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BRIEF ARTICLE

Analysis of demographic characteristics in 3242 young age gastric cancer patients in Korea

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Abstract

AIM: To evaluate the epidemiologic features of young age gastric cancer (GC).

METHODS: Retrospectively, a total of 3242 patients with GC between 18 and 45 years of age and 3000 sex- and age-matched controls were reviewed. All subjects were stratified into 3 groups based on age (A, 18-30 years; B, 31-40 years; C, 41-45 years). Epidemiologic characteristics and risk factors were investigated with reference to their age and gender.

RESULTS: Compared to controls, more frequent intake of high risk diet (P = 0.00075), history of heavy smoking (P = 0.00087), intake of heavy alcohol (P = 0.00091), lower social economic status (P = 0.00083), body mass index > 30 (P = 0.00097), urban residence (P = 0.00065), and more frequent exposure to harmful occupational environments (P = 0.00072) were observed in all age groups and both genders in young age GC. These relationships were weaker in females compared to males of the same age, and were stronger as the age of patients increased. However, in group C of young age GC patients, environmental factors played important roles in females and males with a similar body weight. In females, older age at first delivery (> 35 years), lack of lactation history, nulliparity, and poor nutritional status during pregnancy were significantly associated with an increased risk of GC (P = 0.00034). In this study, 252 patients (7.8%) had a family history of GC with high odds ratio (OR) (3.22-4.21). In particular, family history was more closely associated with GC in males (OR, 4.21 in male *vs* 3.46 in female) and more advanced cases (P = 0.00051).

CONCLUSION: Hormonal associated factors were more commonly associated with females whereas environmental factors were more commonly associated with males in young age GC patients.

Key words: Young age gastric cancer; Epidemiology; Risk factor; Age; Gender

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INTRODUCTION

Although gastric cancer (GC) is considered to be a disease of the middle aged and elderly[1], 2%-15% of patients with GC are younger than 45 years of age (defined as young age GC)[2-5], and there has been an increase in the relative proportion of young age GC compared with older age GC[6-8] especially in young females[8]. Until now, a lot of studies about epidemiologic and clinicopathologic features of GC, including risk factors, have been conducted in the elderly. However, in young age GC, only a few studies with small-sized samples have been conducted. The results of these studies were widely variable within each study[1-8], which may be due to bias or low statistical power. In this study, we reviewed our institution's experience of the demographic and clinicopathologic features of GC in young patients between 18 and 45 years of age (defined as young age GC) from January 1990 to April 2008. Simultaneously, a total of 3000 sex- and age-matched healthy controls living in the same period were enrolled, all of whom received endoscopy at the Department of Gastroenterology and Health Care Center for the evaluation of the risk of young age GC. This retrospective, large-scale, and population-based study with abundant epidemiologic and clinicopathologic information in a single institution may reduce the limitation and bias of small sample-sized studies like those performed previously and confirm more accurate data.

The question of whether young age GC is different from that of older patients has been raised but remains unresolved. According to epidemiologic studies of GC, a marked variation was seen in the incidence of GC according to sex and ethnics[1-8]. This fact suggests that sex hormones may modulate GC risk because the status of sex hormones is dependent on age. Therefore, sex as well as age may be considered simultaneously to precisely evaluate the epidemiologic study of GC including risk factors. Additionally, according to previous data, the demographic and clinicopathologic features of young age GC were somewhat different between patients younger and older than 30 years of age[9]. Therefore, further epidemiologic evaluation of young age GC should be done after subdivision of age into younger and older than 30 years old. Based on these assumptions, we investigated the epidemiologic characteristics and risk factors of young age GC with reference to age and sex in Korea, a country with a high rate of GC.

MATERIALS AND METHODS

Subjects

From January 1990 to April 2008, a total of 21 738 patients were diagnosed with GC at Severance Hospital, Seoul, Korea. Among them, 3 242 patients between 18 and 45 years of age (14.9%) were enrolled in the current study. In same period, a total of 3000 sex- and age-matched individuals who received endoscopy with or without gastrointestinal symptoms at the Department of Gastroenterology and Health Care Center were also enrolled as healthy controls to evaluate the risk of young age GC. All subjects were stratified into 3 groups based on age (A, 18-30 years; B, 31-40 years; C, 41-45 years) at initial diagnosis.

