

# The effects of sex disparities on clinicopathological characteristics and prognosis of 3937 Chinese patients with gastric cancer

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## Research

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# Abstract

**Objective:** To investigate the effects of sex disparities on clinicopathological characteristics and prognosis of 3937 Chinese gastric cancer (GC) patients.

**Materials and methods:** A total of 3937 Chinese patients, including 3098 males (78.7%) and 839 females (21.3%), diagnosed with GC at the General Hospital of Ningxia Medical University of China were selected through inclusion and exclusion criteria, and the prognosis of the patients was followed up. Clinicopathological features were assessed, and univariate and multivariate survival analyses were performed.

**Results:** The ratio of male to female was approximately 3.7:1. Compared to females, male patients were relatively older and had more cigarette smoking and alcohol consumption history, higher percentage of late-stage GC, more proximal tumors, and better differentiation of cancer ( $p < 0.05$ ). There was no significant difference between the male and female patient groups in terms of the cumulative overall survival rate (62.1% vs. 64.8%), 1-year survival rate (69.7% vs. 71.6%), 3-year survival rate (46.6% vs. 48.5%) and 5-year survival rate (20.8% vs. 15.8%). Female patients with cigarette smoking history and male patients in stage IV or without treatment had a poorer prognosis ( $p < 0.05$ ). Age, clinical differentiation, pathologic T stage, pathologic N stage, clinical stage, and surgery type were significantly independent prognostic factors ( $p < 0.05$ ).

**Conclusion:** Sex disparities play an important role in clinicopathological features and prognosis of GC. Considering that the effect of sexual dimorphism in the development and prognosis of GC is complex, further research is warranted.

## Introduction

Sex is a key factor affecting many biological processes, including the development and progression of many different diseases like cancer. Substantial research has shown extensively differences in sex-biased in terms of the incidence various cancers, prognosis, mortality, and treatment response of various cancers [1, 2, 3]. The reasons underlying the observed differences can be generally attributed to gender-biased sociological behaviors such as smoking, alcohol consumption, and delayed diagnosis, or internal factors, including sex chromosomes, hormone levels, immune internal environment, and sex-biased molecular changes. However, the effect of sexual dimorphism on cancer progression is still a relatively under-researched area in oncology.

Gastric cancer (GC) is a malignant tumor derived from the mucosal epithelium of the stomach and is the major cause of cancer related mortality in men and women worldwide [4]. Epidemiological reports have shown that regardless of the etiologies, the incidence of GC is higher in males than in females with a male to female ratio of approximately 2:1 in both American and Chinese patients. Moreover, several other studies have indicated that male patients with GC had worse overall survival (OS) than their female counterparts [5, 6], but some reports have demonstrated a greater survival advantage for male patients compared with female patients in some special populations, such as young people and high-dose alcohol drinkers [6, 7]. Therefore, the results derived from clinical investigation are inconsistent, and the reasons behind the discrepancies remain unclear. To date, very few studies have systematically investigated the general demography, clinicopathological features, and factors associated with mortality in the two groups of patients with GC or assessed whether GC prognosis for men is congruent with that for women.

This retrospective study enrolled 3937 GC patients from Ningxia, the region with the highest incidence of GC in China, and studied the clinical pathology and examined the possible mortality disparity between male and female patients with GC in this region. The potential risk factors associated with mortality were further investigated.

# Methods

## Ethics statement

The study conformed to the principles of the Helsinki Declaration and was approved by the Ethics Committee of the General Hospital of Ningxia Medical University. All patients enrolled in this study were informed that their medical records would be potentially used for scientific research, and that their privacy would be protected at the same time.

