

## Retrospective Study

# Clinicopathological features of patients with middle third gastric carcinoma

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## Abstract

**AIM:** To compared the prognosis of middle third gastric carcinoma (MGC) patients with those of patients with proximal/distal gastric carcinoma (PGC/DGC).

**METHODS:** Of 3299 patients diagnosed with gastric carcinoma who underwent surgery at our hospital over a 15-year period, 919 (27.9%) were diagnosed with MGC. For each patient, the following information was obtained from hospital records: Age, sex, tumor size, depth of invasion, histologic type, nodal involvement, extent of lymph node dissection, hepatic metastasis, peritoneal dissemination, stage at initial diagnosis, operative type, curability, and survival rate.

**RESULTS:** T1 category tumors were more common in patients with MGC than in patients with PGC ( $P < 0.001$ ). Tumor stage (stage I), N category (N0), and T category (T1) significantly influenced the 5-year survival rates for patients with curatively resected tumors. A multivariate analysis showed that age, tumor size, serosal invasion, lymph node metastasis, and curability were significant predictors of survival in patients with MGC. The survival rate for MGC patients was similar to that for PGC/DGC patients (52.8% vs 44.4%/51.4%,  $P = 0.1138$ ). The 5-year survival rate for MGC patients with curative resection was higher than that for MGC patients with non-curative resection (62.9% vs 8.7%,  $P < 0.001$ ).

**CONCLUSION:** These results indicate that tumor

location did not affect the prognosis. Curative resection is important for improving the prognosis of patients with MGC.

**Key words:** Middle third gastric carcinoma; Prognosis; Curative resection

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**Core tip:** The clinicopathological features of the patients with middle third gastric carcinoma (MGC) were reviewed retrospectively. Tumor location did not affect the prognosis. When the MGC group was divided into patients with or without curative resection, the survival rates were higher for patients with curative resection. Therefore, curative resection is important for improving the prognosis of patients with MGC.

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## INTRODUCTION

Although the incidence of gastric carcinoma is declining, it remains one of the leading causes of death from malignant tumors worldwide and advanced gastric carcinoma patients still have unfavorable prognoses<sup>[1]</sup>. Generally, the prognosis of patients with middle third gastric carcinoma (MGC) is better than that of patients with proximal or distal third gastric carcinoma (PGC/DGC)<sup>[2]</sup>; however, few studies have described the follow-up of patients with MGC. Therefore, it is important to analyze the prognostic factors in patients with MGC. We compared the clinicopathological features and outcomes of MGC with those of more proximally or distally located gastric carcinomas.

## MATERIALS AND METHODS

### Patients

Between 1987 and 2004, 3299 patients with gastric carcinoma were admitted to the Division of Gastroenterologic Surgery, Department of Surgery, Chonnam National University Medical School, Gwangju, South Korea. Of these, 919 (27.9%) had MGC. The clinicopathological features of the patients with MGC were reviewed retrospectively. Patients with carcinomas involving the entire stomach were excluded. Following the Japanese classification of gastric carcinoma outlined by the Japanese Research Society for Gastric Cancer<sup>[3]</sup>, the location of each tumor was described as the proximal, middle, or distal third of the stomach. The following information about each patient was obtained from hospital records: Age, sex, tumor size, depth of invasion,

histologic type, nodal involvement, extent of lymph node dissection, hepatic metastasis, peritoneal dissemination, stage at initial diagnosis, operative type, curability, and survival rate.

### Statistical analysis

The survival rates of the patients were calculated using the Kaplan-Meier method, and the relative prognostic importance of the parameters was investigated using the Cox proportional hazards model. The  $\chi^2$  test was used to evaluate the statistical significance of differences, and *P* values less than 0.05 were considered significant.

## RESULTS

Of the 3299 patients diagnosed with gastric carcinoma who underwent surgery at our hospital over a 17-year period, 919 (27.9%) were diagnosed with MGC. Table 1 describes the clinicopathological features of these 919 patients and the 2312 patients with PGC/DGC. There was a significant difference in the mean age of the patients with MGC (55.8 years) compared to the patients with DGC (57.6 years) (*P* < 0.001). Of the 919 patients with MGC, 602 (65.5%) were male and 317 (34.5%) were female. There were more males than females in each group, but there was no significant difference in the sex ratio of each group. Carcinomas in the middle third of the stomach were smaller than were carcinomas in the proximal third of the stomach (4.2 cm vs 4.7 cm), and the difference in mean tumor size was significant (*P* < 0.001).