Epidemiologic and clinicopathologic characteristics

This study included data on each subject's age, sex, lifestyle (e.g. smoking or alcohol, and diet pattern), occupational environment, place of residence, body mass index (BMI), family history of GC, socioeconomic status, and combined diseases. For women, history of oral contraceptive use, pregnancy/delivery (time of first pregnancy/delivery, nutrition conditions during pregnancy, and parity status), lactation, and menstruation were also investigated. Socioeconomic conditions were stratified into 3 groups based on household income epidemiology in Korea. For evaluation of nutritional status during pregnancy, weight gain, electrolyte imbalances and the level of albumin and hemoglobin during pregnancy were investigated. The level of weight gain was estimated according to prepregnant BMI categories as recommended by the Institute of Medicine[10].

For all subjects, hematological (total blood count), biochemical (routine chemistry), and serological [IgG for *Helicobacter pylori* (*H. pylori*)] evaluations including tumor markers [carcinoembryonic antigen, α-fetoprotein (αFP), and cancer antigen (CA125)] were conducted. For GC, tumor location, number of lesions, growth type (Lauren classification), histological type (World Health Organization classification), and TNM stage were analyzed at initial diagnosis, and treatment-related results including overall survival were assessed.

Specimen histology

Tissue samples were stained with hematoxylin and eosin solution. Giemsa staining was also performed to detect *H. pylori* infection. The degree of gastritis, combined glandular atrophy with intestinal metaplasia (IM), and *H. pylori* infection were graded according to the updated Sydney classification[11].

Statistical analysis

The data are presented as median ± SD. Analysis of variance with multiple comparison (Scheffe post hoc) and χ^2 analysis (Pearson) were conducted to compare data among age groups in each different gender using the Statistical Package for the Social Sciences (SPSS/PC+ 13.0, Chicago, IL, USA). Analysis of survival was performed using the Kaplan-Meier method. For comparison of laboratory findings between the cancer groups and controls, *t*-test was conducted. Epidemiologic risk factors of young age GC were evaluated by comparing them with age-matched controls in each different gender using logistic regression with odds ratios (OR) and 95% confidence intervals (CI). A *P* value of less than 0.05 was considered statistically significant.

Table 1 Demographic and clinicopathologic features of young age in control group *n* (%)

Features	Group A (*n* = 350)	Group B (*n* = 1500)	Group C (*n* = 1150)	Whole (*n* = 3000)	*P*-value
Age (median, yr)	24 ± 1.3	34 ± 2.4	44 ± 3.7	35 ± 4.9	NS
Sex					< 0.05
Male	150 (42.9)	750 (50.0)	750 (65.2)	1650 (55.0)	
Female	200 (52.1)	750 (50.0)	400 (34.8)	1350 (45.0)	
Indication of endoscopy					NS
No symptom	117 (33.4)	514 (34.2)	499 (43.4)	1130 (37.7)	
Dyspepsia	211 (60.3)	798 (53.2)	687 (59.7)	1696 (56.5)	
Weight loss	13 (4.7)	26 (1.7)	28 (2.4)	67 (2.2)	
Nausea/poor oral intake	54 (15.4)	155 (10.3)	308 (26.8)	517 (17.2)	
Others	17 (4.9)	37 (2.5)	28 (2.4)	82 (2.7)	
H. pylori (+) & combined IM					< 0.05
Male	5 (3.3)	65 (4.3)	74 (9.9)	144 (8.7)	
Female	11 (5.5)	89 (11.9)	56 (14.0)	156 (11.6)	

Group A, 18-30 years of age; Group B, 31-40 years of age; Group C, 41-45 years of age; Whole, 18-45 years of age. NS: Not significant; IM: Intestinal metaplasia; *H. pylori*: *Helicobacter pylori*.

