Research Article

Clinicopathological Characteristics and Prognosis of Proximal and Distal Gastric Cancer during 1997–2017 in China National Cancer Center

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Background. The prognostic relevance of gastric tumor location has been reported and debated. Our study was conducted to examine the differences in clinicopathological features, prognostic factors, and overall survival (OS) between patients with proximal gastric cancer (PGC) and distal gastric cancer (DGC).

Patients and Methods. Patients with PGC or DGC were identified from the China National Cancer Center Gastric Cancer Database (NCCGDB) during 1997–2017. Survival analysis was performed via Kaplan-Meier estimates and Cox proportional hazards models.

Results. We reviewed 16,119 cases of gastric cancer patients, including 6,479 of PGC and 9,640 of DGC. PGC patients presented as older patients (61.5 versus 56.4 years, \( P < 0.001 \)) and more males (82.9% versus 68.2%, \( P < 0.001 \)). Compared with DGC, PGC was more likely to be in later pT stage (pT3 and pT4, 65.0% versus 52.8%, \( P < 0.001 \)) and lymph node metastasis (54.8% versus 50.9%, \( P < 0.001 \)). In univariate analysis, PGC patients had a worse survival outcome in stage I (Hazard ratio [HR] = 2.04, 95% CI: 1.42-2.94) but a better prognosis in stage IV (HR = 0.85, 95% CI: 0.73-0.98) when compared to DGC patients. However, multivariate analysis demonstrated that PGC was not an independent predictor for poor survival (HR = 1.07, 95% CI: 1.00-1.14). Results from multivariate analysis also revealed that pT4, lymph node metastasis, distant metastasis, no gastrectomy, and Borrmann IV were independent predictors associated with poor survival for both PGC and DGC patients. Additional prognostic factors for PGC patients included underweight (BMI < 18.5) (HR = 1.29, 95% CI: 1.06-1.58), linitis plastica (HR = 2.13, 95% CI: 1.25-3.65), and overweight (23 ≤ BMI < 27.5) (HR = 0.80, 95% CI: 0.71-0.90). During the 20-year study period, the 5-year OS increased significantly for both PGC and DGC, with the increase rate of 91.7% and 67.7%, respectively.

Conclusion. In China, PGC significantly differed from DGC in clinicopathological characteristics and prognostic factors. However, there was no significant relationship between survival outcome and gastric tumor location.

1. Introduction

Gastric cancer (GC) is the third leading cause of cancer-related mortality and the fifth most common cancer globally [1]. Many population-based studies have reported that the incidence of distal gastric cancer (DGC) has gradually declined, while proximal gastric cancer (PGC) has increased obviously during the last decades [2–9].

Researches have indicated that PGC differed from DGC in clinicopathological characteristics [10–13]. For example, one previous study [11] found that PGC patients were more likely to be in an advanced tumor stage and have larger tumor size as compared to DGC. Yu et al. [13] showed that PGC was more common than DGC in males. Moreover, there was no clear agreement on the link between tumor location and overall survival (OS) of GC. Some studies [11, 13–17] reported...
a worse prognosis in patients with PGC compared to DGC, while others [10, 12, 18] have shown no relationship between prognosis and gastric tumor location. Katsuhiko et al. [19] even demonstrated that PGC patients had a longer survival time than DGC after chemotherapy. The inconsistent findings from these previous studies could be partially due to the small sample size, with the population records ranging from 270 to 3,193.

Given the suggested but undecided differences in clinicopathological characteristics and prognosis between PGC and DGC, the aim of our study was to compare the clinicopathological features, prognostic factors, and survival outcomes between PGC and DGC based on the China National Cancer Center Gastric Cancer Database (NCCGCDB) in order to determine whether PGC conveys worse prognosis and provides evidence for the development of guiding strategies for GC patients with different tumor locations.

2. Materials and Methods

2.1. Patient Population. All the study data were abstracted from the NCCGCDB. The NCCGCDB was a clinical gastric cancer database based on a huge retrospective cohort, which was sourced from China National Cancer Center, a single but large-volume institution, and included more than 19,000 patients from all around China from 1997 to 2018. PGC was defined as tumors with the epicenter located in cardia (C16.0) or fundus (C16.1), whereas DGC was defined as lesions of the body (C16.2), antrum (C16.3), or pylorus (C16.4). Changing trends in clinicopathological characteristics and OS of total GC, PGC, and DGC were analyzed in four consecutive time periods: from 1997 to 2002 (period 1), from 2002 to 2007 (period 2), from 2007 to 2012 (period 3), and from 2012 to 2017 (period 4). The geographical locations of these gastric cancer patients can be found in Figure 1.

