 | 0.605/1 | |

NS not specified

Invasive carcinoma was also localized in the stomach body with 39 cases. Off these 39 cases, 21 were between 31 and 35 years old. 11 cases (8.5%) were located in the gastric angle. In all cases, 12 (9.2%) were not specified. The rest of the cases were disseminat-

ed through the esophagus, cardia, fundus, antrum, and the gastric remnant. The ratio male/female shows that female are more susceptible to gastric carcinoma. However, we recorded no significant differences between men and women or between different age

groups in the effect of screening on any outcome, in the location of the cancer through the stomach.

Table 5 a: Clinical symptoms of gastric carcinoma

| Symptoms | Diarrhea | Haematemesi | s Hematochezia | Melena | Vomit | Abdominalgia | Ab. distention | Ab. mass | Weight change |
|-------------|-----------|-------------|----------------|------------|------------|--------------|----------------|-----------|---------------|
| SEX | | | | | | | | | |
| Female | 2/81(2%) | 3/81(4%) | 15/81(19%) | 16/81(20%) | 23/81(28%) | 73/81(90%) | 61/81(75%) | 7/81(9%) | 36/81(44%) |
| Male | 4/49(8%) | 3/49(6%) | 16/49(33%) | 16/49(33%) | 13/49(27%) | 42/49(86%) | 30/49(61%) | 3/49(6%) | 20/49 (41%) |
| AGE (years) | | | | | | | | | |
| ≤20 | 1/8(12%) | 1/8(12%) | 3/8(38%) | 3/8(38%) | 3/8(38%) | 7/8(88%) | 6/8(75%) | 0/8(0%) | 5/8(62%) |
| 21-25 | 1/10(10%) | 0/10(0%) | 4/10(40%) | 4/10(40%) | 3/10(30%) | 9/10(90%) | 7/10(70%) | 1/10(10%) | 7/10(70%) |
| 26-30 | 1/31(3%) | 0/31(0%) | 5/31(16%) | 5/31(16%) | 9/31(29%) | 28/31(90%) | 24/31(77%) | 4/31(13%) | 14/31(45%) |
| 31-35 | 3/74(4%) | 5/74(7%) | 19/74(26%) | 20/74(27%) | 18/74(24%) | 65/74(88%) | 50/74(68%) | 3/74(4%) | 27/74(36%) |
| 36-40 | 0/7(0%) | 0/7(0%) | 0/7(0%) | 0/7(0%) | 3/7(43%) | 6/7(86%) | 4/7(57%) | 2/7(29%) | 3/7(43%) |

Ab. distention, Abdominal distention; Ab. mass, Abdominal mass

Symptoms of stomach cancers usually do not become apparent until it has reached an advanced stage. Most symptoms of gastric cancers are related to the location of the tumor. As the cancer spreads to these other sites along the gastrointestinal tract, symptoms such as vomit, weight lost, abdominal distention may be experienced. The table 5a gives the approximate value of the statistical parameter measured. It's indicates that most of the symptoms occurred during the middle age and affected both men and women.

<u>Table 5b</u>: Logistic regression analysis of the risk of developing cancer gastric symptoms

| Symptoms | Yes | χ^2 | P | 95% Confidence Interval |
|----------------------|------------|----------|------|-------------------------|
| Abdominalgia | 115(88.5%) | .286 | .593 | .192 – 2.566 |
| Abdominal distention | 91(70.0%) | 2.293 | .130 | .214 - 1.219 |
| Vomit | 36(27.7%) | .099 | .753 | .473 - 2.818 |
| Heamatemesis | 6(4.6%) | .390 | .532 | .067 - 4.028 |
| Melena | 32(24.6%) | 1073.796 | .000 | 15.043 - 16.962 |
| Hematochezea | 31(23.8%) | | | -16.97416.974 |
| Diarrhoea | 6(4.6%) | 1.819 | .177 | .556 - 23.939 |
| Abdominal mass | 10(7.7%) | .170 | .680 | .141 - 3.596 |

χ2, Chi-square; P, P-value

We use multiple logistic regressions to evaluate the significance in the frequency of the symptoms between men and women (table 5b). Abdominalgia, abdominal distention, weight lost, vomit, and melena are the most common and frequent symptoms and should be addressed properly when patients come to health center with these complaints. However, for most of the cases, there were no significant differences between men and women in the occurrence of symptoms of the gastric cancer. Only for melena symptom, we found significant association between gender and, women are more likely to develop the symptoms than men (P<0.01; 95% C.I., 15.047-16.962).

