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# Comparison of clinicopathologic profiles and prognosis of gastric cancer in the upper, middle and lower third of the stomach

## A retrospective cohort study

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**Abstract**

Gastric cancer (GC) is the fourth most common cancer in the world and the second most common cancer in China. The aim of this study was to investigate the clinicopathologic profiles and prognosis of GC in the upper third (UT), middle third (MT) and low third (LT) of the stomach.

Five hundred and forty-two patients with GC resected between January 2010 and January 2014 were retrospectively studied and divided in 3 groups according to cancer location: upper third gastric cancer (UTGC) (n = 62); MTGC (n = 131) and LTGC (n = 349). Clinical and pathological parameters including gender, age, tumor size, macroscopic types, histological types, depth of invasion, lymph node metastasis, venous infiltration and lymph embolism were compared among groups. Overall survival (OS) was calculated based on the aforementioned parameters. Univariate and multivariate survival was analyzed and Cox regression was conducted for each location. The prognostic accuracy was determined using receiver operating characteristic curve analysis.

Patients with UTGC was similar to those with MTGC and both were distinct from those with LTGC based on the tumor size, macroscopic types, depth of invasion and 5-year OS. Patients with MTGC were similar to those with LTGC and distinct from UTGC patients based on gender. 5-year OS were lower for patients with UTGC than those with LTGC ($P = .001$) and were comparable between MTGC and LTGC. No significant differences in 5-year OS were observed between UTGC and MTGC. Cox regression revealed that macroscopic types, depth of invasion and lymph node metastasis were the independent prognostic factors for GC patients regardless of locations. Receiver operating characteristic curve analysis revealed that macroscopic types, depth of invasion and lymph node metastasis were the significantly effective prognosis for the 5-year OS in GC patients regardless of locations.

Our results showed that UTGC is distinct from LTGC whereas MTGC shares some characteristics from both UTGC and LTGC.

**Abbreviations:** GC = gastric cancer, OS = overall survival, ROC = receiver operating characteristic, UTGC = upper third gastric cancer.

**Keywords:** clinicopathologic profiles, different location, gastric cancer, prognosis

## 1. Introduction

Gastric cancer (GC) is the second most common cancer in China and the fourth most common cancer in the world.[1–3] The incidence of GC varies in different geographic regions both in China and in the world. Qinghai Province located in the North-Western China is 1 of the provinces having the highest incidence and mortality of GC in China. The distal GC incidence was steadily decreased in the western world, while the proximal GC incidence and prevalence is increasing during the last few decades.[1,4] GC is a heterogeneous disease in clinical and research perspectives. The controversy is not clear regarding the

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clinicopathology and prognosis of GC from the different locations of stomach. According to the Guidelines of the Japanese GC Association,[5] upper third of GC (UTGC) is defined as adenocarcinoma in the upper third of the stomach. Middle third of GC (MTGC) and lower third of GC (LTGC) were defined as adenocarcinoma in the middle third and lower third respectively. Most reports agreed that LTGC has a better prognosis than UTGC worldwide although different survival of GC with different tumor location was reported.[6,7] However, few studies reported the risk factors for the prognosis of MTGC and the comparisons in clinicopathology and prognosis of UTGC, MTGC and LTGC are not yet known.

We previously analyzed the clinicopathologic characteristics and prognosis in Chinese patients with UTGC following radical surgical treatment.[8] The present study conducted a comparison of clinicopathologic characteristics and prognosis between UTGC, MTGC and LTGC.

## 2. Materials and methods

### 2.1. Patients

A total of 542 GC patients undergoing the radical surgical treatment from January 2010 to January 2014 in the Affiliated Hospital of Qinghai University (Xining, China) were enrolled and retrospectively analyzed. All cases were divided into 3 groups according to cancer location including UTGC (n = 62) group, MTGC (n = 131) group and LTGC (n = 349) group which were located in the upper, middle and lower third of the stomach respectively based on the Guidelines of the Japanese GC Association.[5] Information includes the patient's age, sex, tumor size, macroscopic types, histological types, depth of invasion, lymph node metastasis, lymph embolism and tumor location. Guidelines of the Japanese GC Association was used to evaluate the pathologic diagnosis and classification of GC.[5] Lymph node metastasis was evaluated using the International Union Against Cancer TNM classification system.[9] Preoperative evaluation included endoscopic examination with biopsy and computed tomography. Clinical lymph node metastasis was diagnosed by computed tomography. This study was approved by the Review Board of the Affiliated Hospital of Qinghai University. Written informed consent was obtained from each participant.

