Prognostic significance of peritoneal lavage cytology at three cavities in patients with gastric cancer

Yosuke Kano, MD, Shin-ichi Kosugi, MD, PhD, Takashi Ishikawa, MD, PhD, Takahiro Otani, MD, Yusuke Muneoka, MD, Yu Sato, MD, Takaaki Hanyu, MD, PhD, Kotaro Hirashima, MD, PhD, Takeo Bamba, MD, PhD, *and* **Toshifumi Wakai, MD, PhD, FACS,** *Niigata, Japan*

Background. *We sought to determine the prognostic significance of intraoperative peritoneal lavage cytology (CY) at 3 different abdominal cavities and establish the optimal treatment for gastric cancer patients with positive peritoneal cytology (CY1).*

Methods. *A total of 1,039 patients with primary gastric adenocarcinoma who underwent CY at 3 cavities (Douglas' pouch, left subphrenic cavity, and right subhepatic cavity) were enrolled; 116 (11%) patients had at least one positive cavity. We retrospectively analyzed the clinicopathologic characteristics and survival of these 116 patients with CY1.*

Results. *Seventeen (15%) of the patients had negative cytology at Douglas' pouch but positive cytology at one or both of the other cavities. The 116 patients' overall 2-year survival rate was 22.9%, with the median survival time of 11 months. The overall 2-year survival rates for the patients with positive cytology at 1, 2, and 3 cavities were 41.9%, 35.8%, and 15%, with median survival times of 17, 18, and 9 months, respectively ($P < .01$). A multivariate analysis revealed that macroscopic type 4 tumor, R2 resection, lymph node metastasis, and postoperative chemotherapy were independent prognostic factors. Among the CY1 patients with type 4 tumors, there was no substantial difference in survival between the patients who underwent R1 or R2 resection, although the statistical power of this subgroup analysis was low.*

Conclusion. *CY at 3 cavities might be a useful method to decrease the false-negative rate. Palliative gastrectomy for CY1 patients with type 4 tumors is still controversial. (Surgery 2015;158:1581-9.)*

From the Division of Digestive and General Surgery, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan

Peritoneal lavage cytology (CY) has been used to assess the presence of free cancer cells in the peritoneal cavity. Gastric cancer patients with positive peritoneal lavage cytology (CY1) are classified as stage IV according to the Japanese Classification of Gastric Carcinoma and the Cancer Staging Manual of the American Joint Committee on Cancer.[1,2] Thus, it is important to diagnose a gastric cancer patient's CY status accurately to determine the treatment strategy.

With the goal of increasing the sensitivity of CY for detecting free cancer cells in the abdominal cavity, methods that use immunohistochemical or molecular biological techniques were developed[3-5]; however, these techniques were too expensive and troublesome and could be performed only at limited facilities such as university hospitals and large cancer centers. CY at multiple cavities is a less expensive and more feasible method, and it is already widely used in clinical practice.

Although the prognosis of CY1 patients is known to be poor, the optimal treatment for these patients has not yet been established.[6,7] Palliative gastrectomy for CY1 patients remains controversial, in particular. The dual goals of the present study were to evaluate the prognostic significance of intraoperative CY at 3 different abdominal cavities and to establish the optimal treatment for patients with CY1 gastric cancer.

METHODS

Patients. Between January 1987 and December 2012, 1,252 patients with primary gastric adenocarcinoma, excluding patients with adenocarcinoma in the remnant stomach and those with

Accepted for publication April 5, 2015.

Reprint requests: Shin-ichi Kosugi, MD, PhD, Division of Digestive and General Surgery, Niigata University Graduate School of Medical and Dental Sciences, 1-757 Asahimachi-dori, Chuo-ku, Niigata 951-8510, Japan. E-mail: sugishin@med.niigata-u.ac.jp.

0039-6060/$ - see front matter

http://dx.doi.org/10.1016/j.surg.2015.04.004

active concomitant malignancy, underwent operative interventions at the Division of Digestive and General Surgery, Niigata University Medical and Dental Hospital. During this period, we performed routinely CY to detect potential malignant cells in 3 distinct cavities. CY was not performed in 108 patients for various reasons or in 99 patients with clinical T1N0 disease who underwent laparoscopy-assisted gastrectomy. Six other patients were excluded because they underwent CY in only 1 or 2 cavities. Of the remaining 1,039 patients, 116 (11%) were CY1 and were entered into this study (Fig 1). The median follow-up period for censored cases was 29 months. The Ethics Committee of Niigata University approved the use of prospectively collected data for this study, waiving patient consent.