Using the pTNM system, 296 patients with MGC were classified as pT1, 112 as pT2, 410 as pT3, and 101 as pT4. T1 tumors were more common in patients with MGC than in patients with PGC (32.2% vs 13.1%, *P* < 0.001). Using the grade of anaplasia, 324 (35.3%) of the MGC tumors were differentiated and 595 (64.7%) were undifferentiated adenocarcinomas. Of the patients with MGC, 561 (61.1%) had no lymph node metastases (pN0) and 358 (38.9%) had lymph node metastases. Lymph node metastasis was less common in patients with MGC than in patients with PGC (*P* < 0.05).

Hepatic metastases from MGC were found in 20 patients (2.2%), and peritoneal dissemination was present in 81 patients (8.8%). No significant differences were found in the frequency of hepatic metastasis or peritoneal dissemination among the groups. Of the patients with MGC, 396 (43.1%) were classified as either stage III or IV at the initial diagnosis. In MGC patients, 55.6% of the tumors extended to the serosa or adjacent organs (pT3 and pT4), while 72.5% of the PGCs extended beyond the serosa.

Compared with its use in MGC/DGC, total gastrectomy was performed significantly more frequently for the treatment of PGC (85.6% of cases, *P* < 0.001). The curative resection rate for patients with MGC was 83.1%, similar to that for patients with PGC/DGC (81.4%/82.9%,

**Table 1 Clinicopathologic findings of middle, proximal and distal third gastric carcinoma patients**

Variables	MGC ( <i>n</i> = 919) (%)	PGC ( <i>n</i> = 312) (%)	DGC ( <i>n</i> = 2000) (%)	<i>P</i> value
Age (mean, yr)	55.8 ± 11.7	55.8 ± 12.5	57.6 ± 10.7	< 0.001
Gender				0.277
Male	602 (65.5)	219 (70.2)	1327 (66.4)	
Female	317 (34.5)	93 (29.8)	673 (33.6)	
Tumor size (mean, cm)	4.2 ± 2.8	4.7 ± 2.6	3.7 ± 2.3	< 0.001
Depth of invasion				< 0.001
T1	296 (32.2)	41 (13.1)	648 (32.4)	
T2	112 (12.2)	45 (14.4)	307 (15.4)	
T3	410 (44.6)	177 (56.8)	844 (42.2)	
T4	101 (11.0)	49 (15.7)	201 (10.0)	
Histologic type				< 0.001
Differentiated	324 (35.3)	108 (34.6)	941 (47.1)	
Undifferentiated	595 (64.7)	204 (65.4)	1059 (52.9)	
Lymph node dissection				0.018
< D2	215 (23.4)	51 (16.3)	475 (23.7)	
≥ D2	704 (76.6)	261 (83.7)	1525 (76.3)	
Lymph node metastasis				0.045
N (-)	561 (61.1)	125 (40.1)	1217 (60.9)	
N (+)	358 (38.9)	187 (59.9)	783 (39.1)	
Operative type				< 0.001
Total gastrectomy	297 (32.3)	267 (85.6)	75 (3.8)	
Others	622 (67.7)	45 (14.4)	1925 (96.2)	
Hepatic metastasis				0.068
H (-)	899 (97.8)	300 (96.2)	1914 (95.7)	
H (+)	20 (2.2)	12 (3.8)	86 (4.3)	
Peritoneal dissemination				0.556
P (-)	838 (91.2)	282 (90.4)	1829 (91.4)	
P (+)	81 (8.8)	30 (9.6)	171 (8.6)	
Stage				< 0.001
I	356 (38.7)	71 (22.7)	840 (42.0)	
II	167 (18.2)	66 (21.2)	322 (16.1)	
III	223 (24.3)	109 (34.9)	432 (21.6)	
IV	173 (18.8)	66 (21.2)	406 (20.3)	
Curability				0.796
Curative	764 (83.1)	254 (81.4)	1658 (82.9)	
Non-curative	155 (16.9)	58 (18.6)	342 (17.1)	

MGC: Middle third gastric carcinoma; PGC: Proximal third gastric carcinoma; DGC: Distal third gastric carcinoma.

*P* > 0.05).

