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ORIGINAL ARTICLE

Risk factors and oncological impact of positive resection margins in gastrectomy for cancer: are they salvaged by an additional resection?

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Abstract

Background The situation of positive resection margins (PRMs) varies notably between Western and Asian countries. In the West, PRMs are associated with advanced disease and R1, whereas in Asia, PRMs are also considered in early disease because stomach preservation was recently prioritized. Furthermore, PRMs are usually resected to obtain R0. However, the oncological impact of PRMs and additional resection remains unclear. The aim of this study is to evaluate the oncological impact of PRMs in laparoscopic gastrectomy (LG) for clinical stage (cStage) I gastric cancer.

Methods A total of 2121 patients who underwent LG for cStage I gastric cancer between 2007 and 2015 were enrolled. Survival outcomes were compared between patients with PRMs (group P) and those without (group N). Furthermore, prognostic factors were analyzed using multivariate analysis.

Results Twenty-seven patients (1.3%) had PRMs. Patients in group P had upper and more advanced disease, and the 5-year relapse-free survival (RFS) rate was worse in group P compared with group N (76.3% vs. 95.1%, $P=0.003$). The 5-year RFS of patients with pT2 or deeper (pT2–4) disease in group P was significantly worse than that of patients in group N (66.7% vs. 89.5%, $P=0.030$) although that of patients with pT1 was not. Likelihood ratio tests showed that there was a significant interaction between pT status and PRM ($P=0.005$).

Conclusion PRM in cStage I gastric cancer is associated with advanced upper disease. It remains an independent prognostic factor in pT2–4 disease even after an additional resection to obtain R0.

Keywords cStage I gastric cancer · Positive resection margin · Laparoscopic gastrectomy

Introduction

Gastric cancer is one of the top three causes of cancer-related deaths globally [1]. Gastrectomy with systematic lymphadenectomy is a major curative treatment for most patients with this lethal disease. A retrospective analysis of the nationwide registry of the Japanese Gastric Cancer Association, which includes more than 100,000 patients undergoing gastrectomy, reported that the 5-year overall survival rate was 86.9% in patients without residual tumor, and 12.7% in those with definite residual tumor [2]. To achieve the long-term oncological safety of gastric cancer, it is essential to ensure there is no residual tumor. Thus, maintaining a pathologically negative resection margin in gastric transection is the minimum required prerequisite to achieve a cure.

Some patients, however, unexpectedly experience a positive resection margin (PRM) in gastrectomy with curative

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intent. Many previous Western studies revealed that the incidence of PRM in gastrectomy ranged from 1.8% to 18.2% [3]. In the largest study, Bickenbach et al. evaluated 2384 patients who underwent attempted R0 resection [4] and reported that 4.5% of enrolled patients suffered from PRMs that were mostly located in the esophagus or duodenum. Furthermore, nearly 90% of the PRMs were left, which was postoperatively defined as R1. Thus, the Western PRM is associated with advanced disease extending to the adjacent organs and poor survival outcome.

In Asian countries, PRMs are regarded differently because they are also a considerable problem in early disease, although esophageal and duodenal PRMs are important issues in advanced disease. In the recently developed function-preserving gastrectomy for clinical stage I (cStage I) gastric cancer, the stomach is transected closer to the tumor boundary or opportunities of gastric transections are increased to preserve the stomach. Although unexpected PRMs may occur more frequently in such types of surgery, they are usually resected during the same or subsequent surgery to obtain negative resection margins [5–8]. Many Asian surgeons consider that PRMs are a local and temporary problem in surgery. Thus, they believe that PRMs can be negated by an additional resection and that they may not influence long-term oncological outcomes, although there is a concern that transecting the tumor scatters tumor cells into the abdominal cavity. However, no data of long-term oncological outcomes, focusing on patients who suffered from a PRM and underwent an additional resection, are available.

In this study, we retrospectively compared the clinicopathological characteristics and survival outcomes of patients without and with gastric PRMs, who underwent laparoscopic gastrectomy (LG) with gastric transection for cStage I gastric cancer, to elucidate what is associated with PRMs and to determine whether they have an impact on survival outcome after they are additionally resected. The information obtained from this study can help us to avoid PRMs and manage patients who suffer from PRMs in LG for cStage I gastric cancer.