### 2.2. Operative procedures

All patients had undergone a D2 gastrectomy and radical resection (complete removal of the tumor with microscopic examination of margins showing no tumor cells). Surgeons with over 10 years of experiences conduced all operations.

### 2.3. Follow-up

Follow-up after operation was done by telephone and outpatient examinations every 3 months for the first year, every 6 months for the second year, and annually thereafter until at least 5 years after the operation or the date of the patient's death. As of January 31, 2019, the percentage of follow-up was 95.6% (518/542).

### 2.4. Statistical analysis

SPSS 22.0 (SPSS Inc., Chicago, IL) was used to do the statistical analyses. The prognostic accuracy was determined by receiver operating characteristic (ROC) curve analysis. Categorical variables was analyzed by Pearson $\chi^2$ test and Fisher exact test. Kaplan–Meier analysis was used for the survival and univariate analysis and log-rank test was adopted to calculate the significance of the difference between curves. The Cox proportional hazards regression model was applied to perform multivariate analysis. All statistical analyses were 2-sided, and it was considered statistically significant when $P$ value $<.05$.

## 3. Results

### 3.1. Clinical and pathologic parameters of GC patients

As shown in Table 1, there were 374 (69.0%) males in a total of 542 patients with GC undergoing radical operation (Table 1). 44 (8.1%) cases were younger than 40 years old, 357 (65.9%) between 40 and 65 years old and 141 (26.0%) older than 65 years old. In addition, 331 (61.1%) cases had the tumor with diameter of $\leq 5$ cm and 211 (38.9%) cases with diameter of $>5$ cm. The analysis of macroscopic types showed that there were 74 (13.7%) cases in early GC (EGC), 59 (10.9%) in progressive stage (Borrmann1+2), and 409 (75.5%) in invasive type (Borrmann3+4). Furthermore, 146 (26.9%) tumors were differentiated and 396 (73.1) were undifferentiated. For depth of invasion, T1 tumors were found in 71 (13.1%) patients, T2 in 90 (16.6%), and T3 in 266 (49.1%) and T4 in 115 (21.2%) respectively. For lymph node metastasis, 180 (33.2%) patients were N0, 69 (12.7%) were N1, 112 (20.7%) were N2 and 181 (33.4%) were N3 respectively. 420 (77.5%) cases had no lymph embolism. 62 (11.4%) cases had tumors located in the upper third of stomach, 131 (24.2%) and 349 (64.4%) in the middle and lower third of stomach respectively.

### 3.2. Univariate and multivariate analysis of 5-year OS for all GC patients

The 1-, 3-, and 5-year OS for patients with GC were 82.8%, 55.0% and 47.5% respectively. Univariate analysis of the clinical factors affecting the 5-year OS revealed the significant differences in tumor size ($P<.001$), macroscopic types ($P<.001$), histological types ($P=.011$), depth of invasion ($P<.001$), lymph node metastasis ($P<.001$), lymph embolism ($P<.001$) and tumor location ($P=.001$) (Table 1 and Fig. 1). Among these factors, 5-year OS for patients with GC located in upper, middle and lower third of stomach were 35.0%, 43.2%, and 51.4% respectively. Multivariate analysis of the risk factors for 5-year OS identified by univariate analysis showed that macroscopic types (relative risk, RR, 2.084; 95% confidence interval, CI, 1.495–2.906; $P<.001$), depth of invasion (RR, 1.456; 95% CI, 1.216–1.742; $P<.001$) and lymph node metastasis (RR, 1.588; 95% CI, 1.407–1.792; $P<.001$), lymph embolism (RR, 1.485; 95% CI, 1.141–1.932; $P=.003$) and tumor location (RR, 0.693; 95% CI, 0.493–0.975; $P=.035$) were the independent prognostic factors of patients with GC (Table 2).