Table 2 Demographic and clinicopathologic features of young age GC patients *n* (%)

Features	Group A (*n* = 371)	Group B (*n* = 1584)	Group C (*n* = 1287)	Whole (*n* = 3242)	*P*-value
Age (median, yr)	26 ± 3.2	36 ± 2.8	43 ± 1.4	38 ± 5.6	NS
Sex					< 0.05
Male	144 (38.8)	798 (50.4)	805 (62.5)	1747 (53.9)	
Female	227 (61.2)	786 (49.6)	482 (37.5)	1495 (46.1)	
Survival (median, mo)[1]	29.8 ± 4.2	31.7 ± 5.3	33.2 ± 3.8	32.4 ± 3.3	NS
Tumor size (mean, cm)	5.6 ± 3.2	5.2 ± 3.8	4.9 ± 2.9	5.14 ± 4.4	NS
Number					< 0.05
Multiple	1 (0.2)	5 (0.3)	8 (0.6)	14 (0.4)	
Single	370 (99.8)	1579 (99.8)	1279 (99.4)	3228 (99.6)	
Site of disease					< 0.05
Antrum	71 (19.1)	442 (27.9)	617 (48.0)	1130 (34.9)	
Body (lower and middle)	84 (22.6)	365 (23.0)	308 (23.9)	757 (23.3)	
Upper body and cardia	140 (37.8)	428 (27.1)	218 (16.9)	786 (24.2)	
Diffuse	76 (20.5)	349 (22.0)	144 (11.2)	569 (17.6)	
Pathology					< 0.05
Adenocarcinoma					
Male	63 (43.8)	401 (50.3)	499 (62.0)	963 (55.1)	
Female	87 (38.3)	347 (44.1)	250 (51.9)	684 (45.8)	
Signet ring cell carcinoma					
Male	81 (56.2)	397 (49.7)	306 (38.0)	784 (44.9)	
Female	140 (61.7)	439 (55.9)	232 (48.1)	811 (54.2)	
Stage of disease					< 0.05
Localized to stomach	34 (9.2)	190 (12.0)	181 (14.1)	405 (12.5)	
Regional metastasis[2]	71 (19.1)	491 (31.0)	475 (36.9)	1037 (32.0)	
Distant metastasis	266 (71.7)	903 (57.0)	631 (49.0)	1800 (55.5)	
Coincidence of IM					< 0.05
Male	9 (6.3)	168 (21.1)	249 (31.0)	426 (24.4)	
Female	13 (5.7)	121 (15.4)	97 (20.1)	231 (15.5)	
H. pylori (+)	25 (6.7)	378 (23.9)	472 (36.7)	875 (27.0)	< 0.05

[1]Survival analysis was performed using the Kaplan-Meier method; [2]This included node metastasis.

RESULTS

Demographic and clinicopathologic features

The demographic and clinicopathologic features of all subjects enrolled in this study are summarized in Tables 1 and 2. All subjects were Korean. The median age of cancer patients was 38 years and that of controls was 35 years. The male-to-female ratio of young age GC was 1.2:1.0 on the whole, but it was 1.0:1.6 in group A, 1.0:1.0 in group B, and 1.7:1.0 in group C, respectively, with female predominance when patients were younger.

No statistically significant distinctive laboratory findings were observed in young age GC patients compared with controls except slightly decreased hemoglobin and albumin levels in all genders and elevated αFP and CA125 levels in young women with carcinomatosis (data was not shown).

Histologically, young age GC was frequently located in the upper third or whole stomach diffusely as patients were younger (Table 2). The ratio of adenocarcinoma-to-signet ring cell carcinoma was 1.0:1.1 on the whole. However, in females, the ratio was 1.0:1.8 in group A,

1.0:1.4 in group B, and 1.1:1.0 in group C, respectively, whereas in males, it was 1.0:1.3 in group A, 1.0:1.0 in group B, and 1.6:1.0 in group C, respectively. These results may indicate that undifferentiated histology is more predominant when patients are younger (A > B > C, $P < 0.05$) in both genders. This phenomenon is notably more predominant in younger females. With regard to concomitant gastric pathology around cancer, IM was rarely observed in patients younger than 30 years of age (group A) whereas it was frequently observed in group C (Table 2, $P < 0.05$). IM change was more frequently observed in males compared to females within the same age group (Table 2, $P < 0.05$).

