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Lauren Histology and Lymphatic Permeation are Critical Prognostic Factors in Borrmann Type I Gastric Cancer

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Macroscopic Borrmann type I is relatively rare in advanced gastric cancer, and its detailed prognostic traits are unknown. Among 5172 gastric cancer patients between 1971 and 2013, 114 cases with macroscopic Borrmann type I were identified (2.2%), among which 112 displayed clinicopathologic factors. Univariate prognostic factors with statistical significance were initially selected, which were further applied to the multivariate proportional hazards model. Recently, postoperative adjuvant chemotherapy was recommended for stage II/III gastric cancer patients. Results were as follows: (1) Five-year overall survival (OS) was 66% in Borrmann type I gastric cancer. Five-year relapse-free survival (RFS) was 100%, 87.1%, and 65.5% in stage IA, stage IB, and stage II/III, respectively. (2) Multivariate proportional hazard model for OS identified lymphatic permeation [hazard ratio (HR) = 4.8–7.5, $P = 0.0021$] and age (HR = 2.4, $P = 0.026$), while the multivariate analysis for RFS identified histology (HR = 3.5, $P = 0.018$) and lymphatic permeation (HR = 3.5–4.7, $P = 0.049$) as independent prognostic factors. (3) Recurrence was recognized more in liver of the intestinal type histology. Diffuse type histology with robust lymphatic invasion was all attributed to stage II/III, which occurred largely within 1 year and exhibited 49% RFS. Recurrence pattern of Borrmann Type I gastric cancer with intestinal type histology is unique, and patients with high risk for recurrences were enriched in diffuse type histology with robust lymphatic invasion.

Key words: Gastric cancer – Borrmann type I – Lauren histology – Lymphatic permeation – Prognosis

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Gastric cancer is the fourth most common malignancy (989,000 cases in 2008) and the second leading cause of cancer-related death (737,000 deaths) worldwide.[1] Advanced gastric cancer has a poor survival outcome, despite progress in multidisciplinary therapy,[2,3] while early gastric cancer is a curable disease.[4] Among advanced gastric cancers, Borrmann type I and II cancer are supposed to show relatively good outcomes, whereas the outcomes of Borrmann type III and IV cancer are extremely poor.[5–7]

In Japan, D2 gastrectomy followed by postoperative chemotherapy with tegafur/gimeracil/oteracil potassium (S-1) is the standard treatment for pathologic stage II/III advanced gastric cancer,[3] where this strategy is not necessarily satisfactory for pathologic stage III disease.[8] Because patients who undergo D2 gastrectomy followed by postoperative chemotherapy often have inadequate nutritional intake—resulting in postoperative chemotherapy with insufficient dose intensity[9]—neoadjuvant chemotherapy (NAC) is an alternative and promising strategy for high-risk gastric cancers such as type IV or large type III gastric cancer.[10]

This treatment outcome is slightly different in Western countries, where the prognosis of gastric cancer is poorer than in Eastern countries. In Europe, perioperative adjuvant chemotherapy of epirubicin + cisplatin + 5-FU was actually demonstrated to be effective,[11] while in the United States, postoperative adjuvant chemoradiation therapy was proven to be effective.[12] Such adjuvant therapy is likely to be more potent than that in Japan.

Macroscopic feature is a simple prognostic indicator in gastric cancer[5–7]; however, type I gastric cancer is rare. Therefore, its detailed prognostic feature remains elusive due to a lack of detailed prognostic analysis. In this study, we will describe prognostic features of Barrmann type I gastric cancer.

Patients and Methods

Patients

Between 1971 and 2013, a total of 5172 patients with histologically confirmed primary gastric cancer underwent surgery at the Department of Surgery, Kitasato University School of Medicine, Sagamihara, Japan. Among these patients, 114 (2.2%) had a diagnosis of Borrmann type I gastric cancer, as confirmed pathologically on gross examination of resected specimens, and 112 cases were identified after clinicopathologic analysis. The 112 cases were comprised of 57, 51, and 4 in pathologic stage I, stage II/III and stage IV, respectively. For patients with stage I, no adjuvant therapy was administered at all during any period. Since 2000, however, postoperative adjuvant chemotherapy was recommended for stage II/III gastric cancer patients (n = 13). The requirement for informed consent was waived because of the retrospective study design.