### 3.3. Clinicopathological features of patients with GC in each location and comparisons between 3 locations

The results demonstrated the percentage of male patients was higher in UTGC group (91.9%) than that in MTGC (66.4%) ($P=.001$) group or LTGC (65.9%) ($P=.001$) group (Table 3). A significant difference in percentages of cases was observed for tumor size (54.8 vs 34.1%, $P=.002$), macroscopic types (85.5 vs 73.4%, $P=.020$) and depth of invasion (56.5 vs 45.0% for T3; 29.0 vs 19.5% for T4, $P=.012$) between UTGC and LTGC

**Table 1**

**Univariate analysis of factors affecting 5-yr OS of all GC patients according to clinical and pathologic parameters and tumor locations.**

| Category | N (%) | 5-yr OS (%) | *P* value |
|---|---|---|---|
| Gender | | | .354 |
| Male | 374 (69.0) | 46.3 | |
| Female | 168 (31.0) | 50.1 | |
| Age (yr) | | | .071 |
| <40 | 44 (8.1) | 50.8 | |
| 45–65 | 357 (65.9) | 49.2 | |
| >65 | 141 (26.0) | 42.3 | |
| Tumor size (cm) | | | <.001 |
| ≤5 | 331 (61.1) | 55.3 | |
| >5 | 211 (38.9) | 35.4 | |
| Macroscopic types | | | <.001 |
| Early gastric cancer (EGC) | 74 (13.7) | 95.9 | |
| Borrmann1+2 | 59 (10.9) | 60.8 | |
| Borrmann3+4 | 409 (75.5) | 36.7 | |
| Histological type | | | .011 |
| Differentiated | 146 (26.9) | 58.9 | |
| Undifferentiated | 396 (73.1) | 45.1 | |
| Depth of invasion | | | <.001 |
| T1 | 71 (13.1) | 95.7 | |
| T2 | 90 (16.6) | 64.6 | |
| T3 | 266 (49.1) | 40.6 | |
| T4 | 115 (21.2) | 20.7 | |
| Lymph node metastasis | | | <.001 |
| N0 | 180 (33.2) | 78.9 | |
| N1 | 69 (12.7) | 57.8 | |
| N2 | 112 (20.7) | 42.4 | |
| N3 | 181 (33.4) | 16.1 | |
| Lymph embolism | | | <.001 |
| Absent | 420 (77.5) | 53.4 | |
| Present | 122 (22.5) | 27.0 | |
| Venous infiltration | | | .247 |
| Absent | 537 (99.1) | 47.6 | |
| Present | 5 (0.9) | 20.0 | |
| Location | | | .001 |
| U | 62 (11.4) | 35.0 | |
| M | 131 (24.2) | 43.2 | |
| L | 349 (64.4) | 51.4 | |

GC = gastric cancer, OS = overall survival.

groups. Similar but less extensive results were also found between MTGC and LTGC groups.

### 3.4. Univariate analysis of factors affecting 5-year OS in each location and comparisons between 3 locations according to clinical and pathologic parameters

Kaplan-Meier analysis revealed that 5-year OS rate was 35.0%, 43.2%, and 51.4% for patients with UTGC, MTGC, and LTGC respectively (Table 3). When 5-year OS in the 3 locations were analyzed separately, a significant difference was observed between UTGC and LTGC groups ($P=.001$), and also between MTGC and LTGC ($P=.042$) groups. In addition, univariate analysis showed that tumor size, macroscopic types, depth of invasion, lymph node metastasis and lymph embolism are the prognostic risk factors for patients in each of 3 groups (Table 4). The percentage of 5-year OS in UTGC group was lower than that in LTGC group in terms of males (31.0 vs 52.6%, $P=.001$), ages between 45 and 65 years (34.1 vs 54.4%, $P=.001$), tumor size of >5 cm (22.1 vs 38.7%, $P=.036$), macroscopic types of Borrmann3+4 (29.4 vs 39.5%, $P=.029$), undifferentiated histological types (35.0 vs 49.7%, $P=.015$), depth of invasion of T4 (0 vs 23.4%, $P=.032$), lymph node metastasis of N2 (0.67 vs 47.6%, $P<.001$), absent lymph embolism (43 vs 56.2%, $P=.008$) and absent venous infiltration (45.3 vs 53.6%, $P=.001$) (Table 4).