## Patients

This study was conducted in the General Hospital of Ningxia Medical University in Ningxia, China. Relevant data were collected from the medical records. Overall, we recruited 3937 patients with diagnosis of GC confirmed by endoscopy with biopsy and histopathological evaluations between January 2012 and October 2017. There were 839 (21.3%) females and 3098 (78.7%) males. Patient selection complied with the following inclusion criteria: 1. Every patient confirmed with primary GC by endoscopy with biopsy and histopathological evaluations. 2. The patients had complete clinical data. The following exclusion criteria were followed: 1. Diagnosis of neuroendocrine carcinoma, gastric stromal tumor, lymphoma, and other gastric malignant tumors. 2. Metastatic tumor metastatic to the stomach at other sites.

## Data collection and follow-up

The data collected from each patient referred to sex, age, nationality, blood type, history of cigarette and alcohol, family history, treatment methods, date and type of surgery, tumor size, tumor location, Borrmann type, histological grading, tumor pathology, regional lymph nodes distant metastasis, clinical stage, chemoradiotherapy, vital status, and date of death. Related treatments included operative treatment, postoperative chemotherapy, preoperative chemotherapy, simple chemotherapy, untreated. The tumor-node-metastasis (TNM) staging system from the American Joint Cancer Committee/Union International Contre Le Cancer (AJCC/UICC) is the internationally accepted standard for GC staging, and the 7th edition is used throughout this paper. After diagnosis and treatment, each patient was followed up by telephone and mobile phone text messages until January 30, 2019. The follow-up included the survival status of the patients and the specific causes of death and the exact time of death of the patients, as applicable. We considered missing visits in cases of two unsuccessful phone call attempts on the same day and another unsuccessful attempt on the next day. In this retrospective study, survival data were available for 3383 of the 3937 patients (85.9%).

## Statistical analysis

SPSS Version 21.0 for Windows (SPSS Company, Chicago, Illinois, USA) was used for analyses. Comparison between the two groups was performed using the chi-square test for categorical variables and t-test for continuous variables. The survival curves were estimated using the Kaplan–Meier product-limit method. The survival comparison was assessed by performing the log-rank test, and multivariate analysis was performed using Cox regression. Proportional hazards regression models were fitted with computing hazard ratios and the corresponding 95% CI. All statistical tests were two sided, with p-values  $\leq 0.05$  considered statistically significant.

# Results

## Demographic and clinicopathological variables of the male and female patients

As shown in Table 1, a total of 3937 patients with GC were included in this study: 3098 males (78.7%) and 839 females (21.3%). 61.16±10.52 and 58.09±12.23 years. There were differences in the composition ratio between male and female age groups, and the difference was statistically significant ( $p < 0.001$ ). Both men and women had onset before the age of 20, and the incidence increased with age, with a peak between the ages of 60 and 80. Among them, male patients were dominant (53.1% vs. 47.4%) in the elderly group (60–80 years old), whereas female patients were more common before the age of 40 (9.4% vs. 3.1%). Compared with female patients, male patients accounted for the absolute dominance in the two sociological behaviors of smoking history and alcohol history (54.1% vs. 3.1%;  $p < 0.001$ , 45.9% vs. 2.1%;  $p < 0.001$ ). There were no statistically significant differences in blood type, family history, or race/ethnicity distributions between the two groups ( $p = 0.118$ ,  $p = 0.277$ ,  $p = 0.208$ , respectively).

The male patient group, compared with the female counterpart, had higher proportions of late-stage GC (stage III-IV: 57.0% vs. 54.5%), although male and female patients are often diagnosed at advanced stages. Additionally, male patients had higher proportion of the late-stage in the depth of tumor invasion T (T3-T4: 72.4% vs. 68.3%;  $p = 0.040$ ), lymph node metastasis N (61.5% vs. 58.7%), and distant metastasis M (84.3% vs. 82.8%). A dramatic and statistically significant difference ( $p < 0.001$ ) in the location was observed between the two groups; the upper (proximal) third of the stomach was higher for men (29% vs. 15.7%) and lower (distal) third for women (40.4% vs. 53.6%). As for the degree of tumor differentiation, the percentage of poorly differentiated carcinoma in women was more than that in men (53.4% vs. 45.0%), and men had an advantage in the quantity of moderately and highly differentiated adenocarcinomas with better differentiation (35.8% vs. 26.40%), this difference being statistically significant ( $p < 0.001$ ). There were no significant differences in the Borrmann type, Tumor diameter, Surgical type, and Chemotherapy between the male patients and the female patients ( $p > 0.05$ ).