Pathology of gastric carcinoma

The most significant epithelial tumor of the stomach is the adenocarcinoma. Of the 130 specimens of consecutive gastric cancer examined, 10 (7.7%) had well differentiated or moderately differentiated adenocarcinoma.

<u>Table 6</u>: Clinicopathologic characteristics of gastric cancers and their prevalence on the gender and age

| | | | _ | | | _ | | | - | _ |
|-------------------------------------|-------------|-------|-------|-------|-------|-------|--------|------|------------|---------|
| | Age (years) | | | | | | Sex | | | |
| Pathology | €20 | 21-25 | 26-30 | 31-35 | 36-40 | Total | Female | Male | Total | P value |
| Anaplastic carcinoma | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 1 | 1 (0.8%) | 1.000 |
| Mucinous adenocarcinoma | 0 | 0 | 2 | 1 | 0 | 3 | 2 | 1 | 3 (2.3%) | 0.000 |
| Mucoid cell adenocarcinoma | 0 | 0 | 1 | 1 | 0 | 2 | 2 | 0 | 2 (1.5%) | 0.993 |
| Myxocyte adenocarcinoma | 0 | 0 | 2 | 1 | 1 | 4 | 3 | 1 | 4 (3.1%) | 0.000 |
| Poorly differentiated adenocarcinos | na l | 5 | 13 | 46 | 3 | 68 | 48 | 20 | 68 (52.3%) | 0.000 |
| Well differentiated adenocarcinoma | a 2 | 1 | 0 | 6 | 1 | 10 | 3 | 7 | 10 (7.7%) | 0.000 |
| Tubular adenocarcinoma | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 1 | 1 (0.8%) | ref |
| Adenocarcinoma | 3 | 6 | 19 | 56 | 5 | 89 | 58 | 31 | 89(68.5%) | |

Table 6-1 NR, Not Reported; ref, reference category, GIST, Gastric Intestinal Stromal Tumor

| | Age (years) | | | | | | Sex | | |
|-------------------------|-------------|-------|-------|---------------|-------|-------|--------|------|-------------------|
| Pathology | <u>≤20</u> | 21-25 | 26-30 | 31- <u>35</u> | 36-40 | Total | Female | Male | Total |
| Adenocarcinoma | 3 | 6 | 19 | 56 | 5 | 89 | 58 | 31 | 89 (68.5%) |
| GIST | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 1 | 1 (0.8%) |
| Signet ring cell cancer | 3 | 2 | 6 | 14 | 1 | 26 | 13 | 13 | 26 (20.0%) |
| NR | 2 | 2 | 6 | 3 | 1 | 14 | 10 | 4 | 14 (10.8%) |
| Total | 8 | 10 | 31 | 74 | 7 | 130 | 81 | 49 | 130 (100%) |

NR, Not Reported; GIST, Gastric Intestinal Stromal Tumor

Gastric cancer was more likely to be poorly differentiated adenocarcinoma with 68 cases (52.3%) characterized. In each case, neoplastic cells displayed a pure signet ring cell cancer in 20% of the cases (table 6). With multinomial logistic regressions, regardless the nature of the pathology, there was strong evidence between gender and the pathology and female are more likely to develop pathology P<0.001.