The clinicopathological variables tested in our univariate analysis are shown in Table 2. Factors influencing the 5-year survival rate were patient age, sex, tumor size, depth of invasion, histologic type, presence of hepatic metastasis, lymph node invasion, extent of lymph node dissection, and stage at initial diagnosis. When corrected for depth of invasion, tumor stage, and lymph node invasion in the two groups, tumor stage (stage I), N category (N0), and T category (T1) significantly influenced the 5-year survival rates for patients with curatively resected tumors (Table 3). A multivariate analysis showed that age, tumor size, serosal invasion, lymph node metastasis, and operative curability were significant predictors of survival for patients with MGC (Table 4). Figure 1 shows the patient survival rate according to tumor location. The 5-year survival rate for patients with MGC (52.8%) was higher than that for patients with PGC/DGC (44.4%/51.4%), but not significantly (*P* > 0.05). When the MGC group was divided into patients with or without curative

resection, the respective 5-year survival rates were 62.9% and 8.7% (*P* < 0.001) (Figure 2). There were no significant differences in the survival rates among MGC, PGC, and DGC when the patients were divided into early and advanced gastric carcinoma (Figures 3 and 4).

## DISCUSSION

The prognosis of gastric carcinoma varies with tumor location<sup>[4-6]</sup>. Although MGCs are reported to have relatively better outcomes than carcinomas in other parts of the stomach<sup>[2]</sup>, there is limited information on the prognostic factors for MGC. Therefore, we compared the clinicopathological features and prognosis of MGC patients with those of patients with PGC/DGC.

Investigators have discussed various prognostic factors for MGC. Serosal invasion, lymph node metastasis, and lymphatic involvement were found to have significant correlations with prognosis in univariate analyses, and serosal invasion and lymphatic involvement were independent prognostic factors in a multivariate analysis<sup>[7]</sup>.

**Table 2** Univariate analysis of prognostic factors in middle third gastric carcinoma patients

Variables	No. of patients	5-yr survival rate	P value
Age			0.0057
< 65	688	56.0	
≥ 65	231	40.0	
Gender			0.0161
Male	602	48.9	
Female	317	59.9	
Tumor size (cm)			< 0.001
< 5	616	68.5	
≥ 5	303	28.0	
Depth of invasion			< 0.001
T1	296	88.3	
T2	112	75.9	
T3	410	37.8	
T4	101	15.4	
Histologic type			0.0294
Differentiated	324	62.8	
Undifferentiated	595	48.2	
Hepatic metastasis			< 0.001
(-)	899	53.7	
(+)	20	10.8	
Operative type			0.4327
Total	297	52.4	
Others	622	63.6	
Lymph node invasion			< 0.001
N (-)	561	77.5	
N (+)	358	32.7	
Lymph node dissection			< 0.001
< D2	215	18.3	
≥ D2	704	60.0	
Stage			< 0.001
I	356	87.5	
II	167	62.5	
III	223	35.2	
IV	173	14.7	

**Table 3** Influence of T category, and N category on the 5-year survival rate of patients with middle third gastric carcinoma surgically treated with curative intent

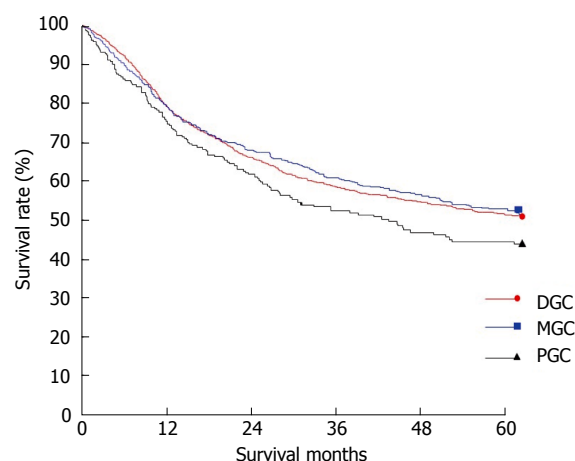
Variables	PGC (n = 254) (%)	MGC (n = 764) (%)	P value
Depth of invasion			
T1	77.6	88.8	0.0477
T2	76.0	76.1	0.7534
T3	44.6	45.1	0.9900
T4	17.3	16.8	0.1698
Lymph node metastasis			
N0	72.3	79.9	0.0270
N1	42.7	49.6	0.6285
N2	33.4	31.0	0.6933
Stage			
I	77.2	87.9	0.0420
II	68.4	63.2	0.5566
III	33.7	36.3	0.5823
IV	17.6	21.8	0.3635

MGC: Middle third gastric carcinoma; PGC: Proximal third gastric carcinoma.