Clinicopathologic Factors

We performed prognostic analysis to identify independent prognostic factors in the 112 patients with Borrmann type I gastric cancer. Pathologic tumor depth, pathologic lymph node metastasis, and pathologic distant metastasis were classified according to the International Union Against Cancer (UICC) TNM staging system, 7th edition.[13] The cytology test was not necessarily informative for all cases, because it was not in use until 2000.

Chemotherapy

The adjuvant chemotherapy trial of S-1 for gastric cancer (ACTS-GC), published in 2007, showed that S-1 is effective as adjuvant chemotherapy; and we participated in this clinical trial.[3] Patients with stage II/III advanced gastric cancer (n = 8) were recommended for and received adjuvant chemotherapy with S-1.

Statistical Analysis

Continuous variables were evaluated by Student's *t*-test; categoric variables were evaluated by Fisher's exact test or the χ^2 test, as appropriate. Survival was calculated by the Kaplan–Meier method. Univariate analyses of prognostic factors for overall survival (OS) or relapse-free survival (RFS) were performed using the log-rank method. OS was defined as time from surgery to death from any causes, and data on surviving patients were censored at the last follow-up. The median follow-up was 59 months (range: 8–250 months). RFS was defined as time from surgery to recurrences, and data on surviving patients or other disease deaths were censored at the last follow-up. Factors with $P < 0.05$ on univariate analysis were subjected to multivariate analysis using a Cox proportional hazards model to identify independent prognostic factors. All calculations were performed with the use of statistical software (JMP 10, SAS Institute Inc, Cary, North Carolina). A

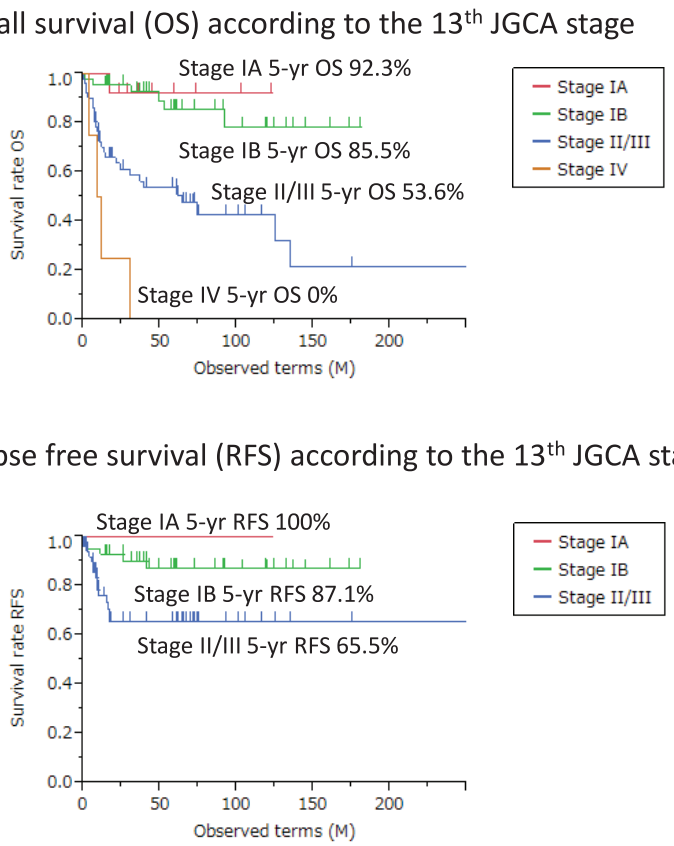

Fig. 1 Kaplan-Meier curves in Borrmann type I gastric cancer. (a) Survival curve for OS is shown according to pStage I to IV. (b) Survival curve for RFS is shown according to pStage I to III.

value of $P < 0.05$ was considered to indicate statistical significance.