Methods

Patients

Consecutive patients with histologically proven gastric adenocarcinoma who underwent LG at the Department of Gastroenterological Surgery, Cancer Institute Hospital, Tokyo, Japan, between January 2007 and December 2015 were enrolled in this study. Among these patients, we excluded those who met any of the following criteria: patients who underwent intended total gastrectomy, patients who were converted to open surgery before harvesting of specimens or patients without cStage I gastric cancer. A flowchart of patient enrollment is shown in Fig. 1. Tumor location was ascertained by upper gastrointestinal endoscopy and clinical depth of tumor by endoscopy, upper gastrointestinal series, and computed tomography findings. Endoscopic ultrasonography was performed in some cases. Tumors were classified according to the third English Edition of the Japanese Classification of Gastric Carcinoma [9]. Differentiated types included papillary and tubular adenocarcinomas, and undifferentiated types included poorly differentiated adenocarcinoma, signet ring cell carcinoma, and mucinous adenocarcinoma. This study was approved by the institutional review board of the Cancer Institute Hospital (approval number: 2020-1311).

Surgical procedure

Indication of each procedure

Laparoscopic distal gastrectomy (LDG) was performed for cStage I gastric cancer located in the middle or lower third of the stomach during the study period. Laparoscopic

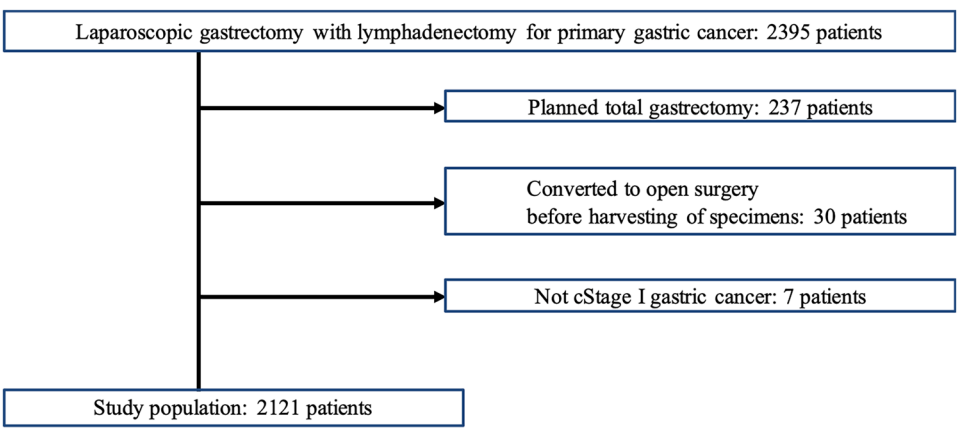

Fig. 1 Flowchart of patient enrollment

pylorus-preserving gastrectomy (LPPG) was applied to cT1N0M0 disease located in the middle to lower third of the stomach, in which the distal boundary was more than 4–5 cm away from the pylorus. Laparoscopic subtotal gastrectomy (LSTG) was defined as laparoscopic distal gastrectomy for tumors located in the upper third of the stomach or tumor invading to the area. LSTG was conducted for cT1 disease in which the proximal boundary was more than 2 cm away from the esophagogastric junction. Laparoscopic proximal gastrectomy (LPG) was performed for cT1N0M0 disease located in the upper third of the stomach. The extent of lymph node dissection was determined according to the Japanese Gastric Cancer Treatment Guidelines [10].

Preoperative management and gastric transection methods

At the initial preoperative endoscopy, biopsies were taken from the tumor and from the proximal and/or distal mucosa with normal appearance. Several days before surgery, marking clips were placed at two proximal and/or two distal biopsy sites on the pathologically confirmed normal mucosa [11]. During surgery, we determined the gastric transection line to be approximately 2 cm away from proximal or distal tumor boundary, which corresponded to the location of intraluminal marking clips by touching or using intraoperative endoscopy, as described previously [11]. The gross proximal or distal margin length was roughly measured on the back table by surgeons other than the operator and assistants based on the information obtained during preoperative examinations including marking clips, and inspected and palpated findings of the resected specimen immediately after the specimen was removed from the surgical field. If the gross margin length was too short to be confirmed as negative or suspicious for cancer, intraoperative frozen section (IFS) analysis of the cutting edge was conducted. However, some surgeons routinely submitted the cutting edge to IFS analysis. When specimens from the resection margin were positive or suspicious for cancer, an additional resection was performed during the same surgery.