<u>Table7</u>: Comparison of serologic tumor markers assays for the diagnosis of the gastric cancer

| Tumors | CEA | | C. | A19-9 | CAI | 15-3 | CA125 | | AFP | | FERROPR | OTEIN | MICROGI | LOBULIN |
|-------------|-------------|---------|------------|---------|-----------|---------|-------------|---------|-------------|---------|------------|---------|-----------|---------|
| | %↑ | P-value | %↑ | P-value | %↑ | P-value | %↑ | P-value | %↑ | P-value | %↑ | P-value | %↑ | P-value |
| SEX | | | | | | | | | | | | | | |
| Female | 6 /33 (21%) | .881 | 9/31 (29%) | .783 | 0/21 (0%) | | 14/26 (54%) | .487 | 1/24 (0.4%) | .492 | 1/19 (0.5% |) | 0/18 (0%) |) |
| Male | 3/15 (20%) | | 4/13 (31%) | | 0/10 (0%) | | 5/13 (38%) | | 1/10 (10%) | | 0/9 (0%) | | 1/9 (11° | %) |
| AGE (years) | | | | | | | | | | | | | | |
| ≤20 | 1/4 (25%) | .810 | 2/4 (50%) | 1.000 | 0/2 (0%) | | 3/4 (75%) | .000 | 0/2 (0%) | 1.000 | 0/2 (0%) | | 0/2 (0%) | |
| 21-25 | 1/6 (17%) | .577 | 1/6 (17%) | .368 | 0/6 (0%) | | 4/6 (67%) | .000 | 0/6 (0%) | 1.000 | 0/6 (0%) | 1.000 | 0/6 (0%) | .998 |
| 26-30 | 2/10 (20%) | .634 | 3/9 (33%) | .661 | 0/5 (0%) | | 5/7 (71%) | .000 | 0/7 (0%) | 1.000 | 1/5 (20%) | .997 | 0/4 (0%) | .998 |
| 31-35 | 4/25 (16%) | .472 | 6/23 (26%) | .485 | 0/18 (0%) | | 6/20 (30%) | | 2/17 (12%) | | 0/15 (0%) | | 1/15 (0.7 | %) |
| 36-40 | 1/3 (33%) | | 1/2 (50%) | | 0/0 (0%) | | 1/1 (100%) | | 0/2 (0%) | | 0/0 (0%) | | 0/0 (0% | .) |

^{. 1.} increase

We compared serologic assays (CEA, CA 19-9, CA 125, CA 15-3, AFP, Ferroprotein and Microglobilin) for their efficacy at detecting gastric cancer. The minimum detectable concentration was slightly higher for CA 125 than for the other assays. The CA 19-9 assay exhibited a significantly higher reference interval for males than for females; otherwise there were no significant differences between the sexes. In this study, the CA125 was the best tumor antigen for use in the diagnosis of gastric cancer.

Course of the disease

The table below gives the approximation of the time consumed before the diagnosis of the clinical symptoms.

Table 8: Approximate timeline between primary infection and clinical diagnosis of the symptoms

| Course the | disease | | | | | |
|-------------|----------|------------|-------------|-----------|----------|-----------|
| | <1 month | 1-6 months | 7-12 months | 1-2 years | >2 years | Total |
| SEX | | | | | | |
| Female | 12(15%) | 42(52%) | 12(15%) | 10(12%) | 5(6%) | 81(62%) |
| Male | 8(16%) | 29(59%) | 3(6%) | 7(14%) | 2(4%) | 49(38%) |
| Total | 20(15%) | 68(52%) | 15(12%) | 17(13%) | 7(5%) | 130(100%) |
| AGE (years) | | | | | | |
| ≤20 | 1(12%) | 6(75%) | 0(0%) | 1(12%) | 0(0%) | 8(6%) |
| 21-25 | 2(20%) | 6(60%) | 1(10%) | 1(10%) | 0(0%) | 10(8%) |
| 26-30 | 6(19%) | 15(48%) | 5(16%) | 3(10%) | 2(6%) | 31(24%) |
| 31-35 | 9(12%) | 41(55%) | 9(12%) | 10(14%) | 5(7%) | 74(57%) |
| 36-40 | 2(29%) | 3(43%) | 0(0%) | 2(29%) | 0(0%) | 7(5%) |
| Total | 20(15%) | 71(55%) | 15(12%) | 17(13%) | 7(5%) | 130(100%) |