### 3.5. Multivariate analysis of factors affecting 5-year OS in each location

As shown in Table 5, macroscopic types, depth of invasion and lymph node metastasis were the independent prognostic factors for the 5-year OS of patients with UTGC (RR, 2.252; 95% CI, 1.137–4.460; $P=.020$ for macroscopic types; RR, 1.699; 95% CI, 1.208–2.389; $P=.002$ for depth of invasion; RR, 1.399; 95% CI, 1.108–1.989; $p=.015$ for lymph node metastasis), MTGC (RR, 2.153; 95% CI, 1.070–4.332; $p=.032$ for macroscopic types; RR, 1.507; 95% CI, 1.280–2.342; $P=.035$ for depth of invasion; RR, 1.481; 95% CI, 1.157–1.896; $P=.002$ for lymph node metastasis) and LTGC (RR, 2.113; 95% CI, 1.394–3.203; $P<.001$ for macroscopic types; RR, 1.496; 95% CI, 1.394–3.203; $P<.001$ for depth of invasion; RR, 1.644; 95% CI, 1.394–3.203; $P<.001$ for lymph node metastasis) respectively.

### 3.6. ROC curve analysis of factors affecting 5-year OS in each location

ROC curve analysis was performed to evaluate the prognostic accuracy of macroscopic types, depth of invasion and lymph node metastasis, 3 independent prognostic factors for the 5-year OS in patients with UTGC, MTGC and LTGC respectively. As presented in Figure 2, macroscopic types, depth of invasion and lymph node metastasis showed significantly effective prognosis for the 5-year OS in patients with UTGC (area under curve [AUC], 0.775; 95% CI, 0.657–0.893; $P=.001$ for macroscopic types; AUC, 0.856; 95% CI, 0.750–0.962; $P<.001$ for depth of invasion and AUC, 0.652; 95% CI, 0.500–0.803; $P=.043$ for lymph node metastasis), MTGC (AUC, 0.663; 95% CI, 0.565–0.761; $P=.001$ for macroscopic types; AUC, 0.672; 95% CI, 0.579–0.765; $P=.001$ for depth of invasion and AUC, 0.755; 95% CI, 0.670–0.840; $P<.001$ for lymph node metastasis) and LTGC (AUC, 0.679; 95% CI, 0.622–0.735; $P<.001$ for macroscopic types; AUC, 0.750; 95% CI, 0.699–0.801; $P<.001$ for depth of invasion and AUC, 0.790; 95% CI, 0.742–0.838; $P<.001$ for lymph node metastasis) respectively.

## 4. Discussion

In present study, we found that 5-year OS for patients with UTGC, MTGC and LTGC were 35.0%, 43.2% and 51.4% respectively. We confirmed our previous study showing that 5-year OS was 38.6% for 126 patients with UTGC following radical surgical treatment in Chinese population [8]. We further extended the previous study by comparing the clinicopathologic characteristics and prognosis in patients with UTGC, MTGC and LTGC respectively.

The novelty of this study is that we added new data to compare and interpret the significance of clinicopathologic characteristics in the prognosis for GC, especially in different locations of the stomach. In addition, these data are from Qinghai Province located in the North-Western China, which is 1 of the provinces having the highest incidence and mortality of GC in China. Our