Results

Survival outcome of Borrmann type I gastric cancer

All clinicopathologic factors investigated in this current study were informative for 112 cases. Of the stage IV gastric cancer patients who underwent surgery, only 4 were actually included in the study (1 for peritoneal dissemination and 3 for liver metastasis). We have shown the Kaplan-Meier curve of OS in all cases (n = 112; Fig. 1a), and RFS in cases excluding stage IV disease (n = 108; Fig. 1b). Five-year OS was 66% in Borrmann type I gastric cancer, and 5-year OS was 92.3%, 85.5%, 53.6%, and 0% in stage IA, stage IB, stage II/III, and stage IV, respectively. Stage IV disease inevitably showed dismal prognosis due to cancer progression in Borrmann type IV gastric cancer. Five-year RFS was 100%, 87.1%, and 65.5% in stage IA, stage IB, and stage II/III, respectively. RFS was superior to OS by over 10% in terms of stage II/III, because deaths other than cancer were defined as events in OS, but not in RFS in this current study, and actual inclusion of other disease deaths were frequently recognized in stage II/III.

Univariate and multivariate prognostic analysis for OS in Borrmann type I gastric cancer

Univariate prognostic factors with statistical significance for OS were initially explored (Table 1). Factors that contributed to poor OS were older patient age ($P = 0.043$); positive margin ($P = 0.04$); larger tumor size ($P = 0.016$); higher degree of lymphatic permeation ($P < 0.0001$); higher degree of vascular permeation ($P = 0.0097$); type of gastrectomy ($P = 0.04$); no use of laparoscopic approach ($P = 0.049$); lymph node dissection level ($P = 0.0032$), and 7th UICC stage ($P = 0.0008$). Lymphatic permeation was categorized into ly0/1, ly2, and ly3, since the Kaplan-Meier curve revealed that prognosis was similar between cases with ly0 and ly1 (data not shown). We did not show prognostic relevance of the individual TNM factors because therapeutic strategy was generally determined based on stage rather than individual TNM factors.

The above univariate negative prognostic factors were applied to the multivariate Cox proportional

hazards model. As a result, the significant independent prognostic factors that remained were lymphatic permeation [$P = 0.0021$, see subclassified HR and 95% confidence interval (CI) in Table 1] and patient age ($P = 0.026$, HR = 2.33, 95% CI: 1.11–5.89). Kaplan-Meier curves for OS were shown according to lymphatic permeation and stage in Borrmann type I gastric cancer (Fig. 2a and 2b). Degree of lymphatic permeation clearly stratify the prognosis of Borrmann type I gastric cancer.

Univariate and multivariate prognostic analysis for RFS in Borrmann type I gastric cancer

More detailed information is required to understand the accurate prognosis of curable Borrmann type I gastric cancer, so we retrospectively investigated information of relapse status and cause of deaths in 108 cases with stage I to III (after exclusion of stage IV disease).

Univariate prognostic factors with statistical significance for RFS were investigated (Table 2). Possible factors representing poor RFS were elderly patient age ($P = 0.046$); positive margin ($P = 0.0003$); larger tumor size ($P = 0.03$); diffuse type histology (Lauren classification; $P = 0.025$); higher degree of lymphatic permeation ($P = 0.03$); lymph node dissection level ($P = 0.0005$); and 7th UICC stage ($P = 0.0051$).

The above univariate negative prognostic factors were applied to the multivariate Cox proportional hazards model. As a result, the significant prognostic factors that remained were diffuse type histology ($P = 0.018$, HR=3.52, 95% CI: 1.24–10.16) and lymphatic permeation ($P = 0.049$, see subclassified HR and 95% CI in Table 2). Kaplan-Meier curves of independent prognostic factors for RFS were shown according to Lauren histology classification and degree of lymphatic permeation in Borrmann type I gastric cancer (Fig. 2c and 2d). Patient age remained as an independent prognostic factor for RFS with marginal significance ($P = 0.097$).