Gastric cancers usually start affecting the certain regions of the stomach after prolonged course and the complications usually arise at the end stage carcinoma. The table 8 shows that the incidence of gastric cancer is higher for patients in the age range from 25 to 35 years. The incidence undoubtedly has been increased by early diagnosis; 1-6 months time period. This early diagnosis could be favorable for patients with gastric carcinoma since the overall survival rate of patients can be increased significantly.

Invasive carcinoma

The incidence of metastasis from gastric carcinoma to various regions of the stomach was studied and correlated with their influence on the gender. The incidence of metastasis increased with deeper tumor invasion in the stomach wall. The relative importance of the incidence of the metastasis in this study is difficult to assess because of few randomization. We use multinomial logistic regression to evaluate the effects of the gender on the incidence of the metastasis on the different organs affected. For overall organs affected there is no incidence for a systematic influence of the gender on the evolution of the metastasis (table 9).

Table 9: Influence of the gender on the distribution of the metastasis through the abdominal region.

| | Sex | | |
|-----------------------------------|--------|------|-------|
| Metastasis | Female | Male | Total |
| Abdominal cavity | 8 | 8 | 16 |
| Abdominal cavity, greater omentum | 0 | 1 | 1 |
| Bladder | 1 | 0 | 1 |
| Bone, pelvic cavity | 1 | 0 | 1 |
| Greater omentum | 1 | 0 | 1 |
| Greater omentum, pelvic cavity | 0 | 1 | 1 |
| Liver | 0 | 1 | 1 |
| Liver, pelvic cavity | 0 | 1 | 1 |
| Ovary | 1 | 0 | 1 |
| Peritoneum | 0 | 1 | 1 |
| Retroperitoneum | 0 | 1 | 1 |
| Total | 12 | 14 | 26 |

Organs include abdominal cavity, greater omentum, bladder, greater omentum, pelvic cavity, liver, ovary, peritoneum and retroperitoneum were examined by using hematoxylin and eosin. All sections were reviewed by pathologists. The size of the metastases was measured. All patients were radiologically analyzed in order to detect metastases.

 $\underline{\textit{Table 10}}$: Distribution of invasive cancer through the region

| | | Se | x | | Percent | |
|--------------|-----------------|--------|------|-------|---------|---------------|
| Infiltration | Organs affected | Female | Male | Tota1 | | 95% C.I. |
| | Mucosa | 1 | 0 | 1 | 1.0% | 1.001 - 1.001 |
| | Sub-mucosa | 7 | 4 | 11 | 10.8% | ref |
| | Muscular | 7 | 5 | 12 | 11.8% | 0.149 - 4.297 |
| | All layers | 48 | 30 | 78 | 76.5% | 0.247 - 3.390 |
| | NR | 18 | 10 | 28 | | |
| | Total | 81 | 49 | 130 | | |

NR, not reported; ref, reference category; percents were calculated without considering the not reported cases.

The depth of invasion correlated strongly with the incidence of the cancer. Invasive carcinoma was detected in all layers in 76.5% of specimens analyzed. Carcinoma was confined to all organs, with the majority of foci occupying the upper half of the mucosa (submucosa) and spreading superficially. In a single case, carcinoma occupied the entire mucosa, without invasion into the submucosa. The estimated relative area of mucosa infiltrated by invasive carcinoma was small (the percentage of mucosa involved by cancer was (1.0%). In 12 cases (11.8%), infiltration was localized in the muscular. The total number of patients was examined, without an apparent relationship to gender or age of the patients. The intensity of the invasion of the regions of the stomach depends on the duration between the onset of the symptoms and the clinical diagnostic.