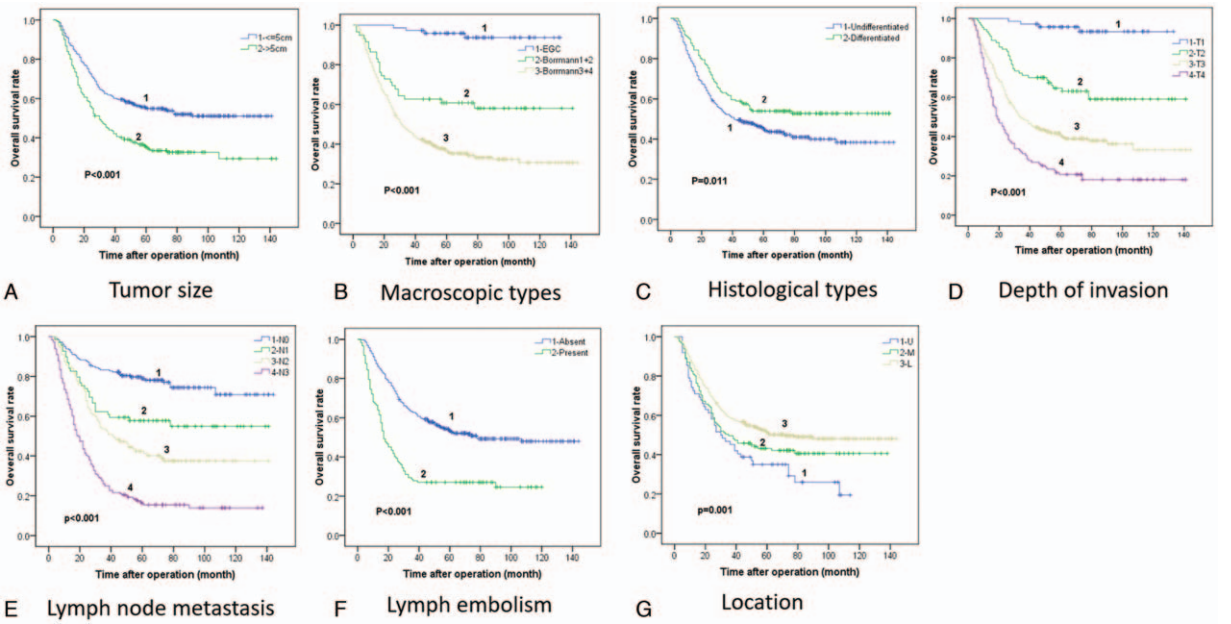


**Figure 1.** OS curves of patients with GC according to clinical and pathologic parameters and tumor locations. GC = gastric cancer, OS = overall survival.

study will provide the evidence for the better prediction of the prognosis for the GC patients in terms of the different location.

The present results showing the poor prognosis in patients with UTGC than those with MTGC or LTGC are consistent with the following the reports. Kim et al compared the prognosis of 271 UTGC patients with that of 2425 patients with MTGC/LTGC and found that the 5-year OS was 49.3% for the former and 57.3% for the latter patients in Korea population.[10] Pinto-de-Sousa et al analyzed the prognosis of 60 UTGC/MTGC patients with those of 162 patients with LTGC and found that the 5-year OS was 20.0% for the former and 50.0% for the latter patients in Portugal population.[11] In Chinese population, Yu et al. demonstrated that 5-year OS was 28.0% for 187 UTGC patients and 51.0% for 777 LTGC patients.[6] Liu et al found that 5-year OS was 27.4% for 73 UTGC patients and 49.5% for 366 LTGC patients.[12] Taken together, these results suggested that patients with UTGC had poor prognosis compared to those with LTGC. However, Wang et al recently reported that the patients with proximal GC (PGC, UTGC) had a better prognosis compared with those with distal GC (DGC, LTGC) in overall population including both the absence and presence of the distant metastasis.[13] The authors also reported that PGC patients in early stage or locally advanced stage had a worse prognosis compared with DGC patients in similar stage, whereas PGC patients with distant metastasis had better prognosis than DGC with distant metastasis. The results suggested that survival between PGC and DGC is stage dependent. Although the reason for the observed difference is currently unclear, the authors speculated that the differences in tumor biology and anatomy between PGC and DGC play a role.[13] The intra-abdominal part of the cardia and fundus are not fully covered by visceral peritoneum perhaps making early PGC more prone to infiltrate the serosa and more inclined to peritoneal metastasis compared with early DGC.[13]

**Table 2**

**Multivariate analysis of factors affecting 5-yr OS of all GC patients.**

| | RR | 95% CI | *P* value |
|---|---|---|---|
| Macroscopic types | 2.084 | 1.495–2.906 | <.001 |
| Depth of invasion | 1.456 | 1.216–1.742 | <.001 |
| Lymph node metastasis | 1.588 | 1.407–1.792 | <.001 |
| Lymph embolism | 1.485 | 1.141–1.932 | .003 |
| Location | 0.693 | 0.493–0.975 | .035 |

CI = confidence interval, GC = gastric cancer, OS = overall survival.

In the present study, we firstly analyzed the clinicopathologic characteristics and prognosis in 542 patients with GC. Univariate analysis identified tumor size, macroscopic types, histological types, depth of invasion, lymph node metastasis, lymph embolism and tumor location as the prognostic factor of 5-year OS. Multivariate analysis identified macroscopic types, depth of invasion, lymph node metastasis, lymph embolism and tumor location as independent prognostic factors of all patients with GC. The results also showed that 5-year OS was 47.5% for all patients with GC. These results are well consistent with the previous reports regarding macroscopic types, depth of invasion, lymph node metastasis and lymph embolism.[7,14,15] The prognostic significance of depth of invasion and lymph node metastases in GC was also previously reported.[8,14,16–18] To examine the influence of separate tumor locations on the survival outcome of GC patients, we divided the 542 GC patients into UTGC, MTGC and LTGC groups and compared the clinicopathologic characteristics and prognosis.