Overall, patients with stage Ⅳ cancer presented with poor prognosis. However, in resectable cancer, particularly in EGC, prognosis was not poorer compared to that of the elderly reported in previous studies (data was not shown). Females presented with more advanced features compared to males of the same age. Among 1495 female patients, 37 (2%) were diagnosed with Krukenberg tumor.

There was no significant difference in survival among age groups (Table 1, $P > 0.05$) on the whole although younger patients and females presented with relatively more advanced stage and poor prognosis. Females with a history of recent pregnancy and delivery showed poorer prognosis.

Risk factors

We evaluated the risk factors of young age GC by comparison of demographic and clinicopathologic features of young age GC with those of sex- and age-matched controls using logistic regression with OR and 95% CIs (Tables 3 and 4). The evaluations were performed after all people were stratified by age and sex with the assumption that older patients may be more frequently exposed to environmental carcinogens and exposed to them for longer than younger patients and that sex hormones may modulate the development of GC. However, we evaluated the influence of hormonal circumstances on the development of GC only in females in this study because a marked variation of sex hormones was rarely observed in young males under 45 years old whereas it was frequently observed in females of reproductive age with regular menstrual changes (Table 4).

In cancer patients, more frequent intake of beef and canned, smoked, and salted food and less frequent intakes of fresh fruit/vegetables (defined as high-risk diet), history of heavy smoking (defined as more than 20 pack-years) and history of heavy alcohol intake (defined as more than 60 g/d) were observed compared with controls in all age groups and both genders, as described previously[12] (Table 3, $P < 0.05$). However, these relationships were somewhat weaker in females compared to males of the same age, and these relationships were stronger as the age of patients increased (Table 3, $P < 0.05$). Lowest socioeconomic status, BMI > 30, and urban residence increased the risk of GC in all groups and both genders (Table 3, $P < 0.05$). Frequent exposure to harmful industrial and occupational environments (excessive electromagnetic waves, toxic chemicals such as asbestos, lead, sulfur granules, and toxic gases such as CO, NO, methane gas, *etc.*) was also closely associated with increased cancer risk in all age groups and both genders (Table 3, $P < 0.05$). However, these associations were stronger in older patients (A < B < C) and males.

H. pylori infection is considered as a very important epidemiologic risk factor of GC in both the young and the old[13,14]. However, in the current study, *H. pylori* positivity was infrequently observed in group A and B, and *H. pylori* positivity alone was not related to increased cancer risk (Table 2). Additionally, *H. pylori* positivity was not different between genders although the prevalence of young age GC was different according to gender. Only concomitant IM change combined with *H. pylori* positivity was related to increased cancer risk (Table 3, $P < 0.05$). This risk factor was weighted in patient older than 40 years of age and males in whom IM change was relatively frequently observed compared to patients younger than 30 years and females in whom these changes were rarely observed (Table 3, $P < 0.05$).

We also found that in females, frequent use of oral contraceptives without progesterone, older age at first delivery (> 35 years), lack of lactation history, and nulliparity were significantly associated with an increased risk of GC (Table 4, $P < 0.05$). Poor nutritional status during pregnancy (defined as weight gain during pregnancy which is lower than the normal level according to prepregnant BMI categories as recommended by the Institute of Medicine[10] was also associated with an increased risk of GC (Table 4, $P < 0.05$). However, age at menarche and the state of menopause didnot influence GC (Table 4, $P > 0.05$). The incidence of other estrogen-associated gynecologic malignancies, such as ovarian, breast, and uterine cancers, were also evaluated and revealed no association with young age GC (Table 4, $P > 0.05$).

In the current study, 252 patients (7.8%) had a family history of GC, which is similar to previous studies[15]. In particular, family history was more closely associated with GC in males and more advanced cases (Tables 3 and 4, $P < 0.05$) but the reason is not known.