### **Univariate and multivariate analyses of overall survival**

In this retrospective study, we obtained survival information for 3383 patients, with a median follow-up of 44.6 months for men and 42.6 months for women. The overall survival rate of the study population was 62.7%. Male patients compared with their female counterparts had lower 1-year survival rates (69.7% vs. 71.6%) and 3-year survival rates (46.6% vs. 48.5%). However, the 5-year survival rate of male patients was higher than that of female patients (20.8% vs. 15.8%). There was no significant difference in survival between male and female patients.

As shown in Table 2 and Fig 1, univariate analysis of survival revealed significant differences based on the following parameters: cigarette smoking, clinical stage, and surgical type ( $p < 0.05$ ). Female patients with a history of smoking had worse prognosis than male ( $p = 0.029$ ). The prognosis of male patients with stage IV and no surgical treatment was worse than that of female patients ( $p = 0.022$ ;  $p = 0.018$ ).

Next, multivariate Cox regression analysis (Table 3) was used to identify the prognostic factors. Age, clinical factors (differentiation, pathologic T stage, pathologic N stage, and clinical stage) and surgery type were significantly associated with overall mortality in the two groups of patients. Smoking was a significantly independent prognostic factor for females, but there was no significant correlation between smoking and the prognosis of men.

## **Discussion**

In this study, demographic and clinicopathological characteristics were firstly analyzed between male and female patients with GC. The prognostic factors for GC patients with different sex were further determined. It was found that male patients with GC significantly differed from their female counterparts as characterized by age distribution, history of smoking and drinking, tumor location, degree of tumor differentiation, and prognosis of stage IV patients.

The overall survival rate of men was higher than that of women, but there was no statistical significance (62.1% vs. 64.8%).

It was observed that the percentage of male patients diagnosed with GC is significantly higher than that of female patients (78.7% vs. 21.3%) with a male to female ratio of approximately 3.7:1. Moreover, the OS rates in male patients were lower than those in female patients (62.1% vs. 64.8%); although this difference did not reach statistical significance, it was consistent with some other previous studies [5, 6]. The reasons underlying the above differences are complex, but they can be generally attributed to (i) external factors such as sex-biased social behaviors like cigarette smoking, alcohol consumption, and delayed diagnosis [1, 8], and (ii) internal factors, including hormonal ones, sex chromosomes, and sex-biased molecular changes. It is well known that smoking is a high-risk factor for many cancers. Both tobacco smoking and tar contain many carcinogens, such as poly-cyclic aromatic hydrocarbons, phenylpyrene, nitroso compounds, epoxides, and nicotine, and can directly stimulate gastric mucosa [9]. A meta-analysis of 42 articles involving GC patients from Asia, Europe, and the United States, showed that the relative risk of developing GC for current smokers was 1.53 times higher compared to those who never smoked [10]. In this study, the proportion of male smokers was much higher than that of females (54.1% vs. 3.1%), which may be one of the reasons for the high incidence of male patients. Meanwhile, the percentage of male alcohol drinking patients was significantly higher than that of women, which may also account for the high incidence of GC in men. A recent meta-analysis study with 34,500 GC patients showed that, compared with non-drinkers, the relative risk value of GC was 1.07 in moderate/mild drinkers, while that of heavy drinkers (> 4 times a day) was 1.2 [11]. Another prospective study in Korea patients showed that severe drinkers ( $\geq 20$  g/d) were significantly associated with GC (HR = 1.73) compared with mild drinkers[12].