<u>Table 11:</u> Incidence of age and sex in the distribution of lymph nodes in various parts of the stomach

| | Age (years) | | | | Sex | | | |
|---------------------------------|-------------|--------|--------|---------|--------|--------|------|-------|
| Lymph node operated | ≤20 | 21-25 | 26-30 | 31-35 | 36-40 | Female | Male | Total |
| C. ventr. Minor, g.g. curvature | (0%) | 3(75%) | 5(31%) | 19(54%) | 3(75%) | 19 | 11 | 30 |
| Greater gastric curvature | (0%) | 1(25%) | 7(44%) | 6(17%) | 1(25%) | 11 | 4 | 15 |
| Curvature ventricular minor | (0%) | 0(0%) | 4(25%) | 9(26%) | 0(0%) | 7 | 6 | 13 |
| Upper pyloric lymph nodes | (0%) | 0(0%) | 0(0%) | 1(3%) | 0(0%) | 1 | 0 | 1 |
| Total | 0 | 4 | 16 | 35 | 4 | 38 | 21 | 59 |

C. ventr. minor; curvature ventricular minor; g.g. curvature: greater gastric curvature

The distributions of the lymph nodes by age and sex are detailed in the table 11. Lymph nodes were most frequently located in the curvature ventricular minor and in the greater gastric curvature. Only one single case was located in the upper pyloric. The incidence of nodes varied in patients aged between 30 to 35 years and are proportionately distributed between the lesser curvature (13 cases) and the greater gastric (15 cases). We also noted that in 30 cases, the presence simultaneous of the lymph nodes in these two parts of the stomach.

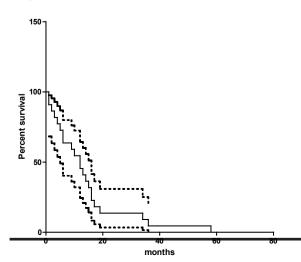


Figure 1: Survival proportions of patients with operated lymph nodes. The curve is defined with a 95% confidence interval.

Comparison of survival rates of patients with operated lymph nodes show a significant differences P < 0.001, QR (95% C.I. = 0.037 (0.01503-0.09541)) with median survival of 12 months (figure 1).

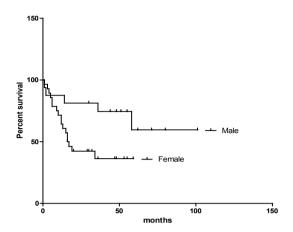


Figure 2: Survival rates curves according to the sex of the patients.

Log-rank Mantel-Cox test show a significant difference between male and female P = 0.0311 OR (95% C.I. = 0.1609 – 0.9170) with a median survival of 16.5 months for females. Men with gastric carcinoma show a better survival rate than females (figure 2).

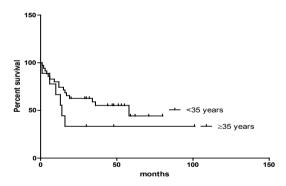


Figure 3: Cumulative survival of patients aged 35 years or less and those aged more than 35 years.

Multivariate analysis showed that there was a significant prognostic factor of survival for gastric carcinoma in patients with operated lymph nodes and in patients' gender. The survival rates of young and older patients did not differ significantly. However, the young patients with gastric carcinoma had a better survival rate than older patients with gastric carcinoma (fig.3). Multivariate analysis showed that age and gender were not independent prognostic factors of survival for gastric carcinoma in young patients.