2.2. Statistical Analyses. Categorical variables were compared using the Chi-squared test and continuous variables were analyzed by Student’s t-test. OS and progression-free survival (PFS) curves were plotted for PGC and DGC groups, respectively, using the Kaplan-Meier method and compared statistically using the log-rank test. Hazard ratios (HRs) and 95% confidence intervals (CIs) were used to estimate the risk of death by employing the multivariate Cox proportional hazards models with adjustment for alcohol consumption, BMI, H. pylori infection, pT stage, pN stage, pM stage, Lauren classification, gastrectomy, surgical margin, HER2 score, linitis plastica, and Borrmann classification between DGC and PGC patients. PGC was more likely to occur in older patients (61.5 versus 56.4 years, P < 0.001). Both groups were predominantly males and PGC has a greater proportion of males than DGC (82.9% versus 68.2%, P < 0.001). Relatively higher percentages of smokers (51.7% versus 33.9%, P < 0.001), alcohol drinkers (41.7% versus 29.0%, P < 0.001), and overweight/obesity (BMI ≥ 23) (56.6% versus 51.2%, P < 0.001) were shown in PGC patients as compared to DGC patients.

As for tumors, PGC patients were more likely to be in later pT stage (pT3 and pT4, 65.0% versus 52.8%, P < 0.001), lymph node metastasis (54.8% versus 50.9%, P < 0.001), intestinal type (18.8% versus 12.2%, P < 0.001), local advanced GC (76.2% versus 65.9%, P < 0.001), and Borrmann I (11.0% versus 4.6%, P < 0.001). The percentages of ever received surgical treatment (81.2% versus 82.3%, P = 0.068) were similar between the two groups. DGC patients more common in diffuse type (17.1% versus 8.6%, P < 0.001), early stage GC (21.5% versus 11.3%, P < 0.001), and distant metastasis (12.8% versus 10.1%, P < 0.001).

Changing trends of clinicopathological features in GC patients were analyzed. The proportion of pT1 tumors increased gradually with time, from 9.5% in period 1 to 22.0% in period 4, whereas the proportion of pT4 had declined from 66.0% in period 1 to 28.1% in period 4. The proportion of patients with pN0 increased from 24.5% in period 1 to 33.5% in period 4, whereas patients with pN3 were gradually decreased from 26.3% in period 1 to 21.5% in period 4. The proportion of pM1 remained relatively stable (from 11.2% to 10.7%) during the past 20 years. In pTNM stage, a significant increase was observed in stages I and II (from 12.0% and 3.8% in period 1 to 24.9% and 17.6% in period 4, resp.), while the proportion of stage III had declined from 63.0% in period 1 to 37.2% in period 4.

3. Results

3.1. Clinicopathological Characteristics. In this study, 16,119 patients were included. The clinicopathological features of 9,640 patients (59.8%) with DGC and 6,479 patients (41.2%) with PGC were compared (Table 1), with an incidence of DGC:PGC = 1.49:1. Among our study population, a higher tumor incidence was found in DGC. There were significant differences in the distribution of age, gender, smoking, alcohol consumption, BMI, H. pylori infection, pTNM stage, Lauren classification, surgical margin, HER2 score, linitis plastica, and Borrmann classification between DGC and PGC patients. PGC was more likely to occur in older patients (61.5 versus 56.4 years, P < 0.001). Both groups were predominantly males and PGC has a greater proportion of males than DGC (82.9% versus 68.2%, P < 0.001). Relatively higher percentages of smokers (51.7% versus 33.9%, P < 0.001), alcohol drinkers (41.7% versus 29.0%, P < 0.001), and overweight/obesity (BMI ≥ 23) (56.6% versus 51.2%, P < 0.001) were shown in PGC patients as compared to DGC patients.

