

ORIGINAL ARTICLE

## Clinicopathological features and prognosis of Borrmann type IV gastric cancer

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### Summary

**Purpose:** Borrmann type IV gastric cancer is still detected at an advanced stage and survival rates for these patients remain poor. The purpose of this study was to provide valuable prognostic and surgical information on patients with Borrmann type IV gastric cancer.

**Methods:** We compared the clinicopathological features of Borrmann type IV gastric cancer with those of other types of gastric cancer. Clinicopathologic features of patients with Borrmann type IV gastric cancer were evaluated as prognostic predictors by univariate and multivariate analyses.

**Results:** The results showed that Borrmann type IV gastric cancer had more advanced and unfavorable clinicopathological factors compared with other Borrmann types. The 5-year overall survival rate was 16.7%, and the median sur-

vival 25 months. The 5-year overall survival rate was influenced by tumor size, depth of invasion, lymph node metastasis, and chemotherapy. Of these, independent prognostic factors were lymph node metastasis (present vs absent, risk ratio 1.855,  $p=0.002$ ) and radical (R0) resection (no vs yes, risk ratio 2.035,  $p<0.001$ ). A significant survival benefit for radical resection was observed, with a 5-year overall survival rate of 30.7% compared with non-radically resected cases (4.8%).

**Conclusions:** Early detection and radical resection were essential to improve the prognosis of patients with Borrmann type IV gastric cancer.

**Key words:** Borrmann type IV, gastric cancer, prognosis, radical resection

### Introduction

The classification of advanced gastric cancer according to Borrmann's criteria is presently accepted widely worldwide by endoscopists, radiologists, and surgeons [1,2]. Eleven to 18 percent of all advanced gastric cancers are thought to be Borrmann type IV gastric cancer [3-5]. Borrmann type IV gastric cancer shows a special morphology both macroscopically and microscopically. It is characterized by less differentiated characteristics and wide invasion which results in diffuse rigidity

of the gastric wall and thickening of the mucosal folds as gastric *linitis plastica* [6]. Although there have been substantial advances in various diagnostic and treatment strategies, most Borrmann type IV gastric cancer cases are not detected in early stage and show poor prognosis. The prognosis of patients with Borrmann type IV gastric cancer is poor, with 5-year overall survival rate after gastrectomy ranging from 10.5 to 27.6% [3-5,7,8].

In this study, we retrospectively analyzed the

records of patients with Borrmann type IV gastric cancer that underwent gastrectomy to clarify the clinicopathological features and prognostic indicators, and to examine the survival benefit of radical resection.

## Methods

### Patients

Between 1992 and 2014, 1865 patients with histologically proven advanced gastric cancer underwent gastrectomy at the Department of General Surgery, The First Affiliated Hospital of Jiamusi University, Jiamusi city, China. Of the advanced gastric cancers examined, 259 (13.9%) were Borrmann type IV, 138 (7.4%) Borrmann type I, 417 (22.4%) Borrmann type II, and 1051 (56.4%) Borrmann type III.

Information on the patient age, sex, tumor size, tumor location, histologic type, depth of invasion, lymph node metastasis, liver metastasis, peritoneal dissemination, stage of disease, radicality of operation, and chemotherapy were obtained from the hospital records. These findings were assessed according to the Japanese General Rules for Gastric Cancer Study in Surgery and Pathology [9]. The American Joint Committee on Cancer (TNM staging system) was used for pathologic staging [10]. Radical resection (R0) was determined the operation leaving no macroscopical or microscopical tumor behind. Informed consent had been obtained, and the Ethics Committee of Jiamusi University approved this study.

Patient follow-up lasted until death or until the cut-off date of Dec 2014, with a mean follow-up time of 28 months (range 2-63). Generally, patients visits were every 3 months for the first year, every 6 months for the next 2 years, and every year for 5 years. Follow-up included routine serum biochemistry, full blood count, and CEA/CA 19.9 tumor markers estimations. Chest x-ray, abdominal ultrasound or abdominopelvic CT scan were performed every 6-12 months, and gastroscopy once a year. After 5 years, the follow-up continued on an annual basis. Only patients who died of gastric cancer were regarded as tumor-related death cases.