Some internal factors, including sex chromosomes and hormone levels are also considered to be a cause of sex differences in the incidence and prognosis of GC. Sex chromosome genes have been particularly highlighted in present research. Yuan et al. found that the most well-known genes with sex-biased expression across cancer types are mainly enriched in the X chromosome [13]. Dunford et al. reported that a subset of X-chromosome genes escaped from X-inactivation, which can protect females from "single-hit" functional loss by "escaping from X-inactivation tumor suppressor" (EXITS) [14]. Several studies have shown male-biased mutations in these genes, which support that EXITS genes play a crucial role in reducing the incidence of cancer in female subpopulations [15-17]. In addition, a number of studies confirmed overexpression of androgen receptors (AR) in tumor tissues, establishing AR as risk factors for high incidence of tumors [18]. Therefore, relatively high AR expression may be one of the internal reasons for the high incidence of GC in men.

It was also observed that, consistent with several other previous reports, both male and female patients with GC were mainly over 60 years old [19, 20], accounting for approximately 50% of their respective numbers. There were more male elderly patients with GC than female patients (55.4% vs. 49.3%). Meanwhile, the mortality rate of the elderly was also higher than those of both the middle-aged and young patients, which may be due to their weaker physical condition, combined with higher vulnerability to acute and chronic diseases, longer periods of smoking, drinking habit, and a history of high salt intake.

In contrast, there was a relatively higher frequency of young patients in the female group compared to the male group (9.5% vs. 3.2%). Consistently, the overall mortality rate of young female patients was higher than that of male patients in the same age group (37.9% vs. 31.8%), which is in line with a recent study involving 875 patients in Brazil [21].

Regarding the difference in the location of tumors between the two sexes, there was a significant difference between the lower-third and the upper-third of the stomach. The proportion of proximal GC in male patients was higher than in

female patients (26.8% vs. 14.8%), whereas the proportion of distal GC in female patients was higher than that in males (50.5% vs. 37.5%). Qiao Luji et al. reported that proximal GC was more common in males, and that the male to female ratio of proximal GC was about 7.96:1 [22]. It was also reported that the rate of occurrence of proximal GC in men was higher than that in women (77.46% vs. 54.85%) [23], which is consistent with our results. Several other researchers showed that distal GC had a higher family history rate than proximal GC, which suggests a genetic predisposition in patients in the distal GC group [24]. We also found that the mortality rate of proximal GC in both male and female patients was higher than that in distal GC, which is consistent with some other previous reports [25, 26].

Because there are no characteristic clinical manifestations in the early stage, GC patients are often in advanced stages at the time of initial diagnosis [4, 5, 27]. Invasive tumors may be closer to tissue blood vessels, nerves, lymphoid vessels, and surrounding organs, so their invasive range is wide, destructive to the body leading to more fatal complications, and are more likely to have distant metastasis [26]. Accordingly, the OS is significantly worse in patients with deeper invasion. Consistently, the pathological TNM stage in this study was usually at a late or advanced stage in both male and female patients. In this study, however, there was no significant difference in OS rate between the two groups in clinical stage I, II, and III, but the mortality rate of stage VI male patients was significantly higher than that in the female population (71.3% vs. 61.0%).

To date, the optimal treatment of GC is still surgery. If the clinical circumstances allow, radical gastrectomy can result in a relatively better prognosis compared with other treatments. In this study, however, we found that both male and female patients with advanced GC did not benefit from palliative gastrectomy and exploratory laparotomy. In addition, the mortality rate of male patients who did not undergo surgical treatment was found to be significantly higher than that of women (64.7% vs. 57.8%).

Although both external and internal factors are highlighted for their potential effects on GC, their cross interaction cannot be overlooked. Interestingly, in this study, it was found that cigarette smoking is an independent prognostic risk factor for female GC patients but not for male patients. Our findings are consistent with the results from Ryberg et al., who reported that female smokers had a significantly higher level of aromatic/hydrophobic DNA adducts in their nontumor tissue than male smokers. These observations suggest that women are more susceptible to tobacco carcinogens, which may cause worse survival in tobacco-induced GC [28].