Recurrence characters of sites in Borrmann type I gastric cancer

Clinicopathologic features of the 20 Borrmann type I gastric cancer patients with recurrences were shown in Table 3. In the patients with intestinal type histology, liver metastasis was uniquely frequently recognized in 7 of 10 (70%) patients, while peritoneal dissemination was more frequently (5/10) found in those with diffuse type histology. Patients with a combination of Lauren histology and lymphatic permeation were at high risk for recurrence, in cases displaying Borrmann type I gastric cancer (Fig. 3); diffuse type histology with robust lymphatic invasion was all included in stage II/III, in which recurrences occurred largely within 1 year after surgery (7/8), and exhibited 49% of RFS in Borrmann type I gastric cancer. Although D2 lymph node dissection was not done for all such high-risk patients, the initial recurrence sites were unlikely associated with a limited lymph node dissection level (Table 3).

Discussion

Borrmann type I gastric cancer is a relatively rare entity among gastric cancers, and there is limited information on prognosis, except that type I gastric cancer has shown better prognosis than type III or type IV gastric cancer.[5] In our current study, we examined the detailed prognostic analysis. Prognosis of pStage IA and pStage IB of the Borrmann type I gastric cancer exhibited excellent prognosis, so surgery can reach satisfactory prognostic outcomes in both stages. A total of 14 patients with pStage IA did not show any recurrences. On the other hand, 42 patients with pStage IB showed 5 recurrences (12%), and such prognosis is consistent with a Japanese nationwide registry of pStage IB gastric cancer in 2002.[14] The 5 recurrences in our cases were all distant ones, comprised of 4 in liver and 1 in bone. Among the 4 liver recurrences, 3 occurred within 1 year after surgery, and early liver metachronous metastasis is often encountered as a recurrence pattern of pStage IB Borrmann type I gastric cancer. Bone metastasis, on the other hand, was recognized in 41 months after operation.

Independent prognostic factors for RFS of the Borrmann type I gastric cancer was finally selected as Lauren diffuse type histology with robust lymphatic permeation (ly2 and ly3). The combination of the 2 prognostic factors enriched patients who exhibited only 49% of RFS, which were all pStage II/III. Such high-risk patients unexpectedly showed nonspecific recurrent sites comprised of peritoneum, liver, and the para-aortic lymph node. This finding suggested that high risk of the Borrmann type I gastric cancer is similar with Borrmann type III or IV gastric cancer in terms of recurrence sites. On the other hand, the most outstanding traits of high-risk Borrmann type I gastric cancer is early onset of recurrence, where 7 recurrences were found, within 1 year after opera-

Table 1 Univariate and multivariate prognostic analysis for overall survival (OS) in 112 Type I gastric cancer

		Univariate analysis (log-rank test)		Multivariate analysis		
Clinicopathologic factors	Patients, n (%)	5-year OS, %	*P* value	Hazard ratio	95% CI	*P* value
Age			0.043			0.026
≥67 years	72 (64)	62.7		2.44	1.11–5.89	
<67 years	40 (36)	78.4		Reference		
Sex			NS			
Male	79 (70.5)	67.1		–	–	
Female	33 (29.5)	70.9		–	–	
Tumor location			NS	–	–	
Upper	58 (51.8)	65.9		–	–	
Middle	30 (26.8)	58.6		–	–	
Lower	24 (21.4)	83.1		–	–	
Positive margin			0.04			NS
No	107 (95.5)	70.0		Reference		
Yes	5 (4.5)	30.0		1.99	0.41–7.55	NS
Histology (Lauren classification)			NS			
Diffuse type	34 (30.4)	60.8		–	–	
Intestinal type	78 (69.6)	71.9		–	–	
Tumor size			0.0016			NS
<4 cm	24 (21.4)	95.7		Reference		
≥4 cm	88 (78.6)	61.4		4.51	0.73–91.20	
Lymphatic permeation			<0.0001[a]			0.0021
ly0	17 (15.2)	90.0		–	–	
ly1	40 (35.7)	89.5		–	–	
ly2	32 (28.6)	60.2		4.83	1.51–17.75	0.0071
ly3	23 (20.5)	31.6		7.49	2.31–28.41	0.0005
ly0/1	57 (50.9)	90.0		Reference		
Vascular permeation			0.0097			NS
v0	17 (15.2)	100.0		Reference		
v1	33 (29.5)	75.0		1.74×10^9	≥1.00	NS
v2	35 (31.3)	52.3		1.08×10^9	≥0.56	NS
v3	27 (24.1)	62.2		1.51×10^9	≥0.81	NS
7th UICC stage			<0.0001			NS
Stage IA	14 (12.5)	92.3		Reference		
Stage IB	43 (38.4)	85.5		3.08	0.14–24.90	NS
Stage II/III	51 (45.5)	53.6		2.95	0.13–23.40	NS
Stage IV	4 (3.6)	0.0		1.08	0.08–29.51	NS
Gastrectomy			0.04			NS
Total gastrectomy	56 (50.0)	56.7		1.92	0.88–4.45	NS
Proximal gastrectomy	13 (11.6)	88.9		1.36	0.27–5.26	NS
Distal gastrectomy	43 (38.4)	77.6		Reference	0.25–3.09	
Laparoscopic gastrectomy			0.049			NS
Yes	12 (10.7)	100.0		Reference		
No	100 (89.3)	65.7		9.52×10^8	0.077–	
Lymph node dissection			0.0032			NS
D1	24 (21.4)	52.90		5.26	0.95–98.40	NS
D1+	21 (18.8)	95.20		Reference		
D2	67 (59.8)	68.10		2.68	0.50–49.73	NS