As for tumors, PGC patients were more likely to be in later pT stage (pT3 and pT4, 65.0% versus 52.8%, P < 0.001), lymph node metastasis (54.8% versus 50.9%, P < 0.001), intestinal type (18.8% versus 12.2%, P < 0.001), local advanced GC (76.2% versus 65.9%, P < 0.001), and Borrmann I (11.0% versus 4.6%, P < 0.001). Both groups
| Table 1: Clinicopathological characteristics by tumor location. |
|---------------------------------------------------------------|
| **Age at diagnosis (years)**                                   |
| Total GC | PGC | DGC | P Value |
| Mean (SD)  | 58.5 (11.4) | 61.5 (10.0) | 56.4 (11.9) | <0.001 |
| Younger (≤35) | 590 (3.7) | 86 (1.3) | 504 (5.2) | |
| Middle-aged (36-65) | 10,842 (67.3) | 4,026 (62.1) | 6,816 (70.7) | |
| Older (≥66) | 4,685 (29.1) | 2,366 (36.5) | 2,319 (24.1) | <0.001 |
| **Gender**                                                   |
| Male | 4,171 (25.9) | 5,374 (82.9) | 6,574 (68.2) | |
| Female | 11,948 (74.1) | 1,105 (17.1) | 3,066 (31.8) | <0.001 |
| **Smoking status**                                           |
| Never smokers | 9,289 (57.6) | 3,065 (47.3) | 6,224 (64.6) | <0.001 |
| Smokers | 6,621 (41.1) | 3,352 (51.7) | 3,269 (33.9) | |
| Current smokers | 4,634 (28.8) | 2,210 (34.1) | 2,424 (25.2) | |
| Ex-smokers | 1,987 (12.3) | 1,142 (17.6) | 845 (8.8) | <0.001 |
| **Alcohol consumption**                                      |
| Never drinkers | 10,398 (64.5) | 3,716 (57.4) | 6,682 (69.3) | |
| Drinkers | 5,496 (34.1) | 2,699 (41.7) | 2,797 (29.0) | <0.001 |
| Current drinkers | 4,752 (29.5) | 2,416 (37.3) | 2,336 (24.2) | |
| Ex-drinkers | 744 (4.6) | 283 (4.4) | 461 (4.8) | <0.001 |
| **BMI (kg/m2)**                                              |
| <18.5 | 1,066 (6.6) | 380 (5.9) | 686 (7.1) | |
| 18.5-22.9 | 6,097 (37.8) | 2,301 (35.5) | 3,796 (39.4) | |
| 23-27.4 | 6,576 (40.8) | 2,760 (42.6) | 3,816 (39.6) | |
| ≥27.5 | 2,028 (12.6) | 909 (14.0) | 1,119 (11.6) | <0.001 |
| **H. pylori**                                                |
| No | 1,247 (7.7) | 437 (6.7) | 625 (6.5) | |
| Yes | 956 (5.9) | 331 (5.1) | 810 (8.4) | |
| Unknown | 13,916 (86.3) | 5,711 (88.2) | 8,205 (85.1) | <0.001 |
| **Pathologic T stage**                                       |
| T0+Tis | 58 (0.4) | 14 (0.2) | 44 (0.5) | |
| T1 | 2,491 (15.5) | 596 (9.2) | 1,895 (19.7) | |
| T2 | 1,376 (8.5) | 441 (6.8) | 935 (9.7) | |
| T3 | 3,019 (18.7) | 1,640 (25.3) | 1,379 (14.3) | |
| T4 | 6,288 (39.0) | 2,573 (39.7) | 3,715 (38.5) | |
| TX | 2,887 (17.9) | 1,215 (18.8) | 1,672 (17.3) | <0.001 |
| **Pathologic N stage**                                       |
| N0 | 4,538 (28.2) | 1,623 (25.1) | 2,915 (30.2) | |
| N1 | 2,281 (14.1) | 983 (15.2) | 1,298 (13.5) | |
| N2 | 2,417 (15.0) | 1,081 (16.7) | 1,336 (13.9) | |
| N3 | 3,799 (23.3) | 1,489 (23.0) | 2,270 (23.6) | |
| NX | 3,124 (19.4) | 1,303 (20.1) | 1,821 (18.9) | <0.001 |
| **Pathologic M stage**                                       |
| M0 | 13,629 (84.6) | 5,555 (85.7) | 8,074 (83.8) | |
| M1 | 1,883 (11.7) | 651 (10.1) | 1,232 (12.8) | <0.001 |
| **pTNM**                                                     |
| 0 | 52 (0.3) | 13 (0.2) | 39 (0.4) | |
| I | 2,989 (18.5) | 825 (12.7) | 2,164 (22.5) | |
| II | 2,112 (13.1) | 929 (14.3) | 1,183 (12.3) | |
| III | 7,354 (45.6) | 3,272 (50.5) | 4,082 (42.3) | |
| IV | 1,883 (11.7) | 651 (10.1) | 1,232 (12.8) | <0.001 |
and alcohol drinking (HR = 0.85, 95% CI: 0.77-0.94) were additional prognostic factors for DGC patients.

The univariate analysis found a survival benefit in patients with DGC (HR = 0.87, 95% CI: 0.82-0.93). After stratification by pTNM stage, further comparison between the two groups showed that, compared to patients with DGC, PGC patients had a worse survival outcome in stage I (HR = 2.04, 95% CI: 1.42-2.94) but a better prognosis in stage IV (HR = 0.85, 95% CI: 0.73-0.98). There was no significant survival difference in stages II and III (P=0.84 and 0.58, resp.). However, the multivariate analysis demonstrated that PGC was not an independent predictor for poor survival (HR = 1.07, 95% CI: 1.00-1.14).

When appropriate significant factors were taken into consideration, multivariate analysis (Table 3) revealed that pT4, lymph node metastasis, distant metastasis, no gastrectomy, and Borrmann IV were independent predictors for poor prognosis in both PGC and DGC patients. Additional factors associated with increased mortality in PGC patients included underweight (BMI < 18.5) (HR = 1.29, 95% CI: 1.06-1.58) and linitis plastica (HR = 2.13, 95% CI: 1.25-3.65). Overweight (23 ≤ BMI < 27.5) was a prognostic factor associated with favorable survival outcomes only for PGC (HR = 0.80, 95% CI: 0.71-0.90). In DGC group, additional factors for poor prognosis were H. pylori infection (HR = 1.52, 95% CI: 1.11-2.07), diffuse subtype (HR = 1.32, 95% CI: 1.04-1.67), and positive on proximal or distal margin (HR = 1.67, 95% CI: 1.16-2.41; HR = 1.57, 95% CI: 1.13-2.17, resp.). Alcohol drinkers, including current drinkers and ex-drinkers, showed better survival for DGC (HR = 0.90, 95% CI: 0.81-0.99, HR = 0.72, 95% CI: 0.56-0.93, resp.).