Evaluation and statistical analysis

Differences in clinicopathological characteristics between patients with PRMs (group P) and those without (group N) were evaluated. We used the Mann–Whitney *U* test to compare the continuous variables, and Chi-squared or Fisher's exact tests to compare the categorical variables between the two groups. A two-sided *P* value <0.05 was considered statistically significant. Multiple logistic regression analysis was performed to identify independent risk factors for PRMs. In this analysis, we used a stepwise method to select variables, with entry and removal limits of $P<0.10$ and $P>0.15$, respectively.

Overall survival (OS) and relapse-free survival (RFS), defined as the interval from the date of gastrectomy to the date of relapse or death from any cause, were estimated using the Kaplan–Meier method and compared between the groups using the log-rank test. The Cox proportional hazards model was performed to identify independent prognostic factors and verify the existence of interactions for RFS. In multivariate analysis, prognostic factors with univariate *P* values of <0.10 were all included. In addition, the likelihood ratio Chi-squared test statistic was used to verify the existence of interactions. All statistical analyses were performed using IBM SPSS statistical software version 22 (IBM, Armonk, NY, USA).

Results

Patient characteristics

The clinicopathological characteristics of the 2121 patients enrolled in this study are summarized in Table 1. PRM occurred in 27 (1.3%) patients. Among them, 25 patients underwent additional resection to obtain R0 resection. Two patients underwent R1 resection, whose pathological remnant tumor tissue was confirmed by formalin-fixed, paraffin-embedded tissue section analysis and refused a second surgery to obtain pathologically negative margins. Significant differences in some preoperative and pathological factors were found between groups N and P. Although all the patients had cStage I disease, the proportion of pT2 or deeper (pT2–4) disease and the incidence of lymph node metastasis in group P were significantly higher than those in group N. Thus, the proportion of pStage II/III tumors in group P was significantly higher than that in group N. Details of the patients with PRMs are presented in Supplemental Table 1.

Risk factors of PRM

Table 2 shows uni- and multivariate analyses to identify risk factors of PRM. The multivariate analysis revealed that a tumor located in the upper third of the stomach was an independent risk factor (odds ratio 19.1; 95% confidence interval [CI] 2.47–148.1).

Long-term outcomes

Survival outcomes of all patients

The median follow-up period after gastrectomy was 61 months (range 1–134 months). Figure 2 shows

Table 1 Baseline characteristics of groups N and P

Variables	Group N $n=2094$	Group P $n=27$	P
Preoperative factors			
Age, median (range)	64 (25–98)	64.5 (37–81)	0.555
Sex (male/female)	1288/806	19/8	0.347
BMI, median (range)	22.5 (14.0–40.7)	23.3 (17.2–29.2)	0.266
Main tumor location (U/M/L)	278/1402/414	12/14/1	< 0.001
Circumferential location (Less/Gre/Ant/Post/Circ)	771/398/397/513/15	7/6/4/10/0	0.534
Pretreatment with ESD (absent/present)	1715/379	26/1	0.072
cTumor size (mm), median (range)	28 (2–120)	35 (12–65)	0.033
Macroscopic type (Sup/Adv)	2046/48	27/0	1.000
cT status (1/2)	1969/125	25/2	0.376
cN status (0/1)	2074/20	27/0	1.000
Operative factors			
Intended procedure (DG/PPG/STG/PG)	1129/690/147/128	8/8/4/7	< 0.001
Performed procedure (DG/PPG/STG/PG/TG)	1147/669/147/126/5	6/4/0/4/13	< 0.001
IFS analysis (absent/present)	1501/593	7/20	< 0.001
Retrieved lymph nodes, median (range)	39 (10–121)	43.5 (22–63)	0.134
Pathological factors			
pTumor size (mm), median (range)	29 (1–210)	50 (15–242)	< 0.001
Histopathological type (Dif/Und)	908/1186	11/16	0.785
Lymphatic invasion (0/1)	1514/580	14/13	0.019
Venous invasion (0/1)	1663/431	21/6	0.834
pT status (1/2/3/4)	1825/175/77/17	17/1/5/4	< 0.001
pN status (0/1/2/3)	1848/170/57/19	18/3/4/2	< 0.001
pStage (I/II/III)	1910/156/28	16/7/4	< 0.001