The results showed that UTGC and MTGC share some common characteristics and prognosis in tumor size, macroscopic types, depth of invasion and 5-year OS that are distinct from LTGC. This study also revealed a relatively higher frequency in males in UTGC group than that in MTGC and LTGC groups, a relatively higher frequency in tumor size of >5 cm, in macroscopic types of III+IV and in depth of invasion of T4 in UTGC and MTGC groups than that in LTGC group. A major factor for prognosis of GC is the depth of invasion through the gastric wall.[19–21] The present results showed that both UTGC and MTGC are surgically resected at higher grades (T4 of depth of invasion) when compared to LTGC cases, which can be explained by the anatomic reasons for the deeper invasion.[19,21]

**Table 3**

**Clinicopathological features of patients with GC in each location and comparisons between 3 locations.**

| | n (%) | | | *P* value | | |
|---|---|---|---|---|---|---|
| **Category** | **U** | **M** | **L** | **U vs M** | **U vs L** | **M vs L** |
| Gender | | | | .001 | .001 | .916 |
| Male | 57 (91.9) | 87 (66.4) | 230 (65.9) | | | |
| Female | 5 (8.1) | 44 (33.6) | 119 (34.1) | | | |
| Age (yr) | | | | .236 | .975 | .076 |
| <40 | 2 (3.2) | 8 (6.1) | 34 (9.7) | | | |
| 45–65 | 41 (66.1) | 88 (67.2) | 228 (65.3) | | | |
| >65 | 19 (30.6) | 35 (26.7) | 87 (24.9) | | | |
| Tumor size (cm) | | | | .171 | .002 | .040 |
| ≤5 | 28 (45.2) | 73 (55.7) | 230 (65.9) | | | |
| >5 | 34 (54.8) | 58 (44.3) | 119 (34.1) | | | |
| Macroscopic types | | | | .324 | .020 | .030 |
| EGC | 3 (4.8) | 11 (8.4) | 60 (17.2) | | | |
| Borrmann1+2 | 6 (9.7) | 20 (15.3) | 33 (9.5) | | | |
| Borrmann3+4 | 53 (85.5) | 100 (76.3) | 256 (73.4) | | | |
| Histological types | | | | .868 | .306 | .250 |
| Differentiated | 14 (22.6) | 31 (23.7) | 101 (28.9) | | | |
| Undifferentiated | 48 (77.4) | 100 (76.3) | 248 (71.1) | | | |
| Depth of invasion | | | | .315 | .012 | .026 |
| T1 | 3 (4.8) | 10 (7.6) | 58 (16.6) | | | |
| T2 | 6 (9.7) | 18 (13.7) | 66 (18.9) | | | |
| T3 | 35 (56.5) | 74 (56.5) | 157 (45.0) | | | |
| T4 | 18 (29.0) | 29 (22.1) | 68 (19.5) | | | |
| Lymph node metastasis | | | | .239 | .679 | .226 |
| N0 | 23 (37.1) | 38 (29.0) | 119 (34.1) | | | |
| N1 | 5 (8.1) | 17 (13.0) | 47 (13.5) | | | |
| N2 | 15 (24.2) | 27 (20.6) | 70 (20.1) | | | |
| N3 | 19 (30.6) | 49 (37.4) | 113 (32.4) | | | |
| Lymph embolism | | | | .644 | .257 | .076 |
| Absent | 46 (74.2) | 93 (71.0) | 281 (80.5) | | | |
| Present | 16 (25.8) | 38 (29.0) | 68 (19.5) | | | |
| Venous infiltration | | | | .523 | .512 | .315 |
| Absent | 58 (93.5) | 120 (91.6) | 315 (90.2) | | | |
| Present | 4 (6.5) | 11 (8.4) | 34 (9.8) | | | |
| 5-year OS rate (%) | 35.0 | 43.2 | 51.4 | .155 | .001 | .042 |

GC = gastric cancer, OS = overall survival.