3.3. Changing Trends of OS and PFS for Patients with PGC and DGC. The changing trends of 5-year OS and PFS for PGC and DGC patients were shown in Figure 2(a). The total 5-year OS for GC, PGC, and DGC was 66.5% (95% CI: 65.5%-67.4%), 63.9% (95% CI: 62.4%-65.5%), and 68.1% (95% CI: 66.9%-69.3%), respectively. For total GC, 5-year OS increased from 44.1% (95% CI: 39.4%-48.7%) in period 1 to 78.4% (95% CI: 77.0%-79.7%) in period 4. The 5-year OS of PGC and DGC rose from 39.6% (95% CI: 32.8%-46.4%) to 75.9% (95% CI: 73.6%-78.1%) and from 47.7% (95% CI: 41.4%-54.0%)
| Prognostic Factors       | PGC group (N=4,716) | DGC group (N=7,228) | PGC versus DGC |
|-------------------------|---------------------|---------------------|----------------|
|                         | HR                  | 95% CI              | HR             | 95% CI        | HR             | 95% CI        | P Value |
| **Age (years)**         |                     |                     |                |                |                |                |
| Younger (≤35)           | 1.00                | 1.00                | 2.00           | 1.50           | 3.22           | <0.001         |
| Middle-aged (36-65)     | 0.47                | 0.33                | 0.65           | 0.94           | 0.77           | 1.14           | 0.52     | 1.12 | 1.03 | 1.21 | 0.008 |
| Older (≥66)             | 0.51                | 0.37                | 0.72           | 1.01           | 0.82           | 1.24           | 0.92     | 1.14 | 1.01 | 1.28 | 0.028 |
| **Gender**              |                     |                     |                |                |                |                |
| Male                    | 1.00                | 1.00                | 1.00           | 1.00           | 1.00           | 1.00           | <0.001   |
| Female                  | 1.04                | 0.91                | 1.19           | 1.07           | 0.98           | 1.17           | 0.12     | 1.13 | 0.98 | 1.30 | 0.097 |
| **Smoking status**      |                     |                     |                |                |                |                |
| Never smoker            | 1.00                | 1.00                | 1.00           | 1.00           | 1.00           | 1.00           | <0.001   |
| Smokers                 | 1.00                | 0.91                | 1.10           | 0.98           | 0.85           | 0.93           | <0.001   |
| Current smokers         | 1.03                | 0.92                | 1.14           | 0.63           | 0.89           | 0.81           | 0.99     | 0.023|
| Ex-smokers              | 0.94                | 0.82                | 1.09           | 0.41           | 0.72           | 0.60           | 0.86     | <0.001|
| **Alcohol consumption** |                     |                     |                |                |                |                |
| Never drinkers          | 1.00                | 1.00                | 1.00           | 1.00           | 1.00           | 1.00           | <0.001   |
| Drinkers                | 0.95                | 0.86                | 1.05           | 0.35           | 0.85           | 0.77           | 0.94     | 0.001|
| Current drinkers        | 0.97                | 0.87                | 1.07           | 0.55           | 0.90           | 0.82           | 1.00     | 0.048|
| Ex-drinkers             | 0.82                | 0.62                | 1.07           | 0.14           | 0.58           | 0.45           | 0.74     | <0.001|
| **BMI (kg/m2)**         |                     |                     |                |                |                |                |
| <18.5                   | 1.24                | 1.02                | 1.51           | 0.033          | 1.12           | 0.96           | 1.32     | 0.16  |
| 18.5-22.9               | 1.00                | 1.00                | 1.00           | 1.00           | 1.00           | 1.00           |         |
| 23-27.4                 | 0.73                | 0.65                | 0.82           | <0.001         | 0.82           | 0.75           | 0.91     | <0.001|
| ≥27.5                   | 0.79                | 0.67                | 0.92           | 0.0024         | 0.73           | 0.63           | 0.85     | <0.001|
| **H. pylori**           |                     |                     |                |                |                |                |
| No                      | 1.00                | 1.00                | 1.00           | 1.00           | 1.55           | 1.09           | 2.21     | 0.016|
| Yes                     | 1.45                | 1.01                | 2.08           | 0.044          | 1.71           | 1.25           | 2.33     | 0.001|
| Unknown                 | 2.36                | 1.80                | 3.09           | <0.001         | 3.31           | 2.60           | 4.21     | <0.001|
| Prognostic Factors |  |  |  |  |  |  |  |  |  |  |  |  |
|-------------------|---|---|---|---|---|---|---|---|---|---|---|---|
|                  | PGC group (N=4,716) |  |  |  |  |  |  |  |  |  |  |  |
|                   | 95% CI |  |  |  |  |  |  |  |  |  |  |  |
|                   | HR     |  |  |  |  |  |  |  |  |  |  |  |
|                   | Lower  |  |  |  |  |  |  |  |  |  |  |  |
|                   | Upper  |  |  |  |  |  |  |  |  |  |  |  |
|                   | P Value |  |  |  |  |  |  |  |  |  |  |  |
| Pathologic T stage|        |  |  |  |  |  |  |  |  |  |  |  |
| T0+Tis            | 3.28   | 0.79 | 13.58 | 0.10 | 2.58 | 0.94 | 7.08 | 0.066 | 2.46 | 0.45 | 13.53 | 0.30 |
| T1                | 1.00   | 1.00 | 1.00 | 2.07 | 1.39 | 3.10 | <0.001 |
| T2                | 1.58   | 1.02 | 2.45 | 0.041 | 3.26 | 2.38 | 4.46 | <0.001 | 0.96 | 0.67 | 1.38 | 0.84 |
| T3                | 3.86   | 2.77 | 5.38 | <0.001 | 8.32 | 6.39 | 10.83 | <0.001 | 0.92 | 0.80 | 1.06 | 0.26 |
| T4                | 6.69   | 4.83 | 9.28 | <0.001 | 12.61 | 9.81 | 16.21 | <0.001 | 1.05 | 0.95 | 1.15 | 0.37 |
| TX                | 11.12  | 7.99 | 15.48 | <0.001 | 27.37 | 21.21 | 35.31 | <0.001 | 0.81 | 0.72 | 0.92 | <0.001 |
| Pathologic N stage|        |  |  |  |  |  |  |  |  |  |  |  |
| N0                | 1.00   | 1.00 | 1.65 | 1.35 | 2.02 | <0.001 |
| N1                | 1.91   | 1.56 | 2.36 | <0.001 | 2.39 | 1.96 | 2.90 | <0.001 | 1.31 | 1.07 | 1.60 | <0.001 |
| N2                | 2.84   | 2.34 | 3.44 | <0.001 | 3.89 | 3.26 | 4.65 | <0.001 | 1.20 | 1.01 | 1.41 | 0.034 |
| N3                | 5.00   | 4.20 | 5.95 | <0.001 | 8.42 | 7.21 | 9.83 | <0.001 | 0.97 | 0.86 | 1.08 | 0.56 |
| NX                | 6.56   | 5.51 | 7.81 | <0.001 | 12.60 | 10.79 | 14.73 | <0.001 | 0.85 | 0.76 | 0.96 | 0.007 |
| Pathologic M stage|        |  |  |  |  |  |  |  |  |  |  |  |
| M0                | 1.00   | 1.00 | 1.28 | 1.18 | 1.38 | <0.001 |
| M1                | 4.96   | 4.33 | 5.68 | <0.001 | 7.45 | 6.73 | 8.25 | <0.001 | 0.85 | 0.73 | 0.98 | 0.027 |
| pTNM              |        |  |  |  |  |  |  |  |  |  |  |  |
| 0                 | 4.06   | 0.99 | 16.71 | 0.052 | 2.25 | 0.71 | 7.14 | 0.17 | 3.16 | 0.53 | 19.05 | 0.21 |
| I                 | 1.00   | 1.00 | 2.04 | 1.42 | 2.94 | <0.001 |
| II                | 2.26   | 1.63 | 3.15 | <0.001 | 4.43 | 3.35 | 5.86 | <0.001 | 1.03 | 0.81 | 1.29 | 0.84 |
| III               | 6.39   | 4.79 | 8.52 | <0.001 | 12.28 | 9.64 | 15.64 | <0.001 | 1.03 | 0.94 | 1.12 | 0.58 |
| IV                | 23.33  | 17.19 | 31.68 | <0.001 | 54.77 | 42.63 | 70.38 | <0.001 | 0.85 | 0.73 | 0.98 | 0.027 |
| Lauren classification|        |  |  |  |  |  |  |  |  |  |  |  |
| Intestinal        | 1.00   | 1.00 | 1.68 | 1.31 | 2.15 | <0.001 |
| Diffuse           | 1.93   | 1.54 | 2.42 | <0.001 | 2.09 | 1.66 | 2.62 | <0.001 | 1.54 | 1.25 | 1.90 | <0.001 |
| Mixed             | 1.54   | 1.22 | 1.94 | 0.0003 | 1.37 | 1.04 | 1.81 | 0.024 | 1.88 | 1.45 | 2.46 | <0.001 |
| Unknown           | 2.76   | 2.35 | 3.24 | <0.001 | 4.45 | 3.64 | 5.44 | <0.001 | 1.05 | 0.97 | 1.13 | 0.22 |
Table 2: Continued.