NS, not significant.

[a]This *P* value is calculated for ly0/1, not separately for ly0 and ly1.

tion among the 8 cases (Table 3). Such prognostic information would be beneficial for a postoperative follow-up schedule or clinical decision for therapeutic strategy in the outpatient center.

The unique recurrence site of the Lauren intestinal type histology of the Borrmann type I gastric cancer was the liver. Nevertheless, Lauren intestinal type Borrmann type I gastric cancer showed good prognosis, which was not required for postoperative adjuvant therapy in our study (Fig. 3), and chemotherapeutic efficacy for recurrent cases rather than empiric chemotherapy should be initially

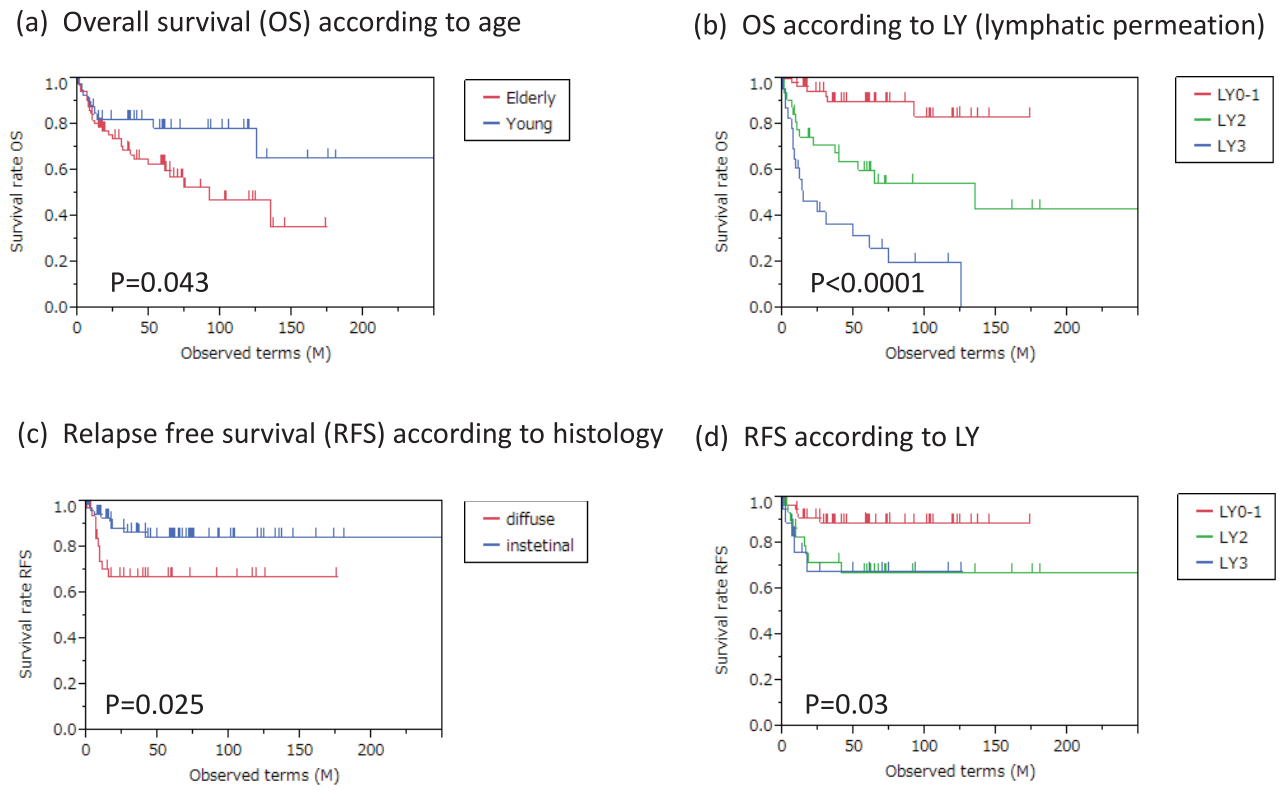

Fig. 2 Kaplan-Meier curves for OS and RFS according to independent prognostic factors in Borrmann type I gastric cancer. (a) Survival curve for OS is shown according to patient age ($P = 0.043$). (b) Survival curve for OS is shown according to lymphatic permeation ($P < 0.0001$). (c) Survival curve for RFS is shown according to Lauren histology ($P = 0.025$). (d) Survival curve for RFS is shown according to lymphatic permeation ($P = 0.03$).

elucidated in the future. Frequent metachronous liver metastasis is recognized in this type of cancer, as the most frequent recurrent site of CRC were liver.[15–17] Lauren intestinal type histology of Borrmann type I gastric cancer is likely to have highly biologic similarities with colorectal cancer. Such similarities with CRC as it relates to recurrence pattern may point to the novel therapeutic strategy for Borrmann type I gastric cancer with intestinal histology. Interestingly, Borrmann type I gastric cancer with Lauren diffuse type histology tended to include more of peritoneal dissemination than Lauren intestinal type histology (Table 3).