BMI body mass index, *U* upper third, *M* middle third, *L* lower third, *Less* lesser curvature, *Gre* greater curvature, *Ant* anterior wall, *Post* posterior wall, *Circ* circumferential, *ESD* endoscopic submucosal dissection, *cTumor size* gross tumor size, *Sup* superficial, *Adv* advanced, *LAG* laparoscopy assisted gastrectomy, *TLG* totally laparoscopic gastrectomy, *DG* distal gastrectomy, *PPG* pylorus-preserving gastrectomy, *STG* subtotal gastrectomy, *PG* proximal gastrectomy, *TG* total gastrectomy, *IFS* intraoperative frozen section, *pTumor size* pathological tumor size, *Dif* differentiated type, *Und* undifferentiated type

Kaplan–Meier estimates of OS and RFS stratified by the margin status. The 5-year OS and RFS rates were significantly lower in group P than in group N (group P: 79.9% vs. group N: 95.6%, $P=0.02$; 76.3% vs. 95.1%, $P=0.003$, respectively).

Survival outcomes of R0-resection patients

To evaluate the survival impact of PRMs after an additional resection, two patients who underwent R1 resection were excluded. Figure 3 shows the RFS curves of patients who underwent R0 resection according to pT status. Although there was no significant difference in the 5-year RFS between the patients with pT1 disease ($P=0.276$) in the two groups, the 5-year RFS of the patients with pT2–4 disease in group P was significantly worse than that of those in group N (66.7% vs. 89.5%, $P=0.030$). The proportion of patients who received adjuvant chemotherapy was not different between the two groups (83.3% vs. 80.4%, $P=1.000$).

Recurrence profiles

Details of recurrence are listed in Supplemental Table 2. The number of recurrences was significantly higher in group P than in group N. Among five patients who experienced recurrence in group P, four patients had pStage II/III disease and one had pStage I disease. Three of the four patients with pStage II/III disease underwent adjuvant S-1 monotherapy. The incidences of peritoneal dissemination and local recurrence were significantly higher in group P than in group N.

Prognostic factors for RFS

Table 3 shows uni- and multivariate analyses of prognostic factors for RFS. We found that PRMs (hazard ratio [HR] 2.69; 95% CI 1.20–6.02) were independently associated with RFS, in addition to pN status, macroscopic type, and age.

Table 2 Univariate and multivariate analyses of risk factors for positive resection margin

Variables	*n*	Univariate analysis		Multivariate analysis	
		OR [95% CI]	*P*	OR [95% CI]	*P*
Age					
≥ 65	1121	1			
≥ 65	1000	1.04 [0.49–2.23]	0.917		
Sex					
Male	1307	1			
Female	814	0.67 [0.29–1.54]	0.350		
Main tumor location					
L	415	1		1	
M	1416	4.13 [0.54–31.5]	0.171	3.82 [0.50–29.2]	0.196
U	290	17.9 [2.31–138.2]	0.006	19.1 [2.47–148.1]	0.005
Pretreatment with ESD					
Absent	1741	1		1	
Present	380	0.17 [0.02–1.29]	0.087	0.14 [0.02–1.04]	0.056
cTumor size (mm)					
< 30	1182	1			
≥ 30	939	1.84 [0.85–3.99]	0.121		
Histology					
Differentiated	919	1			
Undifferentiated	1202	1.11 [0.51–2.41]	0.785		
Intended procedure					
DG	1137	1			
PPG	698	1.64 [0.61–4.38]	0.327		
STG	151	3.84 [1.14–12.9]	0.030		
PG	135	7.72 [2.75–21.6]	< 0.001		
cT status					
cT1	1994	1			
cT2	127	1.26 [0.30–5.38]	0.755		
cN status					
cN0	2101	1			
cN1	20	0.00 [NA]	0.999		