| Prognostic Factors | PGC group (N=4,716) | DGC group (N=7,228) | PGC versus DGC |
|--------------------|---------------------|---------------------|----------------|
|                    | HR                  | 95% CI              | HR             | 95% CI              | HR             | 95% CI              | P Value |
|                    | Lower               | Upper               | P Value        | Lower               | Upper               | P Value               |
| Stage              |                     |                     |                |                     |                     |                     |
| Early stage        | 1.00                | 1.00                | 2.09           | 1.31                | 3.32                | 0.002                 |
| LAGC               | 5.29                | 3.65 7.65           | <0.001         | 9.18                | 7.24 13.04          | <0.001                 |
| Distant            | 25.33               | 17.25 37.20         | <0.001         | 60.25               | 44.52 81.52         | <0.001                 |
| Type of gastrectomy|                     |                     |                |                     |                     |                     |
| Gastrectomy        | 1.00                |                     | 1.24           | 1.15 1.34           | 0.001                |
| No surgery         | 3.01                | 2.71 3.35           | <0.001         | 4.47                | 4.08 4.88           | <0.001                 |
| Surgical Margin    |                     |                     |                |                     |                     |                     |
| Negative           | 1.00                |                     | 1.27           | 1.17 1.38           | 0.001                |
| Positive on the proximal margin | 1.96    | 1.34 2.87       | 0.0006         | 2.98                | 2.07 4.28           | <0.001                 |
| Positive on the distal margin | 2.49    | 1.63 3.79      | <0.001         | 2.56                | 1.85 3.53           | <0.001                 |
| Positive on the proximal and distal margin | 1.08     | 0.27 4.34   | 0.91          | 2.57                | 1.33 4.95           | 0.005               |
| HER2 score         |                     |                     |                |                     |                     |                     |
| 0 (-)             | 1.00                |                     | 1.45           | 1.22 1.73           | 0.001                |
| 1 (+)             | 0.70                | 0.57 0.86           | 0.001         | 0.85                | 0.72 1.02           | 0.073                 |
| 2 (++)            | 0.69                | 0.53 0.89           | 0.005         | 0.66                | 0.51 0.85           | 0.002                 |
| 3 (+++)           | 0.94                | 0.71 1.26           | 0.08          | 0.99                | 0.72 1.38           | 0.96                  |
| Unknown           | 1.72                | 1.49 1.98           | <0.001        | 2.44                | 2.15 2.77           | <0.001               |
| Linitis plastica  |                     |                     |                |                     |                     |                     |
| No                | 1.00                |                     | 1.15           | 1.08 1.23           | 0.001                |
| Yes               | 2.44                | 1.44 4.12           | 0.001         | 2.37                | 1.63 3.44           | <0.001               |
| Borrmann classification |                 |                     |                |                     |                     |                     |
| Borrmann I        | 1.00                |                     | 1.03           | 0.78 1.35           | 0.85                 |
| Borrmann II       | 1.03                | 0.85 1.24           | 0.79          | 0.93                | 0.73 1.17           | 0.52                  |
| Borrmann III      | 1.14                | 0.94 1.38           | 0.20          | 1.13                | 0.90 1.43           | 0.30                  |
| Borrmann IV       | 2.16                | 1.70 2.75           | <0.001        | 2.11                | 1.65 2.73           | <0.001               |
| Unknown           | 2.44                | 1.99 3.01           | <0.001        | 3.09                | 2.44 3.93           | <0.001               |
| Location          |                     |                     |                |                     |                     |                     |
| PGC               | 1.00                |                     |               |                     |                     |                     |
| DGC               | 0.87                | 0.82 0.93           | <0.001        |                     |                     |                     |
Table 3: Multivariate survival analysis by tumor location.

