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# The Value of Palliative Gastrectomy for Gastric Cancer Patients With Intraoperatively Proven Peritoneal Seeding

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**Abstract:** The aim of this study was to evaluate the survival benefit of palliative gastrectomy for gastric cancer patients with peritoneal seeding proven intraoperatively and to identify positive predictive factors for improving survival.

The value of palliative resection for gastric cancer patients with peritoneal metastasis is controversial.

From 2006 to 2013, 267 gastric cancer patients with intraoperatively identified peritoneal dissemination were retrospectively analyzed. Patients were divided into resection group and nonresection group according to whether a palliative gastrectomy was performed. Clinicopathologic variables and survival were compared. Subgroup analyses stratified by clinicopathologic factors and multivariable analysis for overall survival were also performed.

There were 114 patients in the resection group and 153 in nonresection group. The morbidities in the resection and nonresection groups were 14.91% and 5.88%, respectively ( $P=0.014$ ). There, however, was no difference in mortality between the 2 groups. The median survival time of patients in the resection group was longer than in nonresection group (14.00 versus 8.57 months,  $P=0.000$ ). The median survivals among the patients with different classifications of peritoneal metastasis were statistically significant ( $P=0.000$ ). Patients undergoing resection followed by chemotherapy had a significantly longer median survival, compared with that of patients who had chemotherapy alone, those who had resection alone, or those who had not received chemotherapy or resection ( $P=0.000$ ). Results of subgroup analyses showed that except for P3 patients and patients with multisite distant metastases, overall survival was significantly better in

patients with palliative gastrectomy, compared with the nonresection group. In multivariate analysis, P3 disease ( $P=0.000$ ), absence of resection ( $P=0.000$ ), and lack of chemotherapy ( $P=0.000$ ) were identified as independently associated with poor survival.

Palliative gastrectomy might be beneficial to the survival of gastric cancer patients with intraoperatively proven P1/P2 alone, rather than P3. Postoperative palliative chemotherapy could improve survival regardless of operation and should be recommended.

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**Abbreviations:** IGCC = International Gastric Cancer Congress, VOLTGA = Volunteer Team of Gastric Cancer Surgery.

## INTRODUCTION

Gastric cancer is a disease with high incidence and cancer-related deaths worldwide.<sup>1</sup> Surgery is the mainstay of treatment for gastric cancer patients with D2 lymphadenectomy accepted as the standard surgery in East Asia. Although overall survival is improved with the implementation of standard D2 lymphadenectomy and the development of chemotherapy as well as new targeted drugs in recent years,<sup>2–4</sup> the long-term survival rates of advanced cases is still unsatisfactory. Unfortunately, most patients are diagnosed as advanced gastric cancer at presentation in China.<sup>5</sup>

Peritoneal dissemination is the most frequent pattern of metastasis and recurrence in patients with gastric cancer.<sup>6,7</sup> It has been reported that the detection rate of free cancer cells in peritoneal cavity was 44% in patients with serosal invasion.<sup>8</sup> Some patients with gastric cancer even present with peritoneal carcinomatosis. Another challenge is that the diagnosis of peritoneal metastasis is often not made before laparotomy because of absence of ideal techniques with high sensitivity and specificity. Studies reported that 10% to 20% of patients have intraoperatively proven peritoneal seeding, which was not diagnosed preoperatively.<sup>9,10</sup> Therefore, the most suitable therapeutic strategy for such patients is a subject of debate.

There, however, is still controversy about the role of resection in the palliative treatment of patients with peritoneal metastasis. Some investigations reported that gastric resection can prolong the survival of selected patients with P1/P2 peritoneal metastasis without increasing the mortality rate and may be beneficial to reducing symptoms, and enhancing the quality of life.<sup>10–13</sup> It has been reported that the palliative gastrectomy even nonresectional operations could relieve the symptoms associated with cancer, such as enable oral food intake after improving obstructive symptoms, bleeding, and/or pain, and improve the quality of life.<sup>14–16</sup> Some other studies, however, have indicated that palliative gastrectomy has no survival benefit in the setting of peritoneal dissemination and surgical treatment was not recommended in the absence of serious complications, such as tumor bleeding or organ perforation.<sup>5,17,18</sup> In addition, palliative

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resection may lead to the increased risks of surgical morbidity and prolonged hospitalization.<sup>19</sup>

Therefore, there is still no consensus in the value of palliative gastrectomy for gastric cancer patients with intraoperatively proven peritoneal seeding. The aim of this study was to evaluate the survival benefit of palliative gastrectomy for gastric cancer patients with intraoperatively proven peritoneal seeding and to identify positive predictive factors for improving survival.