### Statistics

The intergroup comparisons of clinicopathologic variables were performed with the chi-square test for discrete variables and Student's t-test for continuous variables. Clinicopathologic variables of 192 patients with Borrmann type IV gastric cancer that underwent gastrectomy before Dec 2009 were evaluated as prognostic predictors by univariate and multivariate analyses. The Kaplan-Meier method was used for calculating cumulative survival rates, and the difference between groups was assessed by using the log-rank test. Covariates that remained significant through the univariate analysis were selected for multivariate analysis. Cox

regression was used for multivariate analysis, with backward stepwise elimination model. The accepted level of significance was  $p < 0.05$ . All data analysis was performed using the SPSS for Windows, Version 13.0 software package.

## Results

### Clinicopathological findings

Table 1 summarizes the clinicopathological data of 259 patients with Borrmann IV gastric cancer, and of 1606 patients with other types of gastric cancer, all of whom underwent gastrectomy. There were significant differences in the distribution of age, sex, tumor size, tumor location, histologic type, depth on invasion, lymph node metastasis, peritoneal dissemination, stage of disease, and radicality of operation between the two groups. In the Borrmann type IV group age was younger and females were more frequent. The size of Borrmann type IV gastric cancer was larger than that of other types, and 18.9% of the Borrmann type IV tumors occupied the whole stomach. The frequency of deeper cancer invasion was higher in Borrmann type IV tumors. More poorly differentiated, extensive lymph node metastasis, and peritoneal dissemination were noted in Borrmann type IV tumors than in others types. Borrmann type IV gastric cancer was detected at a stage higher than III in 81.9% of the patients. The rate of operative radicality was lower in Borrmann type IV group.

### Survival and prognostic factors

In patients with Borrmann type IV gastric cancer, the 5-year overall survival rate was 16.7%, and the median survival was 25 months. The 5-year overall survival rate was influenced by tumor size, depth on invasion, lymph node metastasis, radicality of the operation, and chemotherapy (Table 2). A significant survival benefit for R0 resection was observed, with a 5-year overall survival rate of 30.7% compared with non-R0 resected cases (4.8%). Five factors significant in the univariate analysis were included in the multivariate analysis, which indicated that survival was independently influenced by lymph node metastasis and radical resection (Table 3).

## Discussion

This study on Borrmann type IV gastric cancer examined the 12 clinicopathological parameters and identified that factors significantly asso-

**Table 1.** Clinicopathological features of Borrmann type IV gastric cancer versus other Borrmann types

Features	Borrmann I, II, III N=1606 (%)	Borrmann IV N=259 (%)	p value
Age (mean, years)	57.5±12.2	55.8±11.5	0.008
Sex			<0.001
Male	1147 (71.4)	150 (57.9)	
Female	459 (28.6)	109 (42.1)	
Tumor size (mean, cm)	6.9±3.5	10.2±4.8	0.005
Tumor location			<0.001
Upper	249 (15.5)	46 (17.8)	
Middle	275 (17.1)	63 (24.3)	
Lower	947 (59.0)	101 (39.0)	
Whole	135 (8.4)	49 (18.9)	
Histologic type			<0.001
Well and moderate differentiated	531 (33.1)	21 (8.1)	
Poorly differentiated	764 (47.6)	195 (75.3)	
Signet ring cell and mucinous	311 (19.4)	43 (16.6)	
Depth on invasion			<0.001
T1/T2	461 (28.7)	35 (13.5)	
T3	827 (51.5)	147 (56.8)	
T4	318 (19.8)	77 (29.7)	
Lymph node metastasis			<0.001
N0	353 (22.0)	25 (9.7)	
N1	462 (28.8)	75 (29.0)	
N2	542 (33.7)	61 (23.6)	
N3	249 (15.5)	98 (37.8)	
Stage			<0.001
I	314 (19.6)	2 (0.8)	
II	410 (25.5)	45 (17.4)	
III	525 (32.7)	103 (39.8)	
IV	357 (22.2)	109 (42.1)	
Liver metastasis			0.360
Absent	1544 (96.1)	252 (97.3)	
Present	62 (3.9)	7 (2.7)	
Peritoneal dissemination			<0.001
Absent	1489 (92.7)	180 (69.5)	
Present	117 (7.3)	79 (30.5)	
R0 resection			<0.001
Yes	1105 (68.8)	117 (45.2)	
No	501 (31.2)	142 (54.8)	
Chemotherapy			0.183
No	945 (58.8)	141 (54.4)	
Yes	661 (41.2)	118 (45.6)	