| Prognostic Factors | Total (n=11,944) | PGC group (n=4,716) | DGC group (n=7,228) |
|--------------------|------------------|---------------------|---------------------|
|                    | HR 95% CI        | HR 95% CI           | HR 95% CI           |
|                    | P Value          | P Value             | P Value             |
| Alcohol consumption|                  |                     |                     |
| Never drinkers     | 1.00             | 1.00                | 1.00                |
| Current drinkers   | 0.94 0.87 1.01   | 0.88 1.09 0.69      | 0.81 0.99 0.034     |
| Ex-drinkers        | 0.74 0.61 0.89   | 0.62 1.07 0.14      | 0.56 0.93 0.012     |
| BMI (kg/m2)        |                  |                     |                     |
| <18.5              | 1.07 0.95 1.22   | 1.06 1.58 0.011     | 0.96 1.13 0.61      |
| 18.5-22.9          | 1.00             | 1.00                | 1.00                |
| 23.0-27.4          | 0.89 0.83 0.96   | 0.71 0.90 <0.001     | 0.96 1.06 0.44      |
| ≥27.5              | 0.91 0.82 1.01   | 0.80 1.09 0.41      | 0.75 1.01 0.07      |
| H. pylori          |                  |                     |                     |
| No                 | 1.00             | 1.00                | 1.00                |
| Yes                | 1.43 1.13 1.81   | 1.94 1.94 0.11      | 1.52 2.07 0.009     |
| Unknown            | 1.73 1.44 2.08   | 1.23 2.13 <0.001    | 1.82 2.33 <0.001    |
| Pathologic T stage |                  |                     |                     |
| T0+Tis             | 1.66 0.72 3.85   | 0.56 9.94 0.24      | 0.52 4.17 0.46      |
| T1                 | 1.00             | 1.00                | 1.00                |
| T2                 | 1.53 1.05 2.24   | 0.41 1.62 0.57      | 1.89 3.00 0.007     |
| T3                 | 2.65 1.86 3.76   | 0.79 2.73 0.22      | 3.20 4.91 <0.001    |
| T4                 | 3.28 2.32 4.64   | 1.08 3.69 0.028     | 3.77 5.75 <0.001    |
| TX                 | 2.97 2.02 4.36   | 0.76 2.81 0.26      | 3.88 6.23 <0.001    |
| Pathologic N stage |                  |                     |                     |
| N0                 | 1.00             | 1.00                | 1.00                |
| N1                 | 1.36 1.17 1.59   | 1.09 1.69 0.007     | 1.37 1.69 0.0041    |
| N2                 | 1.99 1.73 2.30   | 1.61 2.44 <0.001    | 2.00 2.44 <0.001    |
| N3                 | 3.44 3.01 3.92   | 2.70 4.01 <0.001    | 3.58 4.28 <0.001    |
| NX                 | 1.83 1.41 2.38   | 1.04 2.48 0.034     | 1.91 2.67 <0.001    |
| Prognostic Factors       | Total (n=11,944) |                           |                           |                           |                           |                           |                           |                           |
|--------------------------|------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|
|                          | HR               | 95% CI                    | P Value                   | HR                        | 95% CI                    | P Value                   | HR                        | 95% CI                    | P Value                   |
| Pathologic M stage       |                  |                           |                           |                           |                           |                           |                           |                           |                           |
| MI                       | 1.00             | 3.05                      | <0.001                    | 1.00                      | 2.84                      | <0.001                    | 1.00                      | 2.32                      | <0.001                    |
| Pathologic M stage       |                  |                           |                           |                           |                           |                           |                           |                           |                           |
| M0                       | 1.00             |                           |                           |                           |                           |                           |                           |                           |                           |
| M1                       | 1.00             |                           |                           |                           |                           |                           |                           |                           |                           |
| Lauren classification    |                  |                           |                           |                           |                           |                           |                           |                           |                           |
| Intestinal               | 1.00             |                           |                           |                           |                           |                           |                           |                           |                           |
| Diffuse                  | 1.22             | 0.99                      |                           | 1.22                      | 0.99                      |                           | 1.22                      | 0.99                      |                           |
| Mixed                    | 0.99             | 1.10                      | 0.088                     | 1.06                      | 0.97                      | 0.095                     | 1.44                      | 1.14                      | 0.003                     |
| Unknown                  | 1.30             | 1.11                      | <0.001                    | 1.20                      | 0.97                      | 1.49                      | 1.44                      | 1.14                      | 0.003                     |
| Type of gastrectomy      |                  |                           |                           |                           |                           |                           |                           |                           |                           |
| Gastrectomy              | 1.00             |                           |                           |                           |                           |                           |                           |                           |                           |
| No surgery               | 1.43             | 1.22                      | <0.001                    | 1.48                      | 1.15                      | 1.90                      | 1.44                      | 1.17                      | 1.76                      | <0.001                    |
| Surgical Margin          |                  |                           |                           |                           |                           |                           |                           |                           |                           |
| Negative                 | 1.00             |                           |                           |                           |                           |                           |                           |                           |                           |
| Positive on the proximal margin | 1.49     | 1.14                      | 1.94                      | 0.004                     | 1.24                      | 0.84                      | 1.83                      | 0.29                      | 1.67                      | 1.16                      | 2.41                      | 0.006                    |
| Positive on the distal margin | 1.54  | 1.19                      | 1.99                      | 0.001                     | 1.53                      | 1.00                      | 2.34                      | 0.051                     | 1.57                      | 1.13                      | 2.17                      | 0.007                    |
| Positive on the proximal and distal margin | 0.95 | 0.52                      | 1.72                      | 0.85                      | 0.70                      | 0.17                      | 2.82                      | 0.62                      | 1.10                      | 0.57                      | 2.14                      | 0.77                     |
Table 3: Continued.