## METHODS

### Patients

From February 2006 to December 2013, data of 267 gastric cancer patients with intraoperatively proven peritoneal seeding were collected from a prospective database and retrospectively analyzed. The diagnosis of peritoneal dissemination was based on the operative findings. Patients were divided into a resection group and a nonresection group according to whether the palliative gastrectomy was performed. The preoperative diagnosis of gastric carcinoma was confirmed by endoscopy followed by biopsy. Patients with only positive cytology were excluded for analysis. Patients diagnosed with other gastric malignancies such as lymphoma and gastrointestinal stromal tumor were excluded. Remnant stomach cancers and patients with neoadjuvant chemotherapy were also excluded. The clinicopathologic features, such as sex, age, tumor size, tumor differentiation, tumor location, depth of tumor invasion, and multisite distant metastases (defined as concurrent extraregional lymph nodes metastasis, hepatic metastasis, or other distant metastases besides peritoneal seeding, such as No.16 lymph nodes metastasis etc), classification of peritoneal metastasis, postoperative chemotherapy, morbidity, mortality, and survival outcome were compared between the 2 groups. The West China Hospital research ethics committee approved retrospective analysis of anonymous data. Signed patient informed consent was waived per the committee approval, because it was a retrospective analysis.

### Treatments

The decision to proceed with resection was determined by the operator according to performance status of the patient and feasibility of resection. The following conditions were considered a contraindication to resection: locoregionally advanced disease infiltration of the root of the mesentery, invasion or encasement of major vascular structures (excluding the splenic vessels) or important organs (such as common bile duct), involvement of the descending part of duodenum or pancreatic head requiring pancreatoduodenectomy, significant esophageal involvement requiring transthoracic resection, extensive adhesion or fixation of the tumor. In the resection group, primary tumors and greater omentum were removed regardless of lymphadenectomy and metastasectomy. Total or subtotal gastrectomy was performed according to the location of the primary lesion. Billroth I, Billroth II, or Roux-en-Y anastomosis with mechanical stapler was performed to reconstruct the digestive tract after distal gastrectomy. Esophagogastric anastomosis was used after proximal gastrectomy and Roux-en-Y esophagojejunostomy was applied for total gastrectomy. Bypass or explorative laparotomy was classified into nonresection group. Fluoropyrimidine and platinum regimens were given to the patients who received postoperative chemotherapy. Clinicopathologic terminology was based on the Japanese classification of gastric carcinoma (3rd English version).<sup>20</sup>

### Classification of Peritoneal Seeding

Because there is no detailed classification of peritoneal seeding in the second and third English version of Japanese classification of gastric carcinoma, we classified peritoneal metastasis according to the first English edition of Japanese classification of gastric carcinoma as follows: P0, no peritoneal seeding; P1, disseminating metastasis to the region directly adjacent to the peritoneum of stomach (above the transverse colon including the greater omentum); P2, several scattered metastases to the distant peritoneum and ovarian metastasis alone; and P3, numerous metastases to the distant peritoneum.<sup>21</sup>

### Follow-Up

Patients underwent a follow-up, which was done by telephone calls, letters, or outpatient visits. As of December 31, 2014, the overall follow-up rate was 89.89% (240/267). Eight patients in the resection group and 19 patient in the nonresection group were lost to follow-up. The median follow-up duration was 12.3 months in the resection group and 9.0 months in the nonresection group.

### Statistical Analysis

SPSS 19.0 software (SPSS, Chicago, IL) was used for statistical analyses. Variables of normality were tested, while confirming the normal distribution, where data are expressed as means  $\pm$  standard deviation. Two independent *t*-tests for quantitative data and  $\chi^2$  test or Fisher exact test for categorical data were performed, or data were expressed as medians with a range taking the Spearman test into consideration. Survival was calculated by Kaplan-Meier estimation and the log-rank test. Independent prognostic factors were identified by Cox proportional hazards regression model. A *P* value of less than 0.05 (two-sided) was considered statistically significant.