Discussion

Certain genetic or familial background, and conditions resulting in gastric dysplasia have been reported as definite risk factors for the development of stomach cancer. The use of tobacco, dietary risk factors and excess alcohol consumption also has been implicated as causal elements (21, 22). In our study, the sex distribution of young patients with gastric cancer is interesting with predominance of females in all age (male/female ratio, 0.605/1). The same tendency have been observe by Umeyama et al (23) in patients younger than 30 years, however the number of patients involve in that study

was very small (n = 13). A variety of studies now indicate that there is a strong association between chronic Helicobacter pylori infection and gastric adenocarcinoma (24), especially of the distal stomach (25). Previous studies have suggested that most H. pylori infections are acquired during childhood (26), and factors such as family crowding and unavailability of hot water during childhood have been associated with increased risk of transmission (27). Alternatively, our findings could indicate that infection with H. pylori at a very young age may be a particularly vulnerable period and thus could lead to increased cancer risk. These observations suggest that, environmental factors or diet is becoming important risk factors for gastric cancer among the younger patients in China. As few as 1% to 3% of all gastric carcinomas have an autosomal dominant gastric cancer susceptibility, for which highly penetrated mutations account for the increased risk (28). Cumulative incidence for all cancer is higher in the middle age group ranged between 30 and 40 years. Several studies have shown that younger patients have higher frequencies of gastric cancers located in the body (29), while others have reported a higher frequency in the antrum (30, 31). In our study, a higher frequency of cases with cancer located in the antrum was observed in both groups of patients, for all histological types of carcinomas. Early stage stomach cancer may be symptom less or have vague and non-specific symptoms such as indigestion, tiredness or loss of appetite. Consequently it is difficult to differentiate between benign conditions and early cancer by symptoms alone. Unfortunately the majority of patients present with advanced disease: their symptoms may include nausea, vomiting, pain, weight loss, abdominalgia, abdominal distention, melena. Most symptoms of gastric cancers are related to the location of the tumor. We recorded that abdominalgia and abdominal distention are the most frequently diagnosed symptoms with respectively 115 and 95 cases out of 130 patients. Most stomach cancers (88%) are adenocarcinomas which may be further classified into poorly to moderately differentiated. The most common histological type was poorly differentiated adenocarcinoma (68%). This and the signet ring cell cancers (26%) are the forms most closely corresponding to Lauren's diffuse type. The differentiated and tubular cancers resembling the intestinal tumors comprised 11%, while a few tumors could not be classified by Lauren's criteria. The adenocarcinomas are associated with a history of atrophic gastritis and are generally found in patient's age range between 25 to 35years. In the current study, cancer tumors were most frequently located at the muscularis and submucosa, with these positions in 11% and 12%, respectively. Invasive carcinoma was detected in all layers in 76.5% of specimens analyzed. The depth of invasion into the stomach wall and metastases to lymph nodes dissected from the fresh specimen, on an average more than 59 nodes, were recorded. The areas of tumor growth were recorded in order of importance, in accordance with the circumferential position. Lymph node metastasis is one of the most important determinants of whether minimally invasive surgery for early gastric cancer is appropriate, since lymph node dissection generally is considered unnecessary for early gastric cancer without nodal metastasis. Nodes metastases can be resected with subsequent long term survival, (32) but opinions differ as to the desirable extent of node dissection (33, 34). Surgery is the only potentially curative modality for localized gastric carcinoma. In accordance with most literature reports, curative resection offered the only chance of long-term survival. In this study, the 5-year survival rates of young and older patients did not differ significantly and young patients with gastric carcinoma had a better survival rate than older patients with gastric carcinoma (median survival = 54 months vs 14 months). The role of chemotherapy in prolonging life, either with adjuvant or palliative intent, is controversial. There were many prospective randomized trials for adjuvant chemotherapy after curative resection. Most of the reports demonstrated no survival advantage for adjuvant chemotherapy. Adjuvant chemotherapy was not actively applied for these advanced gastric carcinomas in our institution.

Conclusions

We concluded that pathophysiological process, such as environmental factors and dietary; may interact with genetic factors. A close association has been observed between diffuse gastric cancer and family history in a younger generation of young patients. So that Although H. pylori infection is generally associated with intestinal type gastric cancer in western countries. Some symptoms may be nonspecific and relatively minor, epigastric pain in patients at risk groups should prompt endoscopic evaluation. Further, identification of gastric cancer within young populations necessitates extended biopsy techniques, careful follow-up and appropriate treatment.

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