| Prognostic Factors | Total (n=11,944) |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |
|--------------------|------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                    | HR               | 95% CI   | P Value  | HR       | 95% CI   | P Value  | HR       | 95% CI   | P Value  |
| HER2 score         |                  |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |
| 0 (-)              | 1.00             |          |          | 1.00     |          |          | 1.00     |          |          |          |          |          |          |          |          |          |          |          |          |          |
| 1 (+)              | 0.97             | 0.85     | 1.10     | 0.62     | 0.82     | 0.67     | 1.01     | 0.06     | 1.08     | 0.91     | 1.29     | 0.37     |          |          |          |          |          |          |          |          |          |
| 2 (+++)            | 0.92             | 0.76     | 1.11     | 0.39     | 0.80     | 0.61     | 1.04     | 0.09     | 1.02     | 0.78     | 1.33     | 0.88     |          |          |          |          |          |          |          |          |          |
| 3 (+++)            | 1.16             | 0.93     | 1.45     | 0.19     | 1.13     | 0.84     | 1.52     | 0.43     | 1.15     | 0.82     | 1.61     | 0.42     |          |          |          |          |          |          |          |          |          |
| Unknown            | 1.33             | 1.17     | 1.50     | <0.001   | 1.19     | 0.98     | 1.45     | 0.07     | 1.44     | 1.23     | 1.70     | <0.001   |          |          |          |          |          |          |          |          |          |
| Limitis plastica  |                  |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |
| No                 | 1.00             |          |          | 1.00     |          |          | 1.00     |          |          |          |          |          |          |          |          |          |          |          |          |          |          |
| Yes                | 1.37             | 1.01     | 1.86     | 0.045    | 2.13     | 1.25     | 3.65     | 0.006    | 1.18     | 0.81     | 1.73     | 0.38     |          |          |          |          |          |          |          |          |          |          |
| Borrman classification |              |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |
| Borrman I          | 1.00             |          |          | 1.00     |          |          | 1.00     |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |
| Borrman II         | 0.92             | 0.80     | 1.07     | 0.30     | 0.87     | 0.72     | 1.06     | 0.17     | 0.99     | 0.78     | 1.25     | 0.93     |          |          |          |          |          |          |          |          |          |          |
| Borrman III        | 0.98             | 0.84     | 1.14     | 0.75     | 0.90     | 0.74     | 1.10     | 0.29     | 1.06     | 0.83     | 1.35     | 0.62     |          |          |          |          |          |          |          |          |          |          |
| Borrman IV         | 1.44             | 1.21     | 1.71     | <0.001   | 1.44     | 1.12     | 1.85     | 0.005    | 1.48     | 1.14     | 1.93     | 0.003    |          |          |          |          |          |          |          |          |          |          |
| Unknown            | 1.12             | 0.95     | 1.32     | 0.17     | 1.05     | 0.84     | 1.32     | 0.68     | 1.19     | 0.93     | 1.52     | 0.17     |          |          |          |          |          |          |          |          |          |          |
| Site               |                  |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |
| PGC                | 1.00             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |
| DGC                | 0.94             | 0.88     | 1.00     | 0.058    |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |
Figure 1: The geographical locations of PGC and DGC patients of NCCGDB, 1997–2017.