## RESULTS

### Patient Characteristics

There were 114 patients in the resection group and 153 patients in the nonresection group. Because the tumors were not removed in the nonresection group, some staging information could not be determined, such as pathologic T stage. In the nonresection group, tumors were larger, depth of serosa invasion was greater, and peritoneal seeding was more severe, compared with the resection group. Other parameters, including age, sex, comorbidity, tumor location, tumor differentiation, multisite distant metastases, and postoperative palliative chemotherapy were comparable between the 2 groups. The general clinicopathologic characteristics are summarized in Table 1. In the resection group, 45 patients underwent distal gastrectomy with 3 proximal gastrectomies and 66 total gastrectomies. Nine patients had combined multiorgan resections, including 1 transverse colon, 1 splenectomy, 1 cholecystectomy, 2 oophorectomies, 2 small intestine resections, and 2 hepatectomies. The average number of total harvested lymph nodes and positive lymph nodes were  $30.17 \pm 12.69$  and  $15.32 \pm 12.00$ , respectively. In the nonresection group, 35 by-pass surgeries and 118 explorations were performed.

### Morbidity and Mortality

The overall postoperative morbidity rates were significantly different at 14.91% (17/114) versus 5.88% (9/153) for the resection and nonresection groups respectively (*P* = 0.014). Most of the postoperative complications were pulmonary

**TABLE 1.** General Clinicopathologic Characteristics of the Patients

	Resection Group (N = 114)	Nonresection Group (N = 153)	P Value
Gender			0.491
Female	40	60	
Male	74	93	
Age (yrs)			0.425
<60	63	92	
≥60	51	61	
ASA score			0.343
I	37	46	
II	65	82	
III	12	25	
Weight	57.2 ± 14.6	58.7 ± 21.4	0.548
Comorbidity	68	80	0.231
Pulmonary	28	25	
Digestive	23	28	
Urological	6	12	
Cardiovascular	20	22	
Endocrinal	15	16	
Neurologic	1	1	
Hematological	4	2	
Tumor location			0.130
Upper third	26	39	
Middle third	17	17	
Lower third	57	63	
Linitis plastica	14	34	
Differentiation			0.141
Moderate	5	2	
Poor	109	151	
Tumor size (cm)			0.000
2~5.0	22	10	
5~8.0	53	43	
>8.0	39	100	
Depth of infiltration (T)			0.000
Tx	0	11	
T1	0	0	
T2	2	2	
T3	3	0	
T4a	58	16	
T4b	51	124	
Peritoneal seeding (P)			0.000
P1	62	42	
P2	15	30	
P3	37	81	
Multisite distant metastases			0.576
Yes	20	31	
No	94	122	
Palliative chemotherapy			0.189
Yes	71	83	
No	43	70	

infections. There were 8 and 3 patients who experienced pulmonary infections in the resection and nonresection groups, respectively. One intraluminal hemorrhage, 3 wound infections, 2 intraperitoneal infections, 1 ileus, 1 vertigo, and 1 acute urinary retention were found in the resection group. One anastomotic leakage, 1 wound infection, 2 gastroparesis, and 2 cardiac failures were detected in the nonresection group. According to according to the Clavien-Dindo classification,<sup>22</sup> there were 4 I, 10 II, 2 IIIa, 1 IVa, and 1 V in resection group,

corresponding to 3 I, 3 II, 1 IIIa, 2 IVa, and 1 V in nonresection group ( $P = 0.869$ ). There was no significant difference in postoperative hospital stays ( $11.56 \pm 4.69$  versus  $10.73 \pm 6.78$ , days  $P = 0.259$ ) between the resection and nonresection groups. One patient from the resection group died because of brain infarction, and another patient in the nonresection group died because of intraoperative cardiac arrest. The postoperative mortality was 0.88% versus 0.65% in the resection and nonresection groups ( $P = 1.000$ ), respectively.

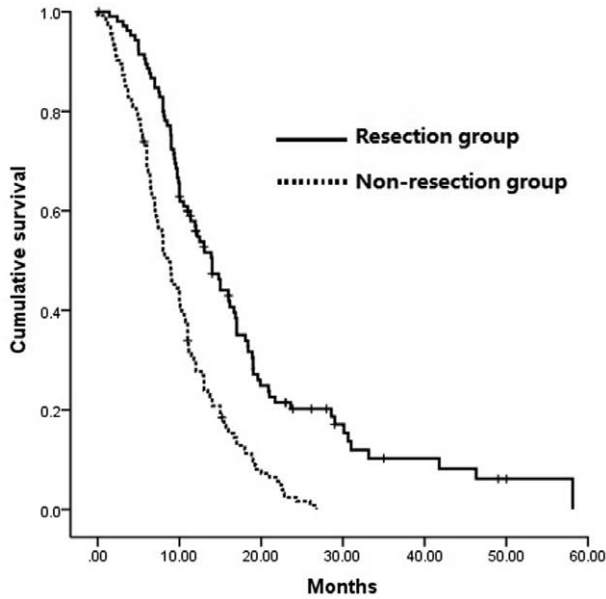


FIGURE 1. Survival curves of resection group and nonresection group for gastric cancer patients with intraoperative proven peritoneal seeding ( $P=0.000$ ).