Overall, environment factors were significantly associated with an increase of GC in all age groups and both genders although these relationships were somewhat weaker in females compared to males of the same age, and these relationships were stronger as the age of patients increased. However, in group C, environmental factors played important roles in females and males with similar weight. In females, hormonal factors associated with reproductive factors, but not menstrual factors, were significantly associated with an increase in GC.

Table 3 Frequency of control group and young age GC, age-adjusted OR estimates and 95% CI by demographic and clinical characteristics, Korea, 1990 to 2008 *n* (%)

Risk factors	GCs		Controls		Age-adjusted OR		95% CI		*P*-value	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
High-risk diet[1]										
Whole	694 (39.7)	440 (29.4)	341 (20.7)	265 (19.6)	2.53	1.71	2.17-2.95	1.34-2.03	< 0.001	< 0.001
Group A	54 (37.5)	40 (27.8)	31 (20.7)	25 (16.7)	2.30	1.50	1.37-3.87	0.87-2.57	0.002	0.034
Group B	311 (39.0)	239 (30.4)	153 (20.4)	151 (20.1)	2.49	1.73	1.99-3.13	1.37-1.29	< 0.001	< 0.001
Group C	329 (40.9)	161 (33.4)	157 (22.0)	89 (22.3)	2.61	1.75	2.08-3.27	1.307-2.37	< 0.001	< 0.001
Heavy smoking[2]										
Whole	528 (30.2)	241 (16.1)	264 (16.0)	137 (10.1)	2.27	1.70	1.93-2.69	1.36-2.13	< 0.001	< 0.001
Group A	51 (35.4)	34 (15.0)	30 (20.0)	19 (9.5)	2.19	1.68	1.30-3.72	0.92-3.05	0.003	0.031
Group B	244 (30.6)	143 (18.2)	119 (15.9)	83 (11.1)	2.34	1.79	1.82-2.99	1.34-2.39	< 0.001	< 0.001
Group C	233 (28.9)	64 (13.2)	115 (15.3)	35 (8.75)	2.25	1.60	1.75-2.89	1.03-2.47	< 0.001	0.035
Heavy alcohol drinking[3]										
Whole	608 (34.8)	168 (11.2)	301 (18.2)	91 (6.7)	2.39	1.52	2.04-2.81	1.34-2.29	< 0.001	< 0.001
Group A	54 (37.5)	26 (11.5)	28 (18.7)	12 (6.0)	2.61	2.02	1.54-4.45	0.99-4.13	< 0.001	0.052
Group B	293 (36.7)	81 (10.3)	142 (18.9)	47 (6.3)	2.48	1.72	1.97-3.14	1.18-2.50	< 0.001	0.005
Group C	261 (32.4)	61 (12.7)	131 (17.5)	32 (8.0)	2.14	1.73	1.68-2.72	1.60-2.54	< 0.001	0.019
Low socioeconomic condition[4]										
Whole	414 (23.7)	323 (21.6)	279 (16.9)	206 (15.3)	1.53	1.53	1.29-1.81	1.26-1.86	< 0.001	< 0.001
Group A	28 (19.4)	44 (19.3)	21 (14)	27 (13.5)	1.42	1.54	0.76-2.64	0.99-3.03	0.003	0.009