**Table 4**

**Univariate analysis of factors affecting 5-yr OS in each location and comparisons between 3 locations according to clinical and pathologic parameters.**

| | 5-yr OS (%) | | | *P* value | | |
|---|---|---|---|---|---|---|
| **Category** | **U** | **M** | **L** | **U vs M** | **U vs L** | **M vs L** |
| Gender | *P*=.267 | *P*=.493 | *P*=.809 | | | |
| Male | 31.0 | 38.4 | 52.6 | .192 | .001 | .058 |
| Female | 26.7 | 49.5 | 48.9 | .790 | .817 | .661 |
| Age (yr) | *P*=.711 | *P*=.690 | *P*=.129 | | | |
| <40 | 50.0 | 50.0 | 50.5 | .780 | .818 | .707 |
| 45–65 | 34.1 | 42.7 | 54.4 | .107 | .001 | .077 |
| >65 | 36.8 | 42.4 | 43.5 | .761 | .460 | .539 |
| Tumor size (cm) | *P*=.033 | *P*=.039 | *P*<.001 | | | |
| ≤5 | 50.0 | 48.7 | 57.9 | .679 | .154 | .160 |
| >5 | 22.1 | 36.1 | 38.7 | .230 | .036 | .474 |
| Macroscopic types | *P*=.027 | *P*=.001 | *P*<.001 | | | |
| EGC | 100.0 | 90.9 | 96.6 | .602 | .664 | .570 |
| Borrmann1+2 | 50.0 | 65.0 | 60.3 | .579 | .741 | .633 |
| Borrmann3+4 | 29.4 | 33.4 | 39.5 | .373 | .029 | .155 |
| Histological type | *P*=.589 | *P*=.080 | *P*=.086 | | | |
| Differentiated | 35.7 | 55.7 | 55.2 | .163 | .066 | .831 |
| Undifferentiated | 35.0 | 38.6 | 49.7 | .427 | .015 | .067 |

(*continued*)

**Table 4**

**(continued).**

| Category | 5-yr OS (%) | | | *P* value | | |
|---|---|---|---|---|---|---|
| | U | M | L | U vs M | U vs L | M vs L |
| Depth of invasion | *P*<.001 | *P*=.001 | *P*<.001 | | | |
| T1 | 100 | 90.0 | 96.5 | .584 | .654 | .553 |
| T2 | 33.3 | 53.5 | 65.5 | .974 | .563 | .504 |
| T3 | 36.7 | 41.3 | 40.2 | .660 | .620 | .979 |
| T4 | 0 | 20.1 | 23.4 | .233 | .032 | .595 |
| Lymph node metastasis | *P*<.001 | *P*<.001 | *P*<.001 | | | |
| N0 | 70.4 | 73.7 | 80.8 | .778 | .133 | .209 |
| N1 | 40.0 | 51.5 | 61.7 | .484 | .361 | .745 |
| N2 | 0.67 | 40.0 | 47.6 | .015 | <.001 | .413 |
| N3 | 0.53 | 16.3 | 18.1 | .308 | .070 | .515 |
| Lymph embolism | *P*=.013 | *P*<.001 | *P*<.001 | | | |
| Absent | 43.0 | 50.0 | 56.2 | .152 | .008 | .216 |
| Present | 12.5 | 26.3 | 30.9 | .716 | .377 | .532 |
| Venous infiltration | *P*=.125 | *P*=.325 | *P*=.258 | | | |
| Absent | 45.3 | 51.2 | 53.6 | .142 | .001 | .067 |
| Present | 35.6 | 42.5 | 45.2 | – | – | .351 |

OS = overall survival.

**Table 5**

**Multivariate analysis of factors affecting 5-yr OS in each location.**

| | U | | M | | L | |
|---|---|---|---|---|---|---|
| | RR (95% CI) | *P* value | RR (95% CI) | *P* value | RR (95% CI) | *P* value |
| Macroscopic types | 2.252 (1.137–4.460) | .020 | 2.153 (1.070–4.332) | .032 | 2.113 (1.394–3.203) | <.001 |
| Depth of invasion | 1.699 (1.208–2.389) | .002 | 1.507 (1.280–2.342) | .035 | 1.496 (1.203–1.861) | <.001 |
| Lymph node metastasis | 1.399 (1.108–1.989) | .015 | 1.481 (1.157–1.896) | .002 | 1.644 (1.402–1.929) | <.001 |

CI = confidence interval, OS = overall survival.