**Long-Term Survival**

The median survival was 14.00 (95% CI: 11.53, 16.47) months in the resection group and 8.57 (95% CI: 7.33, 9.81) months in the nonresection group (Figure 1). The survival difference between the 2 groups was significant ( $P=0.000$ ). The results of subgroup analyses stratified by clinicopathologic factors showed that except for patients with tumor located at upper third ( $P=0.076$ ), P3 patients ( $P=0.138$ ) (Figure 2) and patients with multisite distant metastases ( $P=0.267$ ) (Figure 3), overall survival was significantly better in patients with palliative gastrectomy compared with the nonresection group, even in patients without postoperative chemotherapy (Figure 4). The results of the subgroup analyses are summarized in Table 2.

The median survivals were reanalyzed according to the different classification of peritoneal metastasis and received treatments to investigate their influences. Patients with P1 had a median survival of 12.17 (95% CI: 9.92, 14.42) months compared with 13.00 (95% CI: 9.71, 16.29) months for those with P2 and 8.07 (95% CI: 7.23, 8.91) months for those with P3 ( $P=0.000$ ) (Figure 5). Patients undergoing resection followed by chemotherapy had a significantly longest median survival of 18.37 (95% CI: 16.61, 20.13) months, compared with 11.77 (95% CI: 10.18, 13.36) months for patients who had chemotherapy in the nonresection group, 8.90 (95% CI: 7.69, 10.11) months for those who had resection alone, and 4.73 (95% CI: 3.39, 6.07) months for those who had not received chemotherapy in the nonresection group ( $P=0.000$ ) (Figure 6).

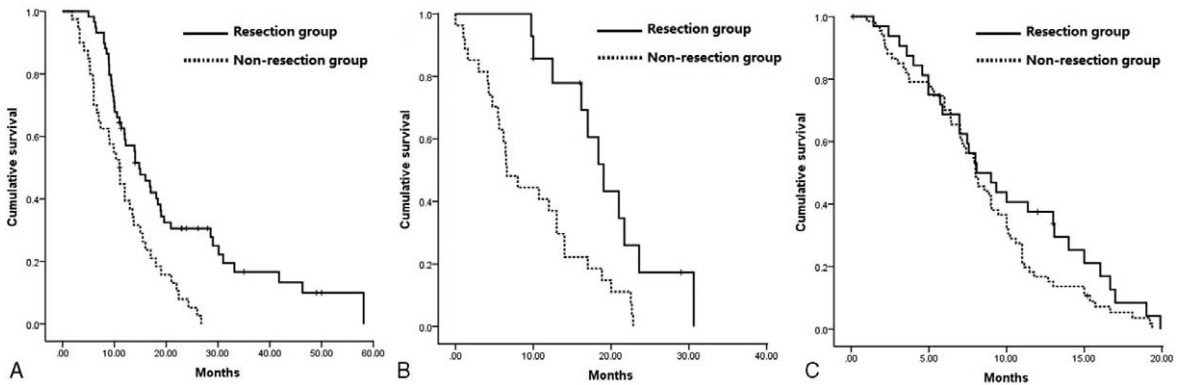


FIGURE 2. Survival curves of resection group and nonresection group for gastric cancer patients with peritoneal seeding stratified by classifications of peritoneal metastasis. A, P1 ( $P=0.000$ ). B, P2 ( $P=0.002$ ). C, P3 ( $P=0.138$ ).