OR odds ratio, *CI* confidence interval, *L* lower third, *M* middle third, *U* upper third, *ESD* endoscopic submucosal dissection, *cTumor size* gross tumor size, *DG* distal gastrectomy, *PPG* pylorus-preserving gastrectomy, *STG* subtotal gastrectomy, *PG* proximal gastrectomy

Subgroup analysis

Forest plots with HRs for RFS according to pT status are shown in Fig. 4. The HR of pT2–4 disease indicated that the RFS of group N was better, and that of pT1 disease indicated that neither the RFS of group P nor N was better. The likelihood ratio test revealed a significant interaction between pT status and PRM ($P = 0.005$).

Discussion

In this retrospective comparative study, we identified three new findings concerning the occurrence and prognostic value of PRMs in cStage I gastric cancer. First, PRMs were more likely to occur in unexpectedly advanced tumors located on the upper gastric body. Second, PRMs remained an independent predictor of worse survival even after an additional resection to obtain R0. Third, the impact of PRMs on patients' prognosis varied depending on the pathological depth of tumor invasion. These new findings imply that PRMs may occur in patients with upper gastric cancer in which the extension and depth cannot be accurately estimated. PRMs in pT2–4 disease are significantly associated with worse survival and may indicate that invisible metastases have already spread to distant sites. However, it may not be completely deniable that transecting the tumor scatters tumor cells.

Recently, the incidence of upper-third gastric cancer, including early gastric cancer, has increased in Asia [12–14].

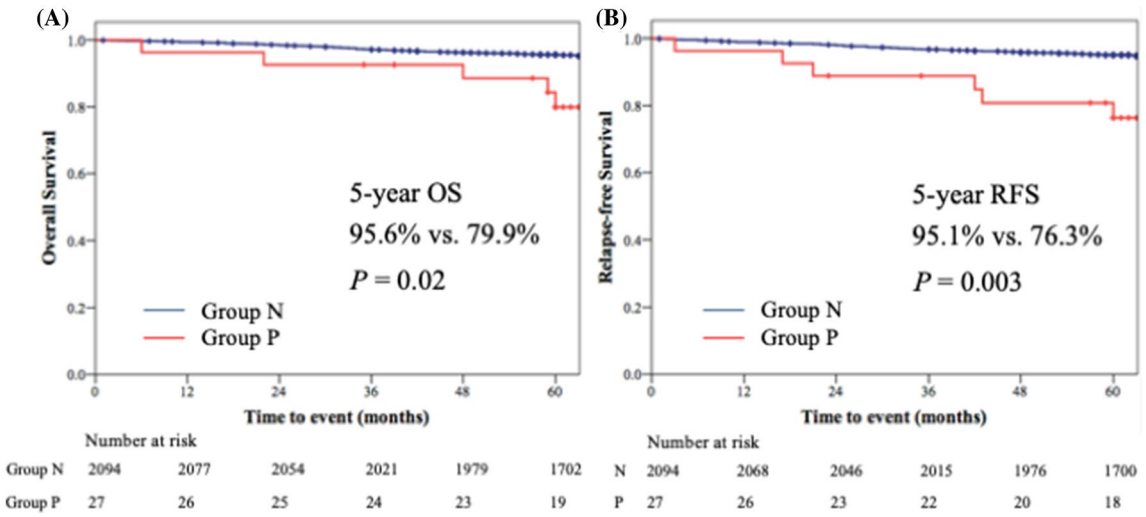

Fig. 2 Kaplan–Meier estimates of overall survival (**A**) and relapse-free survival (**B**) for all patients stratified by the margin status. The 5-year overall survival and relapse-free survival rates were significant lower in group P than in group N (red, group P; blue, group N)