## Conclusion

In summary, the sex factor plays an important role in the occurrence and development of GC. Compared with female patients, male GC patients have higher incidence, older age distribution, more extensive high-risk factors, and more proximal GC, as well as higher mortality among stage IV patients. Although no significant difference was observed in 1-year, 3-year, or 5-year survival rates between male and female patients and sex is not found to be an independent prognostic factor with GC in this study, more in-depth research is needed as the effect of sexual dimorphism is complex. This study has some limitations. This is a retrospective study with a certain amount of data missing and some uncontrollable factors which may affect the results of the study. Besides, patients only from one highly incident center in China were included. Therefore, future multicenter studies, including patients from low-incidence areas are strongly recommended.

## Abbreviations

GC: Gastric cancer;

OS: Overall survival;

TNM: Tumor-node-metastasis staging system;

AJCC: American Joint Committee on Cancer;

UICC: Union for International Cancer Control;

OR: Odds ratio;

EXITS: Escape From X-inactivation Tumour Suppressor;

AR: Androgen Receptor.

## **Declarations**

### **Author's Contributions**

PC, WW, XZ, DZ, Qian Z, JY, and JW collected patient information and followed up all patient survival status. XZ, ZC, JC, and QZ interpreted the collected data and generated tables and figures for the data. XZ and QZ wrote the manuscript. ZC and WY edited the manuscript. WY and JR supervised the study. All authors have read and approved the manuscript.

### **Ethics approval and consent to participate**

The study conformed to the principles of the Helsinki Declaration and was approved by the Ethics Committee of the General Hospital of Ningxia Medical University. All patients enrolled in this study were informed that their medical records would be potentially used for scientific research, and that their privacy would be protected at the same time.

### **Availability of data and materials**

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

### **Consent for publication**

Not applicable.

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### **Declaration of interests**

The authors declare that they have no conflict of interest.

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## Tables

**Table 1. Demographic and clinicopathological variables of the Male and Female patients with gastric cancer**

Variables	Gastric Cancer Cases, No. (%)		$\chi^2$	<i>p</i>
	Male (n=3098)	Female (n=839)		
Age (years)			63.842	0.001
<20	3 (0.1)	1 (0.1)		
21-40	96 (3.1)	79 (9.4)		
41-60	1283 (41.4)	345 (41.1)		
61-80	1644 (53.1)	398 (47.4)		
≥80	72 (2.3)	16 (1.9)		
Smoking			700.500	0.001
Yes	1677 (54.1)	26 (3.1)		
No	1421 (45.9)	813 (96.9)		
Alcohol			234.373	0.001
Yes	823 (26.6)	18 (2.1)		
No	2275 (73.4)	821 (97.9)		
Blood type			5.875	0.118
A	809 (26.1)	211 (25.1)		
B	850 (27.4)	205 (24.4)		
AB	267 (8.6)	69 (8.2)		
O	761 (24.6)	236 (28.1)		
Unknown	411 (13.3)	118 (14.1)		
Family history			2.567	0.277
No	2814 (90.8)	774 (92.3)		
alimentary canal	255 (8.2)	61 (7.3)		
Other system	29 (0.9)	4 (0.5)		
Ethnicity			3.143	0.208
Han	2412 (77.9)	677 (80.7)		
Hui	647 (20.9)	153 (18.2)		
Others	39 (1.3)	9 (1.1)		
T stage			4.2	0.04
T1-T2	664 (21.4)	212 (25.3)		
T3-T4	1738 (56.1)	457 (54.5)		