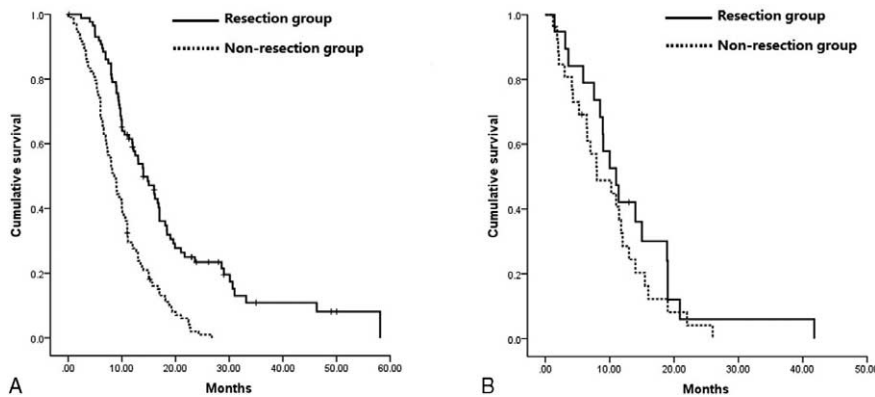
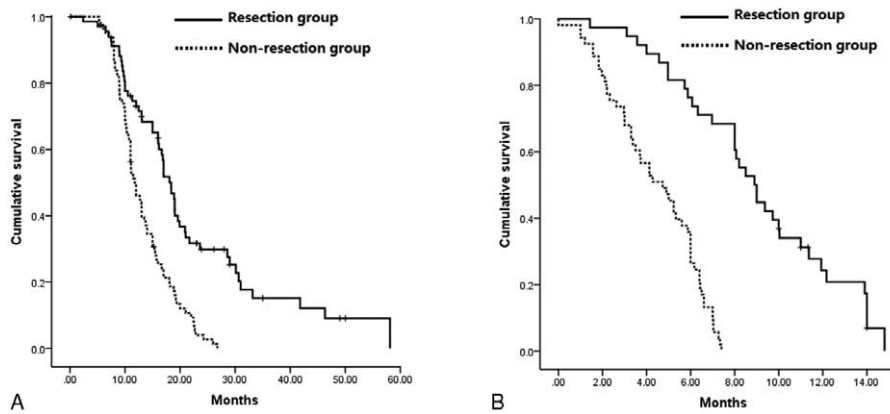


FIGURE 3. Survival curves of resection group and nonresection group for gastric cancer patients with peritoneal seeding stratified by multisite distant metastases. A, Peritoneal seeding only ( $P=0.000$ ). B, With multisite distant metastases ( $P=0.267$ ).

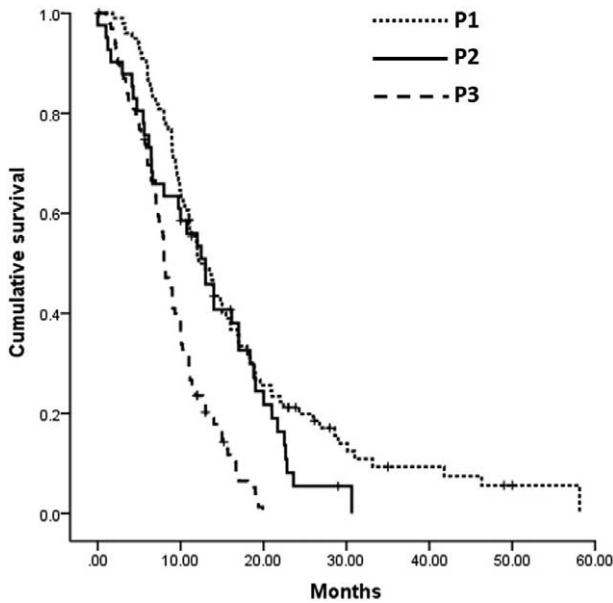


**FIGURE 4.** Survival curves of resection group and nonresection group for gastric cancer patients with peritoneal seeding stratified by postoperative chemotherapy. A, With chemotherapy ( $P=0.000$ ). B, Without chemotherapy ( $P=0.000$ ).