Group B	191 (23.9)	168 (21.4)	135 (18.0)	122 (16.3)	1.43	1.40	1.12-1.84	1.082-1.81	0.004	0.011
Group C	195 (24.2)	111 (23.0)	123 (16.4)	57 (14.2)	1.63	1.80	1.27-2.10	1.27-2.56	< 0.001	0.001
Urban residence										
Whole	947 (54.2)	805 (53.8)	711 (43.1)	574 (42.5)	1.56	1.58	1.37-1.79	1.36-1.83	< 0.001	< 0.001
Group A	84 (58.3)	132 (58.1)	67 (44.7)	99 (49.5)	1.48	1.42	0.93-1.23	0.973-2.08	0.002	0.073
Group B	454 (56.9)	434 (55.2)	331 (44.1)	322 (42.9)	1.67	1.64	1.37-2.04	1.34-2.00	< 0.001	< 0.001
Group C	409 (50.8)	239 (49.6)	313 (38.9)	153 (38.2)	1.44	1.60	1.18-1.76	1.21-2.08	0.003	0.001
Occupational environment										
Whole	588 (33.6)	331 (22.1)	315 (19.1)	181 (13.4)	2.15	1.84	1.84-2.52	1.51-2.24	< 0.001	< 0.001
Group A	44 (30.6)	47 (20.7)	24 (16.0)	29 (14.5)	2.31	1.54	1.32-4.05	0.93-2.56	0.004	0.094
Group B	263 (33.0)	181 (23.0)	140 (18.7)	98 (13.1)	2.14	1.99	1.69-2.71	1.52-2.61	< 0.001	< 0.001
Group C	281 (34.9)	103 (21.4)	151 (20.1)	54 (13.5)	2.13	1.74	1.69-2.68	1.22-2.50	< 0.001	0.003
Family history of GC[5]										
Whole	150 (8.6)	102 (6.8)	36 (2.2)	28 (2.1)	4.21	3.46	2.91-6.10	2.26-5.29	< 0.001	< 0.001
Group A	11 (7.6)	14 (6.2)	3 (2.0)	4 (2.0)	4.05	3.22	1.10-14.84	1.04-9.95	0.035	0.042
Group B	68 (8.5)	53 (6.7)	17 (2.3)	15 (2.4)	4.01	3.54	2.34-6.90	1.98-6.34	< 0.001	< 0.001
Group C	71 (8.8)	35 (7.2)	16 (2.1)	9 (2.3)	4.17	3.40	2.43-7.15	1.62-7.17	< 0.001	0.001
H. pylori (+) & combined IM										
Whole	367 (21.0)	231 (15.5)	144 (8.7)	156 (11.6)	2.78	1.40	2.26-3.42	1.13-1.74	< 0.001	< 0.001
Group A	11 (7.6)	13 (5.7)	5 (3.3)	11 (5.5)	2.40	1.04	0.71-7.08	0.46-2.39	0.051	0.192
Group B	155 (19.4)	121 (15.4)	65 (4.3)	89 (11.9)	2.54	1.35	1.87-3.46	1.00-1.81	< 0.001	0.045
Group C	201 (25.0)	97 (20.1)	74 (9.9)	56 (14.0)	3.04	1.55	2.28-4.06	1.08-2.22	< 0.001	0.017
BMI > 35										
Whole	374 (21.4)	270 (18.1)	201 (12.4)	159 (11.8)	1.94	1.65	1.63-2.37	1.34-2.04	< 0.001	< 0.001
Group A	30 (20.8)	35 (15.4)	18 (12.0)	19 (9.5)	1.93	1.74	1.09-2.35	0.96-3.15	0.043	0.066
Group B	176 (22.1)	139 (17.7)	95 (12.7)	89 (11.9)	1.95	1.60	1.49-2.56	1.20-2.12	< 0.001	0.001
Group C	168 (20.9)	96 (19.9)	92 (12.3)	51 (12.8)	1.89	1.70	1.43-2.49	1.78-2.46	< 0.001	0.005