CRC is well known to occur as a result of accumulation of driver gene mutations,[18] which is different from a large proportion of gastric cancer[19]; and such driver gene abnormalities could be an excellent landmark for molecular targeted therapy as shown in several outstanding reports describing biomarker potential of K-ras mutation or epidermal growth factor receptor (EGFR) genomic amplification against anti-EGFR monoclonal antibody therapy.[20,21] Early colorectal tumorigenesis was well known to be accompanied by beta-catenin pathway subsequent to K-ras pathway activation through mutations of the APC and K-ras genes.[22,23] Intestinal type gastric cancer was also frequently proven to harbor beta-catenin mutation[24,25] and K-ras gene mutation,[26] different from diffuse type gastric cancer or esophageal cancer.[27] These findings also supported the notion that intestinal type Borrmann type I gastric cancer may also be a similar molecular entity with CRC.

Liver metastasis of CRC was optimally controlled by adjuvant 5-FU/LV/oxaliplatin therapy at present.[28] Even in gastric cancer, oxaliplatin is effective and a phase III clinical trial showed that oxaliplatin showed similar effect with cisplatin, and regimens including oxaliplatin are promising.[29] S-1 can increase 5-FU concentration in the liver through gimeracil effect with attenuation of gastrointestinal toxicity through oteracil effects, and S-1 in combination with concurrent other agents may reduce liver metastasis of CRC.[30] S-1, in combination with

Table 2 Univariate and multivariate prognostic analysis for RFS in 108 Type I gastric cancer