**TABLE 2.** Survival Analysis Stratified by Clinicopathologic Factors

	Resection Group (N = 114)		Nonresection Group (N = 153)		P Value
	N	MST (Months) [95% CI]	N	MST (Months) [95% CI]	
Gender					
Female	40	13.07 [6.60, 19.54]	60	7.13 [5.56, 8.70]	0.000
Male	74	14.00 [10.99, 17.01]	93	10.10 [8.23, 11.97]	0.000
Age (yrs)					
<60	63	12.17 [7.75, 16.59]	92	9.07 [7.27, 10.87]	0.001
≥60	51	16.17 [12.80, 19.54]	61	8.00 [6.76, 9.24]	0.000
Tumor location					
Upper third	26	11.30 [6.79, 15.81]	39	8.17 [2.12, 14.22]	0.076
Middle third	17	15.00 [13.25, 16.75]	17	10.00 [4.41, 15.59]	0.002
Lower third	57	14.00 [9.03, 18.97]	63	8.00 [6.13, 9.87]	0.000
Linitis plastica	14	12.47 [8.36, 16.58]	34	8.87 [6.00, 11.74]	0.049
Differentiation					
Moderate	5	-*	2	-*	-*
Poor	109	13.90 [11.41, 16.39]	151	8.57 [7.34, 9.80]	0.000
Tumor size (cm)					
2~5.0	22	14.80 [9.64, 19.97]	10	6.50 [4.45, 8.55]	0.000
5~8.0	53	16.03 [12.91, 19.16]	43	9.87 [7.21, 12.53]	0.000
>8.0	39	10.00 [8.87, 11.13]	100	8.17 [6.53, 9.81]	0.020
Depth of infiltration (T)					
Tx	0	-*	11	-*	-*
T1	0	-*	0	-*	-*
T2	2	-*	2	-*	-*
T3	3	-*	0	-*	-*
T4a	58	13.07 [8.60, 17.54]	16	7.13 [3.89, 10.37]	0.001
T4b	51	14.00 [11.61, 16.39]	124	8.87 [7.47, 10.28]	0.000
Peritoneal seeding (P)					
P1	62	14.80 [11.39, 18.21]	42	11.00 [9.14, 12.86]	0.000
P2	15	19.03 [15.73, 22.33]	30	6.60 [3.94, 9.26]	0.002
P3	37	8.07 [5.63, 10.51]	81	8.00 [6.84, 9.16]	0.138
Multisite distant metastases					
Yes	20	11.00 [7.63, 14.37]	31	8.00 [2.84, 13.17]	0.267
No	94	14.00 [10.93, 17.07]	122	8.57 [7.55, 9.59]	0.000
Palliative chemotherapy					
Yes	71	18.37 [16.61, 20.13]	83	11.77 [10.18, 13.36]	0.000
No	43	8.90 [7.69, 10.11]	70	4.73 [3.39, 6.07]	0.000

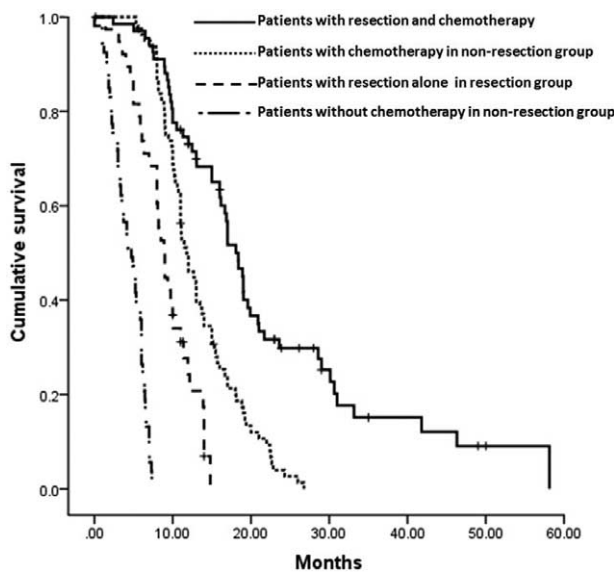
\* The analyses were not performed because of the too small sample size. MST = median survival time.



**FIGURE 5.** Overall survival of gastric cancer patients with peritoneal seeding stratified by classifications of peritoneal metastasis regardless of the treatments ( $P=0.000$ ).

**Multivariable Analysis for Overall Survival**

The univariate survival analysis revealed that sex, tumor size, depth of infiltration, classifications of peritoneal seeding, palliative chemotherapy, and resection were associated with survival (Table 3). In multivariate analysis, P3 disease ( $P=0.000$ ), absence of resection ( $P=0.000$ ), and lack of chemotherapy ( $P=0.000$ ) were identified as independently associated with poor survival after adjusting for age, sex, tumor location, histologic differentiation, tumor size, T stage, classifications of peritoneal seeding, multisite distant metastases, and palliative chemotherapy and resection (Table 3).



**FIGURE 6.** Overall survival of gastric cancer patients with peritoneal seeding according to treatments received ( $P=0.000$ ).

**DISCUSSION**

Often, peritoneal dissemination is difficult to diagnose before surgery. Approximately 10% to 20% of patients with peritoneal seeding are discovered at the time of operation.<sup>9,10</sup> Although efforts on intraperitoneal chemotherapy, systemic chemotherapy, and operations etc have been recently made to this condition to improve the prognosis, there are still many debatable issues about the treatments, including the value of palliative resection for patients with peritoneal metastasis.