Unknown	696 (22.4)	170 (20.2)		
Lymph Node Metastasis			1.638	0.201
Yes	1362 (44.0)	361 (58.7)		
No	851 (27.5)	254 (41.3)		
Unknown	885 (28.6)	224 (26.7)		
M stage			0.867	0.352
M0	2060 (66.5)	570 (67.9)		
M1	383 (12.4)	118 (14.1)		
Unknown	655 (21.1)	151 (18.0)		
TNM <sup>a</sup> stage			6.107	0.107
I	537 (17.3)	169 (20.1)		
II	495 (16.0)	142 (16.9)		
III	1003 (32.40)	246 (29.3)		
IV	418 (13.5)	130 (15.5)		
Unknown	645 (20.8)	152 (18.1)		
Tumor diameter			1.04	0.903
<4cm	851 (27.5)	236 (28.1)		
4-8cm	888 (28.7)	226 (26.9)		
8-12cm	212 (6.8)	60 (7.2)		
>12cm	37 (1.2)	11 (1.3)		
Unknown	1110 (35.8)	306 (36.5)		
Location			66.791	0.001
Proximal	829 (26.8)	124 (14.8)		
Midpiece	871 (28.1)	242 (28.8)		
Distal	1163 (37.5)	424 (50.5)		
Unknown	235 (7.6)	49 (5.9)		
Differentiation			37.293	0.001
Poor	1393 (45.0)	448 (53.4)		
Middle	767 (24.8)	153 (18.2)		
Well	341 (11.0)	69 (8.2)		
Unknown	597 (19.2)	169 (20.2)		
Bormann's type			3.411	0.333

Type I	389 (12.6)	122 (14.5)		
Type II	491 (15.8)	119 (14.2)		
Type III	757 (24.4)	203 (24.2)		
Type IV	732 (23.6)	208 (24.8)		
Unknown	729 (23.5)	187 (22.3)		
Her2			3.831	0.147
1+	446 (14.4)	134 (16.0)		
2+	298 (9.6)	67 (8.0)		
3+	167 (5.4)	38 (4.5)		
Unknown	2184 (70.6)	599 (71.5)		
Surgical type			3.23	0.779
No surgery	1040 (35.1)	385 (34.8)		
Radical Subtotal Gastrectomy	1521 (51.4)	416 (52.1)		
Total Gastrectomy	309 (10.4)	84 (10.5)		
Expanded Radical Gastrectomy	14 (0.5)	2 (0.3)		
Palliative Subtotal Gastrectomy	54 (1.8)	9 (1.1)		
Exploratory Laparotomy	22 (0.7)	8 (1.0)		
Chemotherapy			0.871	0.929
No chemotherapy	2085 (67.4)	557 (66.4)		
Postoperative chemotherapy	782 (25.3)	224 (26.7)		
Preoperative chemotherapy	40 (1.3)	10 (1.2)		
Chemotherapy	190 (6.1)	48 (5.7)		

Note: aTNM stage is based on the AJCC Cancer Staging Manual, seventh edition (2010).

Abbreviations: AJCC, American Joint Committee on Cancer.

**Table 2. Univariate survival analysis comparing the impact of demographical and clinicopathological factors of patients with gastric cancer between different sex**

Variables	Gastric Cancer Cases, No. (%)				<i>p</i>
	Males (%)	<i>p</i>	Females (%)	<i>p</i>	
Age		0.001		0.001	
<40	27 (31.8)		22 (37.9)		0.377
41-60	372 (33.9)		84 (29.5)		0.144
61-80	686 (47.6)		168 (47.9)		0.984
≥80	58 (69.0)		12 (66.7)		0.678
Smoking		0.704		0.016	
Yes	609 (42.2)		16 (64.0)		0.029
No	516 (41.7)		268 (39.4)		0.194
Alcohol drinking		0.44		0.55	
Yes	293 (40.6)		5 (31.2)		0.511
No	830 (42.5)		276 (40.1)		0.279
Blood type		0.757		0.413	
A	283 (40.7)		78 (42.4)		0.861
B	287 (38.7)		57 (32.8)		0.220
AB	95 (41.1)		21 (38.9)		0.249
O	260 (39.3)		75 (39.1)		0.979
Ethnicity		0.536		0.42	
Han	868 (41.5)		216 (38.4)		0.240
Hui	241 (43.6)		61 (45.9)		0.924
Others	14 (41.2)		4 (44.4)		0.758
Family history		0.697		0.837	
No	1019 (41.9)		260 (40.1)		0.366
Alimentary canal	93 (41.7)		20 (38.5)		0.660
Other system	12 (47.8)		1 (33.3)		0.822
T stage		0.001		0.001	
T1-T2	76 (13.0)		184 (15.1)		0.407
T3-T4	724 (47.8)		377 (47.5)		0.972
N stage		0.001		0.001	
N0	120 (16.1)		47 (21.1)		0.091