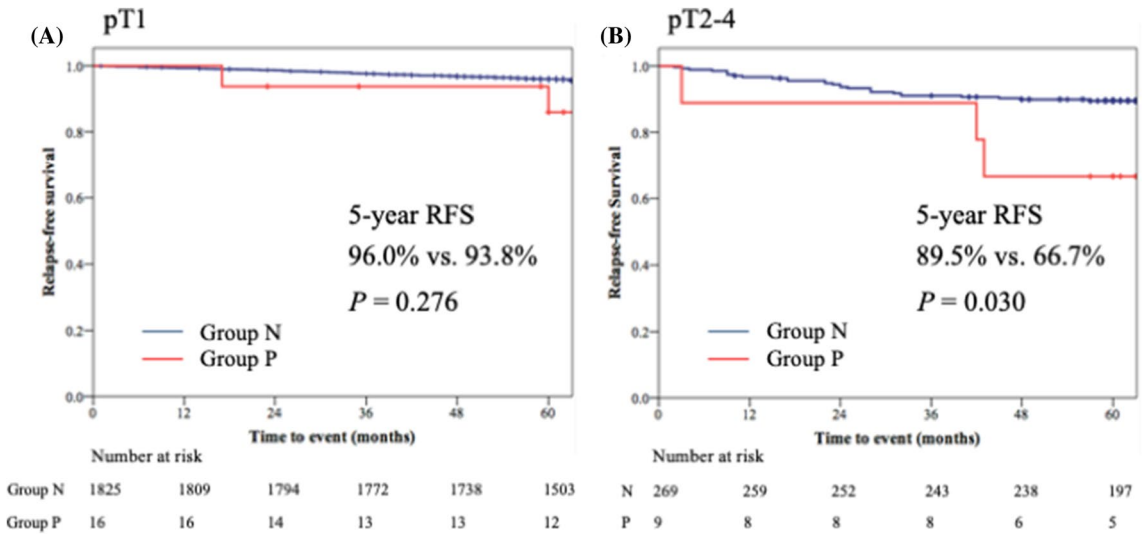

Fig. 3 Relapse-free survival curves for patients who underwent R0 resection stratified by pT status. Although there was no significant difference among patients with pT1 tumors for the two groups, RFS in group P with pT2–4 tumors was significantly worse than that in group N (red, group P; blue, group N)

Laparoscopic total gastrectomy (LTG), LPG, and LSTG are all technically feasible surgical procedures for such lesions. Several studies have shown that LPG and LSTG have surgical and nutritional benefits over LTG [15–19]. Therefore, there are increasing opportunities for function-preserving gastrectomy such as LPG or LSTG to be selected. However, these procedures have a critical oncological problem in that it is difficulty to ensure an adequate surgical margin. We previously reported that the median length of the pathological margin from the tumor boundary to the gastric transection line was 1.5 cm in LSTG and 2.5 cm in LPG, which was significantly shorter than that of the proximal margin in LTG specimens [20]. In the present study, conversion to LTG was required in 2.6% of patients for whom LSTG was planned and in 5.2% of patients for whom LPG was planned due to PRMs. Moreover, the multivariate analysis in the present study revealed that tumors located in the upper third of the stomach were an independent risk factor for PRMs. Although unexpected tumor spread can be found at any location in the stomach, the high incidence of PRMs in the upper third of the stomach is apparently caused by the narrower space for transecting the stomach. We should improve the accuracy of preoperative diagnosis to prevent PRMs caused by underestimation of the tumor extension or

Table 3 Univariate and multivariate Cox proportional hazards analysis for relapse-free survival