From our study, the results showed that median survival was significantly longer in the resection group, compared with the nonresection group. This is supported by other studies.<sup>10-13</sup> Removal of the tumor may reduce the complications caused by the primary tumor and increase the comfort of patients.<sup>12</sup> In addition, the increased efficacy of chemotherapy and lowered body metabolism by reducing tumor size after gastrectomy as well as immunologic benefits in terms of reduced level of cytokine and immunosuppressant produced by tumors may contribute to the improved survival.<sup>12</sup> Although the interim analysis of randomized trial (REGATTA trial), which investigated the role of gastrectomy in the management of incurable advanced gastric cancer seemed not favor the gastrectomy group with 2-year overall survival rate being 25.1% compared with 31.7% of chemotherapy group ( $P=0.68$ ), the results of subgroup analysis for peritoneal seeding was not given.<sup>23</sup> And the final results are still anticipated. Another randomized trial (GYMSSA trial) showed us cytoreductive surgery combined with intraperitoneal and systemic chemotherapy in selected patients with peritoneal carcinomatosis can achieve prolonged survival.<sup>24</sup>

To determine the appropriate surgical candidates for palliative gastrectomy, we performed subgroup analyses stratified by clinicopathologic factors. The results showed overall survival of the resection group was not significantly better for patients with tumor located at upper third, compared with the nonresection group. Although our results were not statistically significant, we found palliative resection could show a benefit trend for survival in patients whose tumor was located at the upper third. Probably there is type II error concerning our results. So, maybe new studies with larger sample sizes are needed. With respect to the classifications of peritoneal seeding, we analyzed the median survival according to the different classifications of peritoneal metastasis. The results showed patients with P1 or P2 had better median survival than that of P3 ( $P=0.000$ ). Hioki et al<sup>10</sup> also reported there was a significant overall improved survival for those in the P1 and P2 groups than in the P3 group. Gretschel et al<sup>25</sup> demonstrated that the median survival of patients with P1, P2, or P3 were 9.9 months, 8.2 months, or 7.6 months, respectively. Furthermore, our results of subgroup analysis stratified by classifications of peritoneal metastasis showed P3 rather than P1/P2 patients, could not benefit from palliative gastrectomy. Xia and Hioki et al<sup>10,11</sup> reported gastric cancer patients with P1/P2 and well/moderately differentiated tumors were likely to have an improved survival after gastrectomy. Surgical approach should not be taken into account for those patients with P3 gastric cancer. Patients with P3 disease did not benefit from additional surgery compared with chemotherapy alone.<sup>25</sup> Mariette et al<sup>26</sup> reported only localized seeding without signet ring cell histology had a survival benefit after palliative resection. In addition, our univariate analysis of clinicopathologic factors revealed that classifications of peritoneal seeding, palliative resection were associated with the survival. In multivariate analysis, both P3 disease and absence of resection were

**TABLE 3.** Prognostic Factors on the Univariate and Multivariate Analysis

	Univariate HR (95 % CI)	P Value	Multivariate HR (95 % CI)	P Value
Gender				
Male	1		1	
Female	1.393 [1.054, 1.840]	0.020	1.094 [0.799, 1.497]	0.576
Age (yrs)				
<60	1		1	
≥60	0.864 [0.659, 1.133]	0.290	1.161 [0.865, 1.559]	0.320
Tumor location		0.638		0.694
Upper third	1		1	
Middle third	0.863 [0.535, 1.390]	0.544	1.284 [0.760, 2.167]	0.350
Lower third	0.953 [0.682, 1.332]	0.779	0.991 [0.689, 1.425]	0.961
Linitis plastica	1.165 [0.778, 1.746]	0.459	1.116 [0.723, 1.722]	0.619
Differentiation				
Moderate	1		1	
Poor	1.179 [0.523, 2.660]	0.692	0.971 [0.409, 2.305]	0.948
Tumor size (cm)		0.011		0.135
2~5.0	1		1	
5~8.0	1.154 [0.714, 1.866]	0.559	1.697 [0.992, 2.903]	0.054
>8.0	1.680 [1.054, 2.677]	0.029	1.698 [0.977, 2.950]	0.060
Depth of infiltration (T)		0.027		0.645
Tx	1		1	
T2	0.576 [0.125, 2.669]	0.481	0.473 [0.094, 2.377]	0.364
T3	0.524 [0.113, 2.432]	0.410	0.439 [0.087, 2.220]	0.320
T4a	0.375 [0.183, 0.768]	0.007	1.031 [0.473, 2.248]	0.939
T4b	0.578 [0.292, 1.142]	0.115	0.892 [0.440, 1.811]	0.752
Peritoneal seeding (P)		0.000		0.000
P1	1		1	
P2	1.302 [0.884, 1.918]	0.182	1.300 [0.864, 1.954]	0.208
P3	2.579 [1.876, 3.544]	0.000	2.271 [1.583, 3.258]	0.000
Multisite distant metastases				
Yes	1.259 [0.901, 1.760]	0.178	1.287 [0.892, 1.855]	0.177
No	1		1	
Palliative chemotherapy				
Yes	0.167 [0.120, 0.231]	0.000	0.071 [0.047,0.108]	0.000
No	1		1	
Resection				
Yes	1		1	
No	2.257 [1.696, 3.004]	0.000	3.399 [2.298, 5.029]	0.000