		Univariate analysis (log-rank test)		Multivariate analysis		
Clinicopathologic factors	Patients, n (%)	5-year OS, %	*P* value	Hazard Ratio	95% CI	*P* value
Age			0.036			NS (0.097)
≥67 years	71	73.7		4.12	1.01–28.03	
<67 years	37	89.7		Reference		
Sex			NS			
Male	76	80.2		–	–	
Female	32	76.8		–	–	
Tumor location			NS			
Upper	57	71.4		–	–	
Middle	27	84.0		–	–	
Lower	24	91.5		–	–	
Positive margin			0.0003			NS
No	103	81.2		Reference		
Yes	5	40.0		2.4	0.45–10.63	
Histology (Lauren classification)			0.025			0.018
Diffuse type	33	67.1		3.52	1.24–10.16	
Intestinal type	75	84.5		Reference		
Tumor size			0.03			NS
<4 cm	24	74.2		Reference		
≥4 cm	84	95.0		5.04	0.63–109.38	
Lymphatic permeation			0.03			0.049
ly0/1	57	89.1		Reference		
ly2	32	67.4		4.68	1.32–18.71	0.016
ly3	19	66.9		3.45	0.80–15.15	NS
Vascular permeation			NS			
v0	17	100.0		–	–	
v1	33	77.8		–	–	
v2	32	76.3		–	–	
v3	26	69.2		–	–	
13th JGCA stage			0.0051			
Stage IA	14	100.0		Reference		
Stage IB	43	87.1		3.60×10^8	0.23–	NS
Stage II/III	51	65.2		3.18×10^8	0.15–	NS
Gastrectomy			NS			
Total gastrectomy	54	69.0		–	–	
Proximal gastrectomy	13	83.9		–	–	
Distal gastrectomy	41	89.9		–	–	
Laparoscopic gastrectomy			NS			
Yes	12	80.2		–	–	
No	96	79.1		–	–	
Lymph node dissection			0.0005			NS
D1	23	48.50		3.64	0.088–0.83	0.022
D1+	21	85.70		1.7	0.34–6.64	NS
D2	64	87.20		Reference		

[a]This *P* value is calculated for ly0/1, not separately for ly0 and ly1.

oxaliplatin as a designated SOX regimen, is being used to demonstrate noninferiority of oxaliplatin to cisplatin (G-SOX trial)[31] and might be promising, especially for liver recurrence of the Borrmann type I intestinal histology.

Type I gastric cancer prognosis has been shown to be excellent compared to type III/IV gastric cancer, and our RFS result is consistent with the previous reports. On the other hand, RFS was superior to OS by over 10% in stage II/III Borrmann type I gastric cancer. Detailed analysis elucidated that the rate of death other than cancer progression within 5 years after operation is unexpectedly high in pStage II/III cases than in pStage IA/IB. Actually in our study, age was an independent prognostic factor for OS, but not for RFS. These results may be due to more inclusion of operation-related deaths, or postoperative course with poor condition for elderly in pStage II/III cases, which was barely found in patients with pStage IA/IB. Given that approximately half of the

Table 3 Recurrence and clinicopathologic features of Borrmann type I gastric cancer