Variables	*n*	Univariate analysis		Multivariate analysis	
		HR [95% CI]	*P*	HR [95% CI]	*P*
Age					
< 65	1121	1		1	
≥ 65	998	3.60 [2.46–5.26]	< 0.001	3.08 [2.06–4.59]	< 0.001
Sex					
Male	1305	1		1	
Female	814	0.66 [0.46–0.94]	0.023	0.80 [0.55–1.16]	0.234
Location of tumor					
L	415	1		1	
M	1414	0.52 [0.36–0.75]	< 0.001	0.71 [0.48–1.06]	0.096
U	290	0.90 [0.56–1.45]	0.664	0.57 [0.19–1.68]	0.303
Macroscopic type					
Superficial	2071	1		1	
Advanced	48	4.12 [2.16–7.86]	< 0.001	2.79 [1.40–5.55]	0.003
pTumor size (mm)					
< 30	1103	1		1	
≥ 30	1016	1.41 [1.02–1.95]	0.036	1.15 [0.82–1.61]	0.430
Histology					
Differentiated	918	1		1	
Undifferentiated	1201	0.52 [0.38–0.72]	< 0.001	0.73 [0.51–1.04]	0.083
Intended procedure					
DG	1136	1		1	
PPG	697	0.38 [0.24–0.60]	< 0.001	0.78 [0.47–1.30]	0.343
STG	151	1.18 [0.67–2.07]	0.563	2.03 [0.74–5.58]	0.171
PG	135	1.15 [0.64–2.05]	0.641	1.74 [0.53–5.69]	0.357
pT status					
pT1	1841	1		1	
pT2-4	278	2.24 [1.55–3.24]	< 0.001	1.51 [0.99–2.31]	0.057
pN status					
pN0	1865	1		1	
pN+	254	3.34 [2.36–4.73]	< 0.001	2.65 [1.81–3.87]	< 0.001
Resection margin					
Negative	2094	1		1	
Positive	25	2.64 [1.20–5.80]	0.016	2.69 [1.20–6.02]	0.016

HR hazard ratio, *CI* confidence interval, *pTumor size* pathological tumor size, *DG* distal gastrectomy, *PPG* pylorus-preserving gastrectomy, *STG* subtotal gastrectomy, *PG* proximal gastrectomy

depth, especially when performing limited gastrectomy for tumors located in the upper gastric body. Furthermore, we should submit the cutting edge to IFS analysis to confirm the pathological negativity of the resection margin for such disease.

In the present study, PRMs were associated with advanced disease and more aggressive biology. This result is similar to previous studies [21–23]. Moreover, despite being associated with more advanced disease, PRMs were an independent predictor of RFS. However, because there was a significant interaction between pT status and PRMs in the likelihood ratio test, the multivariate analysis in all included patients was meaningless and only the result of the subgroup analysis is significant. These findings have important implications for surgeons. If a pathological examination reveals incomplete tumor removal, an additional resection to achieve an R0 resection can completely salvage patients who have pT1 disease. Therefore, we should not hesitate to perform an additional resection for patients with pT1 disease and PRMs. However, patients with pT2–4 disease and PRMs have worse survival even when R0 by an additional resection is achieved. This may indicate that an additional resection to achieve R0 may not be enough for these patients. When IFS analysis in surgery reveals PRMs, the pathological depth is usually unreliable. Thus, it may be quite reasonable that the surgery is complete after a negative resection margin

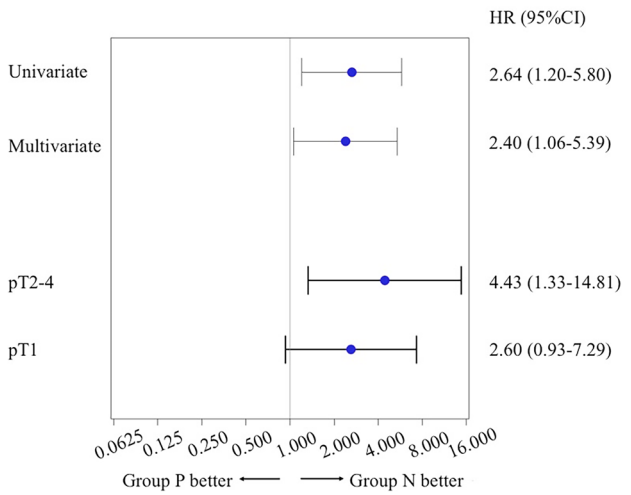

Fig. 4 Forest plot showing hazard ratios for relapse-free survival according to pT status. The HR of pT2–4 disease indicated that the RFS group N was better, and that of pT1 disease indicated that neither the RFS of group P nor N was better