Figure 2: (a) The changing trends of 5-year OS of PGC and DGC from period 1 to period 4. (b) The changing trends of PFS of PGC and DGC from period 1 to period 4.

There was also an increase in PFS of PGC and DGC groups during the 20 years (Figure 2(b)). The total PFS for GC, PGC, and DGC was 82.0% (95% CI: 81.1%-82.9%), 82.3% (95% CI: 80.9%-83.8%), and 81.9% (95% CI: 80.7%-83.0%), respectively. The PFS of PGC and DGC in period 1 was 72.9% (95% CI: 65.5%-80.3%) and 66.2% (95% CI: 59.4%-73.0%), respectively, while the PFS of PGC and DGC in period 4 was 84.2% (95% CI: 82.1%-86.3%) and 86.9% (95% CI: 85.3%-88.4%), respectively.

4. Discussion

In this study, the clinicopathological characteristics of PGC patients presented differently with DGC patients. Although two groups were predominantly males, PGC had a greater proportion of males than DGC. This was similar to some
previous reports [13, 20, 21]. Yu et al. [13] reported that the gender ratio (M:F) in PGC was up to 5:1. This may be due to poor diet and unhealthy habits in men, such as smoking or alcohol consumption [22].

In addition, our study demonstrated that PGC presented to be more frequent in older patients as compared to DGC, which was similar to two published Chinese reports [13, 21]. In contrast, Park et al. from Korea [12] had shown that PGC patients were more likely to be younger. Two European studies, however, had reported no association between age and tumor location [10, 17]. These differences may be partly attributed to the genetic distinction from populations of different countries.

A primary finding of our study was that PGC was not independently associated with overall mortality, although it has long been thought to confer worse prognosis [11, 13–17]. In the univariate analysis stratified by stage, PGC patients with stage I had worse survival when compared with DGC patients, while there was no statistical survival difference between the two groups with stages II–III. However, PGC patients with stage IV had better survival than DGC. Therefore, the variations of prognosis between PGC and DGC may be related to various stage distributions existing in different studies. The reason for survival differences between PGC and DGC by stage has stayed unclear to date, and we speculate that those in tumor biology between PGC and DGC play a role.

Interestingly, the multivariate analyses reported that BMI was an independent prognostic factor for PGC patients but not for DGC patients. Moreover, a higher BMI was associated with survival benefits, while a lower BMI was associated with higher mortality, which has not been described previously. Our study also identified that no gastrectomy was an adverse independent predictor for both PGC and DGC patients, suggesting that surgery was necessary to improve survival outcomes for resected GC. Today, systematic D2 lymphadenectomy with the goal of complete (R0) resection has long been thought to confer worse prognosis [11, 13–17]. These differences may be partly attributed to the genetic distinction from populations of different countries.

In conclusion, PGC significantly differed from DGC in clinicopathological characteristics and prognosis factors. However, there was no significant relationship between survival outcome and gastric tumor location.

Data Availability

The data used to support the findings of this study are included within the article in Tables 1, 2, and 3.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

Authors’ Contributions

Lulu Zhao and Huang Huang contributed equally to this work. All authors made substantial contributions to the intellectual content of this paper.

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