HR = hazard ratio.

identified as independently associated with poor survival. Hence, based on the results, we consider P3 is an important negative factor for prognosis and patients with P3 should not have resections performed. Kikuchi et al<sup>27</sup>, however, demonstrated that palliative gastrectomy should be given to patients regardless of metastasis to the peritoneum, as the extent of peritoneal metastases did not significantly affect the prognosis. Regarding multisite distant metastases, studies have suggested that there is no survival benefit from noncurative gastrectomy for patients with multiple sites of metastasis, which in accordance with our result.<sup>5,28</sup> Therefore, we believe palliative gastrectomy may be beneficial to the survival of selected patients with P1/P2 alone based on the results. Patients with P3 are not suitable for gastrectomy and chemotherapy should be considered.

We also analyzed the effectiveness of different treatment strategies. Our results showed patients undergoing resection followed by chemotherapy had a significant longer median survival compared with that of patients who had chemotherapy

alone, those who had resection alone or those who had not received chemotherapy or resection ( $P=0.000$ ). And the survival of patients who had resection alone was inferior to those who had chemotherapy alone (Figure 6). Also, our subgroup analyses showed that even if overall survival of the resection group for patients without postoperative chemotherapy was significantly better compared with the nonresection group, the median survival was less than those of patients with postoperative chemotherapy in nonresection group (Table 2, Figure 4). In this study, the univariate and multivariate analyses also showed that palliative chemotherapy was associated with the survival, and lack of chemotherapy went against survival. Thereby, we suggest that it is necessary for patients who underwent palliative gastrectomy because of peritoneal seeding to receive chemotherapy after the operation. Ko et al<sup>15</sup> also recommended noncurative resection followed by chemotherapy for incurable gastric cancer in terms of survival.

Laparoscopic exploration might be helpful to detect peritoneal seeding with high sensitivity and specificity. The degree

of peritoneal seeding also could be precisely defined by laparoscopy.<sup>25</sup> Laparoscopy should be focused on identifying all patients with P3 disease, who might not benefit from resection and should be treated with chemotherapy.<sup>25</sup> Patients with P3 may obtain the opportunity for an additional gastrectomy after induction chemotherapy.<sup>29</sup> Although it was reported that peritoneal dissemination disappeared in 46% of patients and the frequency of R0 resection was increased after the induction chemotherapy for patients with P1/P2,<sup>30,31</sup> there is no convincing evidence for a survival benefit of induction chemotherapy over surgery in patients with P1/P2. Actually, the longest survival time was 58.13 months for patients with P1 and could be considered to be cured in our studies. Well-designed prospective trials are needed to evaluate the role of chemotherapy and surgery.

In this study, the overall postoperative morbidity rate was higher in the resection group than that of the nonresection group, which was significantly different. Other studies also reported noncurative gastrectomy may increase postoperative morbidity and prolong hospital stay in patients with distant metastasis.<sup>32,33</sup> This is reasonable and our results are comparable with similar previous reports.<sup>34,35</sup> There were no significant differences in postoperative hospital stay and mortality between the resection group and the nonresection group. Therefore, we consider palliative gastrectomy for gastric cancer patients with intraoperative proven peritoneal seeding still could be considered a safe procedure with acceptable incidence of morbidity and mortality.

There are also some limitations of this study. Firstly, possible selection bias, detection bias, and performance of analysis bias might exist in a retrospective study.<sup>36</sup> Actually in the nonresection group, the tumor was larger, depth of serosa invasion was greater, and the peritoneal seeding was more severe, which may influence the survival results. We, however, have performed subgroup analyses and multivariate analysis to adjust for the shortcomings. Regardless, large scale randomized controlled trials are needed to explore the survival benefit and safety of palliative gastrectomy for gastric cancer patients with intraoperatively proven peritoneal seeding.

## CONCLUSIONS

In conclusion, palliative gastrectomy might be beneficial for the survival of gastric cancer patients with intraoperatively proven P1/P2 alone, rather than P3. Postoperative palliative chemotherapy could improve survival regardless of operation and should be recommended.

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