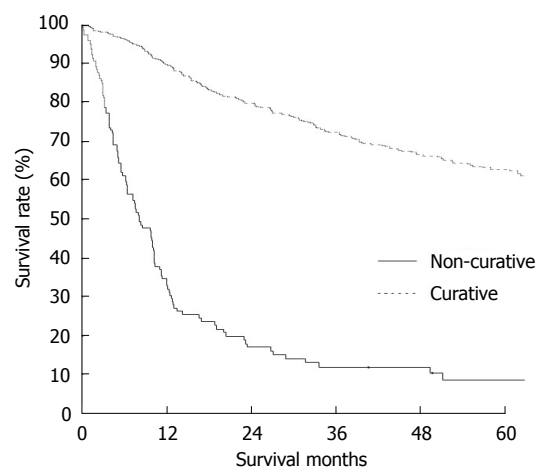
Other authors have reported similar findings<sup>[8,9]</sup>. An anterior location was clearly an independent prognostic factor for patients with MGC based on a multivariate

**Table 4** Multivariate analysis of survival for middle third gastric carcinoma patients

Variables	Risk ratio	95%CI	P value
Age (< 65 <i>vs</i> ≥ 65)	1.78	1.24-2.55	0.002
Tumor size (mm) (< 50 <i>vs</i> ≥ 50)	1.51	1.03-2.21	0.036
Serosal invasion (negative <i>vs</i> positive)	2.46	1.45-4.15	0.001
Lymph node metastasis (negative <i>vs</i> positive)	2.48	1.59-3.87	0.000
Curability (curative <i>vs</i> non-curative)	3.46	2.29-5.23	< 0.001

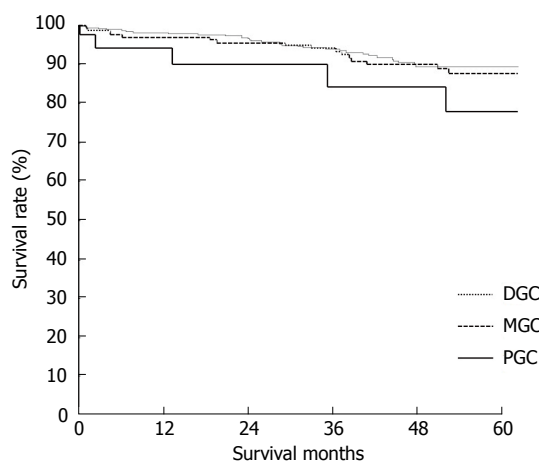


**Figure 1** Survival curves for middle third gastric carcinoma, proximal third gastric carcinoma and distal third gastric carcinoma. 5-year survival rate: MGC = 52.8%, PGC = 44.4%, DGC = 51.4%;  $P = 0.1138$ . MGC: Middle third gastric carcinoma; PGC: Proximal third gastric carcinoma; DGC: Distal third gastric carcinoma.

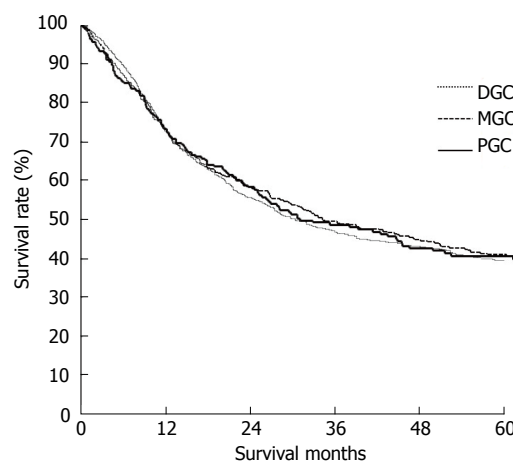


**Figure 2** Survival curves for middle third gastric carcinoma according to curability. Five-year survival rate: curative = 62.9%, non-curative = 8.7%;  $P < 0.001$ .

analysis. It has been postulated that tumors in the anterior wall metastasize more easily to the peritoneum compared with tumors elsewhere because there are no organs on the abdominal side of the anterior wall<sup>[5]</sup>. This explanation seems reasonable, although others do not agree<sup>[7]</sup>. In this study, we found that age, tumor size, serosal invasion,



**Figure 3** Survival curves of early middle third gastric carcinoma, proximal third gastric carcinoma and distal third gastric carcinoma. MGC = 87.8%, PGC = 77.9%, DGC = 89.5%;  $P = 0.0936$ . MGC: Middle third gastric carcinoma; PGC: Proximal third gastric carcinoma; DGC: Distal third gastric carcinoma.