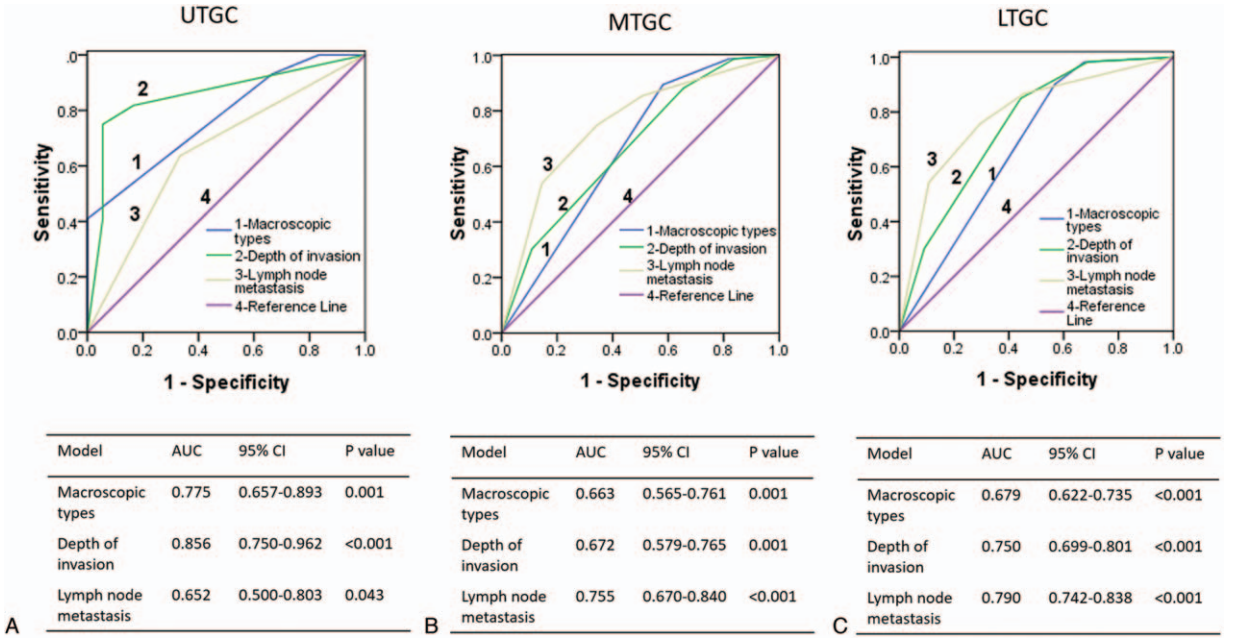


**Figure 2.** ROC curves for patients with UTGC, MTGC and LTGC in terms of macroscopic types, depth of invasion and lymph node metastasis. ROC = receiver operating characteristic, UTGC = upper third gastric cancer.

The relative frequency of gender in MTGC group were distinct from that in UTGC group and similar to that in LTGC group. A higher ratio of male:female was found in UTGC group (11.4:1) compared to that in MTGC (2.0:1) group or in LTGC group (1.9:1). These results are well consistent with the previous reports [22,23] and confirm the assumption that male cases are more easily exposed to exogenous factors including smoke or alcohol involved in the pathogenesis of UTGC.[24]

Comparison of 5-year OS between UTGC, MTGC and LTGC groups based on the clinic and pathologic characteristics revealed significant differences in some subsets. The percentage of 5-year OS in UTGC group was lower than that in LTGC group in terms of males, ages between 45 and 65 years, tumor size of >5 cm, macroscopic types of borrmann 3 + 4, undifferentiated histological types, depth of invasion of T4, lymph node metastasis of N2, absent lymph embolism and absent venous infiltration. These results confirm that GC is a heterogeneous disease.

For all 3 locations, multivariate analysis identified macroscopic types, depth of invasion and lymph node metastasis as the common factors for prognosis, which are in consistent with the results of other studies.[14,25] The prognostic significance of lymph node metastasis is also in consistent with other reports.[6,7] In addition, ROC curve analysis revealed that macroscopic types, depth of invasion and lymph node metastasis showed significantly effective prognosis for the 5-year OS in patients regardless of locations.

The imitation of this study is that this was a retrospective study at a single institution. In addition, TNM stage and diffuse type are not included in the present study, which will be investigated in the future study.

## 5. Conclusion

In summary, the present study suggested that patients with UTGC were similar to MTGC patients and distinct from LTGC patients in several respects. Cox regression identified macroscopic types, depth of invasion and lymph node metastasis as prognostic factors for patients with GC in the 3 locations.

## Author contributions

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