Nx <sup>b</sup>	559 (46.8)		131 (45.3)	0.956
M stage		0.001		0.001
M0	586 (32.4)		158 (32.6)	0.772
M1	232 (62.3)		60 (64.5)	0.090
TNM stage		0.001		0.001
I	52 (11.0)		20 (13.2)	0.443
II	114 (26.0)		38 (32.2)	0.165
III	416 (47.4)		95 (47.0)	0.862
IV	246 (71.3)		64 (61.0)	0.022
Location		0.001		0.012
Proximal	335 (46.7)		49 (49.0)	0.588
Midpiece	301 (40.1)		85 (41.7)	0.781
Distal	375 (37.1)		123 (34.3)	0.369
Differentiation		0.001		0.04
Poor	524 (43.3)		155 (40.8)	0.359
Middle	257 (38.8)		39 (31.0)	0.175
Well	71 (30.0)		10 (23.3)	0.407
Bormann's type		0.001		0.001
I	103 (31.0)		29 (27.1)	0.486
II	118 (26.9)		33 (32.7)	0.265
III	266 (40.2)		54 (33.5)	0.176
IV	303 (47.9)		91 (50.8)	0.568
Her2		0.906		0.857
1+	125 (31.2)		38 (33.6)	0.604
2+	78 (30)		17 (29.3)	0.999
3+	46 (31.1)		11 (33.3)	0.747
Surgical type		0.001		0.001
No surgery	506 (64.7)		122 (57.8)	0.018
Radical Subtotal	366 (27.3)		102 (28.3)	0.510
Total	118 (43.2)		30 (46.2)	0.442
Expanded Radical	7 (50.0)		0 (100.0)	0.417
Palliative Subtotal	29 (64.4)		3 (50.0)	0.504