Patients	Age	Sex	Location	Lymphatic permeation	V	Margin positive	Histology	Size	Operation	Surgery method	LN Dissection	pStage (13th)	Recurrence, mo	Recurrence sites
1	Elderly	F	L	ly0–1	1	No	Diffuse	Large	DGR	Open	D1	Stage IB	11	Liver
2	Elderly	F	U	ly0–1	3	No	Diffuse	Large	TGR	Open	D1	Stage II/III	9	Liver
3	Elderly	F	M	ly2	2	No	Diffuse	Large	DGR	Open	D2	Stage II/III	6	LN/liver
5	Elderly	F	M	ly2	3	No	Diffuse	Large	DGR	Open	D2	Stage II/III	15	Peritoneum
6	Elderly	F	M	ly2	1	No	Diffuse	Large	TGR	Open	D1	Stage II/III	9	Peritoneum/#16 LN
4	Elderly	M	U	ly2	2	No	Diffuse	Large	TGR	Open	D2	Stage II/III	4	Peritoneum
9	Young	F	U	ly3	1	Yes	Diffuse	Large	TGR	Open	D1+	Stage II/III	6	Peritoneum
7	Elderly	M	U	ly3	2	No	Diffuse	Large	TGR	Open	D1	Stage II/III	8	#16 LN
8	Elderly	M	U	ly3	3	No	Diffuse	Large	TGR	Open	D1+	Stage II/III	6	LN/liver/lung/peritoneum
10	Elderly	M	M	ly3	2	Yes	Diffuse	Large	TGR	Open	D1	Stage II/III	0	R2
11	Elderly	M	U	ly0–1	3	No	Intestinal	Large	TGR	Lap	D1+	Stage IB	2	Liver
12	Young	M	U	ly0–1	1	No	Intestinal	Small	PGR	Lap	D1	Stage IB	26	Liver
13	Elderly	M	U	ly0–1	3	No	Intestinal	Large	TGR	Open	D2	Stage IB	3	Liver/#16 LN
14	Elderly	M	U	ly0–1	1	No	Intestinal	Large	PGR	Open	D1	Stage II/III	10	Liver
15	Young	M	U	ly2	1	No	Intestinal	Large	TGR	Open	D2	Stage IB	41	Bone
16	Elderly	M	U	ly2	1	No	Intestinal	Large	TGR	Open	D1	Stage II/III	17	Liver
17	Elderly	M	U	ly2	1	No	Intestinal	Large	TGR	Open	D2	Stage II/III	16	Liver/peritoneum
18	Elderly	M	U	ly2	1	No	Intestinal	Large	TGR	Open	D1	Stage II/III	5	Peritoneum
19	Elderly	F	L	ly2	1	Yes	Intestinal	Large	DGR	Open	D1	Stage II/III	0	R2
20	Elderly	M	U	ly3	1	No	Intestinal	Large	TGR	Open	D2	Stage II/III	17	Liver

DGR, distal gastrectomy; lap, laproscopic surgery; LN, lymph node; TGR, total gastronomy; V, vascular permeation.

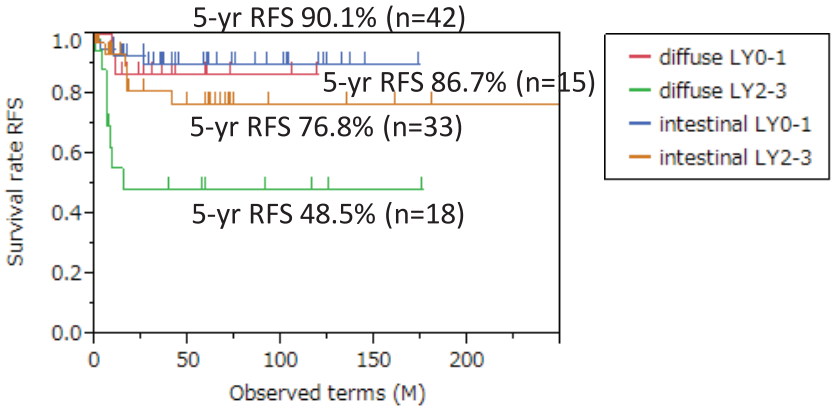

Fig. 3 Kaplan-Meier curves for RFS by combination of independent prognostic factors of Lauren histology and lymphatic permeation. Combination of histology and ly-stratified prognosis. Combination of diffuse type histology with robust lymphatic permeation (ly2-3) enriched patients with high risk for recurrence.

cases of type I gastric cancer are located at the upper portion, there are many operative factors potentially related to other disease deaths within 5 years, such as proximal gastrectomy, extended lymph node dissection including splenectomy, postoperative chemotherapy, and surgery for elderly. Distant metastasis and peritoneal dissemination were actually main obstacles to treatment failure in our data. It may therefore be thought to be wise to select a safer operation and adjuvant strategy expecting better QOL in Borrmann type I gastric cancer expecting a relatively good prognosis.

In conclusion, recurrence pattern of Borrmann type I gastric cancer with intestinal type histology is unique in liver metastasis like CRC, and patients with high risk for recurrence were enriched in diffuse type histology with marked lymphatic invasion. Recurrence in high-risk patients occurs during the very early postoperative course, and adjuvant therapy is thought to be needed to improve prognosis. Most importantly, Borrmann type I gastric cancer showed a relatively good prognosis, and it may be wise to select a safer operation and adjuvant strategy if a better QOL is expected.

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