[1]High-risk diet is defined as more frequent intake of beef and canned, smoked, and salted food and less frequent intake of fresh fruit/vegetables; [2]Heavy smoking is defined as more than 20 pack-years; [3]Heavy alcohol intake is defined as more than 60 g/d; [4]Socioeconomic conditions were evaluated by household income, stratified into 3 groups based on income epidemiology in Korea. This condition comes under the lowest income group; [5]Family history was defined as first-degree relative with GC. The 3000 normal controls included 1650 males and 1350 females. Group A, 18-30 years of age, *n* = 350; Group B, 31-40 years of age, *n* = 1500; Group C, 41-45 years of age, *n* = 1150; Whole, 18-45 years of age, *n* = 3000. The 3242 young age GC included 1747 males and 1495 females. Group A, 18-30 years of age, *n* = 371; group B, 31-40 years of age, *n* = 1584; group C, 41-45 years of age, *n* = 1287; whole, 18-45 years of age, *n* = 3242. GC: Gastric carcinoma; OR: Odds ratio; CI: Confidence interval; BMI: Body mass index.

DISCUSSION

Although epidemiologic characteristics of young age GC were varied according to geographical regions and ethnicity, near-universal findings were commonly demonstrated in each article for epidemiologic studies of young age GC, which are as follows: (1) female dominance, (2) located in the upper area, (3) diffuse growth types, (4) undifferentiated histology (particularly signet ring cell carcinoma), and (5) advanced stage and poor prognosis, which were different from those of the elderly[1-8] although some studies showed different results. On the whole, we also observed similar results to those described previously. However, there are several different points in our study compared with previous studies.

Table 4 Frequency of control group and young age GC, age-adjusted OR estimates and 95% CI by hormonal and reproductive characteristics, Korea, 1990 to 2008 *n* (%)

Risk factors	GCs	Controls	OR	95% CI	*P*-value
Frequent use of oral contraceptives	432 (28.9)	201 (14.0)	2.50	2.06-3.00	< 0.001
Age at first pregnancy (≥ 5 mo)[1]					
Age < 25	225 (15.1)	243 (17.0)	0.86	0.70-1.05	0.127
Age ≥ 25, < 35	848 (56.7)	977 (68.3)	1.05	0.73-1.50	0.438
Age ≥ 35	422 (28.2)	211 (14.7)	2.27	1.89-2.73	< 0.001
Parity (live births)					
Nullipara or few (1-2)	779 (52.1)	487 (34.0)	2.11	182-2.45	< 0.001
Many (≥ 3)	431 (28.8)	629 (44.0)	0.52	0.44-0.60	< 0.001
History of lactation	313 (20.9)	414 (28.9)	0.68	0.58-0.79	< 0.001
Poor nutritional status[2]	252 (16.9)	122 (8.5)	2.12	1.73-2.73	< 0.001
Age at menarche (yr)					
Age < 12	308 (20.6)	258 (18.0)	1.18	0.98-1.14	0.078
Age ≥ 12, < 16	956 (63.9)	930 (65.0)	0.95	0.62-1.44	0.102
Age ≥ 16	231 (15.5)	243 (17.0)	0.89	0.73-1.09	0.262
Premenopausal state (preoperative)	134 (9.0)	138 (9.6)	0.92	0.72-1.18	0.526
Other gynecologic malignancy[3]	19 (1.3)	16 (1.1)	1.14	0.58-2.22	0.237

[1]Pregnancy was maintained for at least 5 mo; [2]This condition was during pregnancy; [3]These conditions included estrogen-associated cancers such as breast, ovarian, and uterine. GC *vs* control = 1495 *vs* 1431.

In this study, we evaluated the epidemiologic features of young age GC after subdividing young patients into 3 age groups and 2 genders under assumption that the effects of sex hormones and environmental factors may be influenced by age; hormonal activities reach a peak around 30 years of age and decline slightly with age, and exposure of environmental carcinogens may be more frequently and longer in the old based on previous studies[16-20].

For demographic risk factors, our study supports the previous results[12]. Environmental factors such as life style, socioeconomic status, occupation, resistance, and IM change with *H. pylori* infection in gastric mucosa were statistically significantly associated with young age GC, particularly in males and older patients. Generally, environmental factors might play important roles in the initiation of cancer development. Several life style factors, such as a history of smoking or alcohol use, and diet, are common weighty risk factors[12]. Low socioeconomic conditions were particularly associated with the intestinal type of GC as those in this income bracket are more likely to be exposed to poor quality food, which may cause intestinalization of the gastric mucosa at a relatively young age. Additionally, few have access to health care services and notification of IM changes in stomach may become delayed. Over the past few decades, people have been exposed to harmful industrial occupational materials called "endocrine disruptors" as societies have undergone rapid industrialization. These endocrine disruptors are thought to be carcinogens. Therefore, the industrialized occupational environment may influence the increase of GC development at a younger age[13]. In same period, females also were exposed to similar harmful environment circumstances. However, these associations were weaker in aged-matched females. We guess the reasons that male patients might have more frequent and prolonged exposure to environmental carcinogens than females is due to social positions[14]. Some epidemiologic data have pointed to an association between *H. pylori* infection and increased risk of young age GC[21,22]. Of course, *H. pylori* infection is a critical environmental factor of GC in old age, particularly intestinal type[16], and IM change was combined in most *H. pylori*-associated GC. However, the prevalent histology of young age GC was diffuse-type cancer, and prevalence of IM change was rare in young age GC. In this study, the association between *H. pylori* infection and increased risk of young age GC was more common in older patients and males than in younger patients and females. Therefore, we suggest that *H. pylori*-associated risk factors may play a limited role in the development of young age GC according to age and gender.