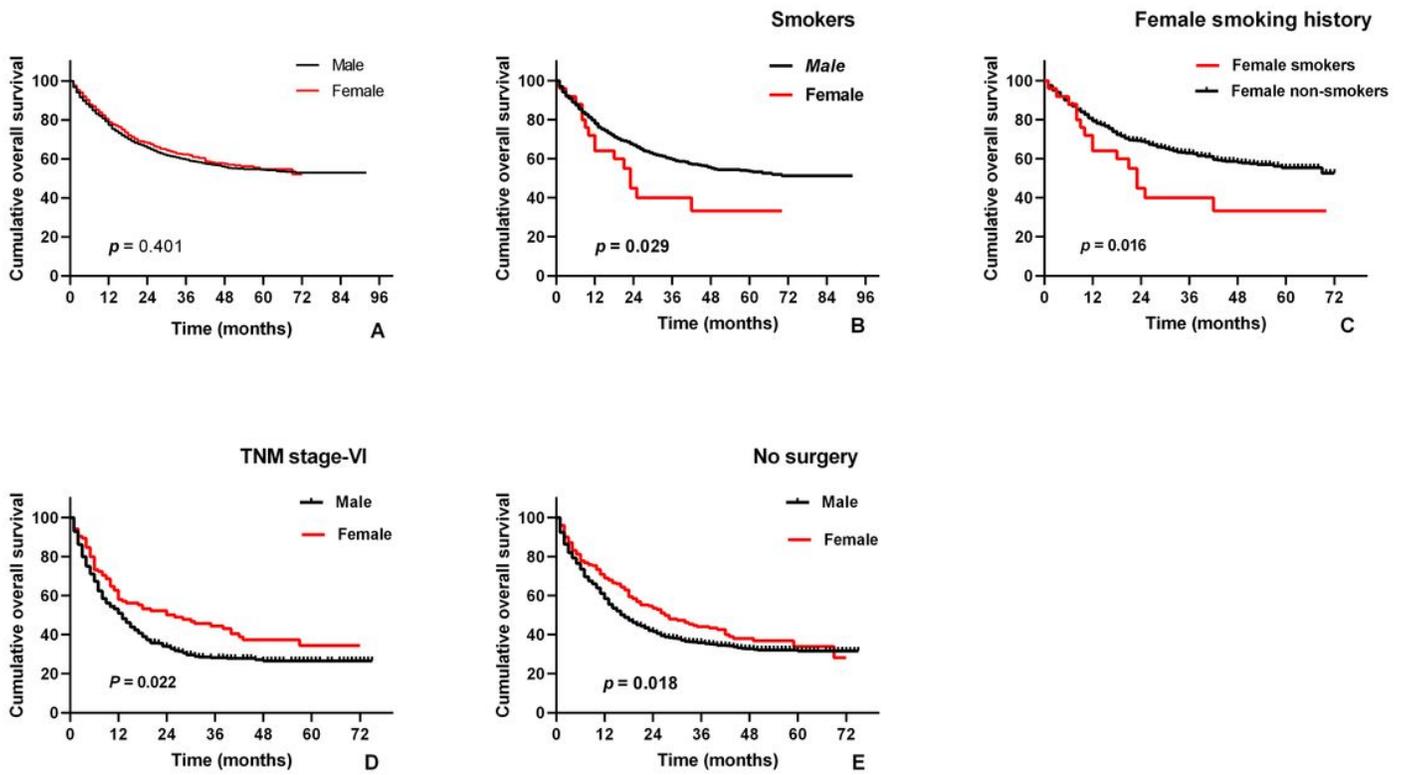
Exploratory Laparotomy	18 (85.7)	5 (71.4)	0.877
Chemotherapy			
Postoperative	221 (33.2)	64 (35.0)	0.488
Preoperative	16 (50.0)	2 (28.6)	0.377
Chemotherapy	105 (65.2)	22 (59.5)	0.432

Note: bNx Positive lymph node metastasis (N1, N2, N3)

**Table 3. Multivariate survival analysis of independent prognostic factors for patients with gastric cancer.**

Variables		Males			Females		
		<i>p</i>	HR	95.0% CI	<i>p</i>	HR	95.0% CI
Age	>60	0.001	1.636	1.327-2.018	0.018	1.683	1.093-2.593
Smoking	Yes	0.479	1.098	0.658-1.299	0.043	1.237	1.006-1.521
Surgery	Palliative	0.001	3.724	2.870-6.830	0.001	3.425	1.948-6.020
T	T3-T4	0.001	2.12	1.515-2.966	0.017	2.033	1.034-3.643
N	Nx	0.001	3.256	2.437-4.349	0.002	2.288	1.366-3.834
cTNM	II-III	0.001	2.156	1.067-2.891	0.040	1.754	1.026-3.000
Differentiation	Poor	0.001	1.63	1.245-2.135	0.043	2.005	1.021-3.936

## Figures



**Figure 1**

Comparison of survival curves for GC patients in different demographic and clinicopathological features. The survival curves were estimated using the Kaplan–Meier product-limit method.  $p < 0.05$  was considered statistically significant. A. The overall survival curves of GC patients in different sex groups ( $p = 0.401$ ). B. Survival curves of GC patients with smoking history in different sex groups ( $p = 0.029$ ). C. Survival curves of smoking history and non-smoking history groups in female GC patients ( $p = 0.016$ ). D. Survival curves of GC patients with stage IV in different sex groups ( $p = 0.022$ ). E. Survival curves of GC patients without surgical in different sex groups ( $p = 0.018$ ).