has been maintained by additional resection and the surgical field has been irrigated using a larger amount of normal saline solution as usual. However, establishing the proper management of patients after surgery who have been determined to have pT2–4 disease and a PRM is challenging. If the location of the PRM is not the esophagus or duodenum, in which an additional resection is technically difficult, we recommend an additional resection in the second surgery. Generally, R1 disease caused by a PRM has poor survival outcome, with a 5-year OS rate ranging 25.8%–51.9% [24–26], while the 5-year RFS of patients with pT2–4 and PRMs in this study was 66.7%, which is relatively favorable. Although disease in which PRMs occur may already have distant metastasis, a PRM can be a sole residual tumor and an additional resection might be able to eradicate the tumor. Furthermore, more careful postoperative surveillance and more intensive adjuvant chemotherapy may be additionally considered for such aggressive disease.

It is unclear why PRMs in patients with pT2–4 were associated with worse survival even though the PRMs were additionally resected and R0 was obtained. There are three potential causes. First, it may be caused by a difference in tumor location between patients in groups P and N. More patients with a PRM had upper disease. We previously reported that patients with cStage I upper-third gastric cancer experienced significantly shorter survival compared with those with middle- to lower-third gastric cancer [27]. However, this may not be the cause because PRMs were an independent prognostic factor. Second, unexpected extending disease may be associated with unpredicted distant diseases. For example, scirrhous-type gastric cancer is sometimes observed as only a small mucosal or submucosal disease even though it spreads throughout in the whole gastric body. Such disease is usually transected because the tumor extension is underestimated. Furthermore, this type of disease already has microscopic peritoneal seeding and distant lymph node metastasis in some patients. Undetectable local spread may represent undetectable distant spread; that is, its essentially hypermalignant nature induces both local and distant failure. Third, transecting the tumor may seed tumor cells in the peritoneal cavity or the systemic circulation. Murata et al. demonstrated that cancer cells that had disseminated into the peritoneal cavity during curative D2 gastrectomy for gastric cancer were viable, proliferative, and tumorigenic and could give rise to peritoneal metastasis [28]. Physically, tumor cells can readily spill into the abdominal cavity. However, whether the spilling cells turn into peritoneal metastasis is unclear, even avoiding touching the tumor during surgery is thought to be a fundamental technique to avoid unexpected tumor spreading. Such a tumor-spreading hypothesis may be explained by the fact that pT2–4 disease containing more tumor volume than pT1 was only associated with worse survival. Furthermore, the incidence of peritoneal recurrence was significantly higher in patients with PRMs in this study. Nonetheless, the true cause is impossible to elucidate and care should be taken regardless, either by conducting postoperative surveillance or by administering more intensive chemotherapy to patients who suffer from PRMs.

Our study had several limitations. First, it was a single-institutional and retrospective study. We recruited 2121 patients, a relatively large number, who underwent LG for cStage I gastric cancer under the same strategy and procedure. However, only 153 RFS and 27 PRM events were obtained from the 2121 patients. This small number of events seemed to affect the robustness of the analyses results. Second, this study did not reveal the causal relationship between PRMs and poor survival outcomes. In other words, it is unclear whether tumors that initially have highly malignant potential are more likely to cause PRMs or whether the occurrence of PRMs worsened the patients' prognosis. However, it is impossible to address this question because a prospective study to test whether PRMs increase recurrence is unethical. Thus, even a retrospective study such as the current report is important to understand the relationship between PRMs and prognosis.

Despite the inevitable limitations of this study, we conclude that PRMs in cStage I gastric cancer are associated with upper location of the disease and unexpectedly advanced disease. Even though it is additionally resected to obtain R0, it remains an independent predictor of worse survival in pT2–4 disease. Although additional resection can salvage patients with pT1 disease and PRMs, more careful postoperative surveillance or intensive adjuvant chemotherapy may be required for patients with pT2–4 disease

and PRMs. At least, we should take the utmost care when determining a gastric transection line, using accurate preoperative diagnoses and precise intraoperative maneuvers for all patients.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10120-021-01238-w.

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Declarations

Conflict of interest The authors declare no conflicts of interest.

Ethical approval All procedures were conducted in accordance with the ethical standards of institutional and national committees responsible for human experimentation and with the 1964 and later versions of the Declaration of Helsinki.

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