ciated with survival after gastric resection were two: lymph node metastasis and radical resection.

Although the ability to diagnose gastric cancer has improved significantly, Borrmann type IV gastric cancer is still detected at an advanced stage and survival rates for these patients remain poor [3,7]. Kitamura et al. reported only 3.0% of the patients with Borrmann type IV gastric cancer belonged to II type (no stage I) [11]. Ostuji et al. and Chen et al. reported that the 5-year overall survival of patients with Borrmann type IV gastric cancer was only 10.5% and 11.3%, respectively [4,5]. In our study, 18.2% of patients with Bor-

rmann type IV gastric cancer belonged to stage I (2 patients) and II (45 patients), and the 5-year overall survival of patients with Borrmann type IV gastric cancer was 16.7%.

With regard to Borrmann type IV gastric cancer, the benefit of radical resection is clear [3,7]. Kim et al. reported that the 5-year overall survival rate of Borrmann type IV was significantly better in patients achieving radical resection than in those with non-radical resection (33.4 vs 8.1%,  $p < 0.01$ ) [3]. In this research, a significant survival benefit for radical resection was observed, with a 5-year overall survival rate of 30.7% compared with non-radically

**Table 2.** Clinicopathologic factors and survival

Factors	Number of patients	5-year survival rate (%)	p value
Tumor size (cm)			0.025
<8	120	18.3	
≥8	72	13.9	
Depth on invasion			0.008
T2	25	24.0	
T3	109	19.3	
T4	58	8.6	
Lymph node metastasis			0.004
N0	18	22.2	
N1	55	27.3	
N2	45	17.8	
N3	74	6.8	
R0 resection			<0.001
Yes	88	30.7	
No	104	4.8	
Chemotherapy			0.009
Yes	85	21.2	
No	107	13.1	

resected cases (4.8%). Lymph node metastasis was reported to be one of the important prognostic factors of gastric cancer [12,15]. In patients with Borrmann type IV gastric cancer, as well as in patients with large gastric cancer, we found that lymph node metastasis was an independent prognostic factor.

Because there is no appropriate therapeutic strategy for Borrmann type IV gastric cancer, various types of therapy such as chemotherapy, immunotherapy, and hormone therapy have been examined for their potential survival benefit [16-

**Table 3.** Multivariate analysis (Cox proportional hazard model)

Variables	Risk ratio	95% Confidence interval	p value
Lymph node metastasis (present vs absent)	1.855	1.260-2.733	0.002
R0 resection (no vs yes)	2.035	1.507-2.748	<0.001

18]. Sasaki et al. reported that chemotherapy, including TS-1, has a greater antitumor effect and improve the survival time for Borrmann type IV gastric cancer than conventional chemotherapy including 5-FU, methotrexate, mitomycin, or cisplatin [17]. In this study, chemotherapy based on 5-FU and leucovorin was administered to patients and the 5-year overall survival rate was significantly better in patients with chemotherapy vs those without chemotherapy.

In conclusion, in patients with Borrmann type IV gastric cancer, lymph node metastasis and radical resection were two independent prognostic factors for long-term survival. On the basis of the above findings, there are two essential factors for improving the prognosis of patients with Borrmann type IV gastric cancer: early detection and a radical (R0) resection.

### Conflict of interests

The authors declare no conflict of interests.

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