**Figure 4** Survival curves of advanced middle third gastric carcinoma, proximal third gastric carcinoma and distal third gastric carcinoma. MGC = 40.8%, PGC = 40.6%, DGC = 39.1%;  $P = 0.7586$ . MGC: Middle third gastric carcinoma; PGC: Proximal third gastric carcinoma; DGC: Distal third gastric carcinoma.

lymph node metastasis, and curability were independent predictors of survival in patients with MGC in a multivariate analysis.

The operation type for patients with MGC is controversial. One prospective randomized trial conducted in Italy stated that distal gastrectomy was sufficient for treating tumors located in the middle third of the stomach if a cancer-free microscopic margin could be achieved<sup>[10]</sup>. However, that study included a relatively small number of MGCs. Therefore, many surgeons still recommend total gastrectomy for MGC because they are concerned about the possibility of local recurrence due to the short proximal resection margin and less extensive lymph node dissection in distal gastrectomy<sup>[11,12]</sup>. In a separate report, distal gastrectomy was performed in only 39.3% of patients with a middle third advanced gastric carcinoma for the same reasons, although the authors stated that the type of gastric resection and length of the proximal resection margin did not affect the long-term prognosis. They also reported that distal gastrectomy was sufficient to achieve a tumor-free resection margin in many cases<sup>[13]</sup>. Other authors have reported that if curative surgery can be performed, the long-term prognosis of patients with MGC is not affected by the extent of gastric resection, and a distal gastrectomy is feasible<sup>[14-16]</sup>. When determining the type of operation for MGC, we also stress tumor-free resection. The statistical analysis in this study showed that operation type was not a prognostic factor.

Generally, the prognosis of patients with MGC is better than that of patients with PGC/DGC<sup>[2]</sup>; the present study showed that tumor location did not affect the prognosis. We thought that the possible reason was due to similar curative resection rates. A significant difference in survival between patients with early and advanced gastric carcinomas has been reported<sup>[7]</sup>. We also found a significant difference in survival rates between patients with early (87.8%) and advanced (40.8%) gastric carcinomas. The survival rate for patients with MGC was 52.8%, and the cumulative survival rate for patients with

MGC was slightly better than that for patients with PGC/DGC. When the MGC group was divided into patients with or without curative resection, the respective 5-year survival rates were 62.9% and 8.7%. Furthermore, we evaluated the relationship between the survival of patients with gastric carcinoma after curative resection and the depth of invasion. There was no significant difference in cumulative survival between the groups when the depth of invasion was that of T2-T4 tumors.

In patients with MGC, as the tumors progress the lymph nodes around the splenic artery and hilum are also frequently involved<sup>[5]</sup>. Several studies have reported that the incidence of lymph node metastasis is 9.7%-20% along the splenic artery and 9.2%-17% at the splenic hilum in advanced PGC and MGC<sup>[17-19]</sup>. In our department, splenectomy is not routine for patients with advanced MGC. However, we perform a splenectomy when the tumor invades the spleen directly or when metastasis to the splenic hilar lymph nodes or lymph nodes around the splenic artery is suspected.

Regarding adjuvant chemotherapy, we administered postoperative chemotherapy to select patients according to the pathologic findings instead of tumor location. Since the chemotherapeutic regimen varied during the study period, we did not analyze the effect of postoperative adjuvant chemotherapy.

In conclusion, our results show that tumor location did not affect the prognosis of MGC. When the MGC group was divided into patients with or without curative resection, the survival rates were higher for patients with curative resection. Therefore, curative resection is important for improving the prognosis of patients with MGC.

## COMMENTS

### Background

The prognosis of patients with middle third gastric carcinoma (MGC) is better



than that of patients with proximal or distal third gastric carcinoma; however, few studies have described the follow-up of patients with MGC.

### Research frontiers

The prognosis of gastric carcinoma varies with tumor location. Although MGCs are reported to have relatively better outcomes than carcinomas in other parts of the stomach, there is limited information on the prognostic factors for MGC.

### Innovations and breakthroughs

The authors did not find any difference in survival rates according to the tumor location. When the MGC group was divided into patients with or without curative resection, the survival rates were higher for patients with curative resection.

### Applications

The study shows the importance of curative resection in patients with MGC.

### Terminology

The stomach is anatomically divided into three portions: The upper (U), middle (M), and lower (L) parts. If more than one portion is involved, all involved portions should be described in order of degree of involvement, the first indicating the portion in which the bulk of the tumor is situated.

### Peer-review

These authors provided an overall review of the middle third gastric cancer. These authors described several clinico pathological parameters of MGC compared to PGC/DGC. In this article, authors also demonstrated the significant difference between curative resection is one of the prognostic factors for MGC. It is interesting and acceptable for publication.

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