GC incidence varies considerably according to studies[1-8]. In our series, the male-to-female ratio was 1.2:1.0 on the whole, but it was 1.0:1.6 in group A, 1.0:1.0 in group B, and 1.7:1.0 in group C, respectively, with female predominance as patients were younger (Table 2). The reason for this higher number of female patients in the younger group is not yet known. However, the role of the sex hormones, especially estrogen, has been suggested[16-20] although the results have varied among different studies. Some investigators asserted their protective effects on GC whereas others emphasized the opposite. The differences may be derived from geographical or ethnic differences, or the relatively small-sized sample number[23,24]. Our study may support the harmful role of estrogen in young age GC in females. In accordance with these results, we observed a close relationship between GC development and hormonal circumstances in young females (Table 4). Additionally, the effect of counter action of progesterone was not noted in many studies asserting the protective effects of estrogen on GC development. Our results may imply

that excessive exposure to estrogen without counter exposure to progesterone is related to an increase in the development of GC in young females.

In conclusion, our study demonstrated that the epidemiologic characteristics including risk factors of young age GC were different according to age and gender. Hormonal factors were more commonly associated with females, particularly in the younger age group, whereas environmental factors were more commonly associated with males, particularly in the older age group.

The development of GC is influenced by a combination of environmental factors and specific genetic alterations including hormonal factors and the role of genetics is considered to be greater in younger patients than older patients[25]. Thus, further investigations of the molecular genetics of young age GC are needed to support the results of our study.

COMMENTS

Background

Two percent to fifteen percent of patients with gastric cancer (GC) are younger than 45 years of age and there has been an increase in the relative proportion of young age GC compared with older age GC, especially in young females. The question of whether young age GC is different from that of older patients has been raised but remains unresolved. Thus, an epidemiologic study about young age GC is significantly important clinically.

Research frontiers

The development of GC is influenced by a combination of environmental factors and specific genetic alterations including hormonal factors. The role of genetics is considered to be greater in younger patients than older patients. According to epidemiologic studies of GC, a marked variation was seen in the incidence of GC according to sex and ethnicity. Sex hormones are considered to modulate the risk of development of GC. Also, according to previous data, the demographic and clinicopathologic features of young age GC were somewhat different between patients younger and older than 30 years of age.

Innovations and breakthroughs

Until now, only a few studies with small-sized samples have been conducted in young age GC patients. However, this retrospective, large-scale, and population-based study with abundant epidemiologic and clinicopathologic information in a single institution may reduce the limitations and bias derived from small sized sample studies like those conducted previously, and confirm more accurate data. The authors also evaluated the epidemiologic features of young age GC after subdividing young patients into 3 age groups and 2 genders under the assumption that the effects of sex hormones and environmental factors may be influenced by age; hormonal activities reach a peak around 30 years of age and decline slightly with age, and exposure to environmental carcinogens may be more frequent and longer in the old, based on previous studies.

Applications

The authors' study demonstrated that the epidemiologic characteristics and the development risk of young age GC were affected by both environmental factors and hormonal factors, especially sex hormones, with different factors contributing a different degree of risk according to age and gender. Their study demonstrated that hormonal factors were more commonly associated with females, particularly in the younger age group, whereas environmental factors were more commonly associated with males, particularly in the older age group. This knowledge may help to clarify the exact pathophysiology of young age GC and help devise an appropriate treatment approach.

Peer review

This paper is thought to be an excellent epidemiologic study surveying risk factors for stomach cancer in patients aged 45 or younger. It is an interesting study of significant clinical importance. However, there are some limitations to the study that require attention from the authors.

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