Peritoneal lavage cytology (CY). The cytological examination was performed routinely immediately after laparotomy or at the staging laparoscopy, before manipulation of the primary tumor, regardless of the preoperative clinical stage. Physiologic normal saline (100 mL) was instilled and aspirated from each of the following areas sequentially: Douglas' pouch, the left subphrenic cavity, and the right subhepatic cavity. New syringes and tubes were used for each sample collection to prevent contamination. The collected specimens were immediately referred to the pathology department and stained by the Papanicolaou method. Two cytotechnologists and a cytopathologist examined all of the slides to reach a diagnosis by consensus.

Benign or intermediate cells on peritoneal cytology were defined as negative peritoneal cytology (CY0), and cancer cells on peritoneal cytology were defined as CY1. Cases that were "suspicious of malignancy" in the cytological diagnosis were classified as CY0.[1] Patients with at least 1 positive cavity on CY were regarded as CY1 in the present study.

Operative interventions and histopathologic examination. The operative interventions for the 116 patients with CY1 included exploratory laparotomy or staging laparoscopy, gastrojejunostomy, and gastrectomy, which were selected individually based on the local and peritoneal tumor spread. The extent of systematic lymph node dissection is defined according to the type of gastrectomy.[8] In principle, D1 lymph node dissection, including mainly perigastric nodes, is involved in a modified surgery. D2 lymph node dissection, including mainly perigastric and suprapancreatic nodes, is involved in a standard surgery. D0 is defined as lymph node dissection less than D1.

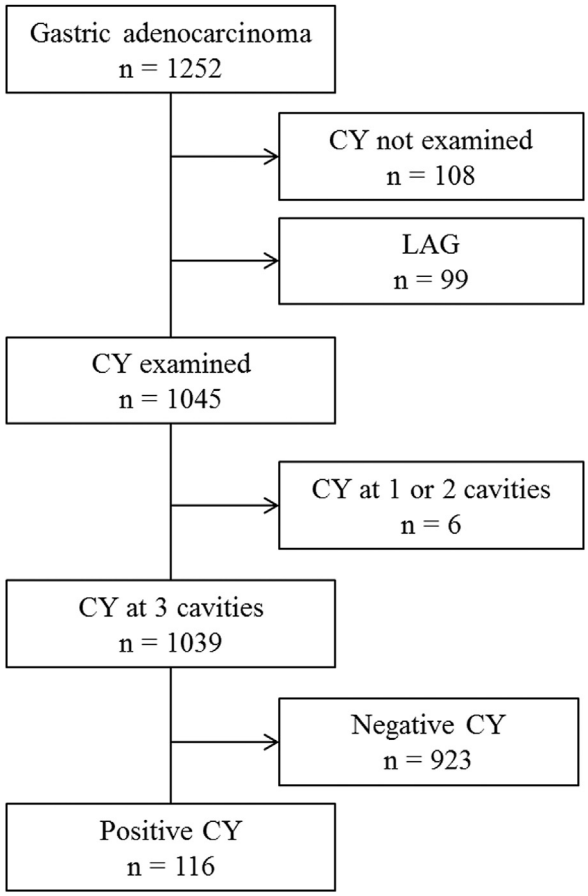

Fig 1. Schema of patients with primary gastric adenocarcinoma who underwent peritoneal lavage cytology. *CY,* Peritoneal lavage cytology; *LAG,* laparoscopy-assisted gastrectomy.

A pathologic examination of the resected specimen was performed in the patients who underwent gastrectomy, and the tumor was described and staged according to the Japanese Classification of Gastric Carcinoma, which was revised as being almost identical to the TNM classification of the Joint Committee on Cancer/International Union Against Cancer.[1,2] The histologic types were divided into 2 groups: the differentiated group included papillary and tubular adenocarcinomas, and the undifferentiated group included poorly differentiated adenocarcinomas, signet-ring cell carcinomas, and mucinous adenocarcinomas.

Statistical analysis. We used SPSS statistical software ver. 17.0 for Windows (IBM, Armonk, NY) for all statistical analyses. Statistical comparisons were made by use of the Mann-Whitney *U* test for continuous variables and the χ^2 or Fisher exact test for categorical variables. A post-hoc power analysis was performed using G* power software, version 3.1. The survival rates after operative

interventions were calculated using the Kaplan-Meier method, and differences between the survival curves were assessed using the log-rank test. We performed a univariate analysis to elucidate potential prognostic factors of the CY1 patients, and these factors were evaluated by a multivariate analysis using the Cox proportional hazard model and a backward step-wise procedure. We used $P < .10$ as a cutoff value to select variables from the univariate analysis for the multivariate model.

RESULTS

Patient characteristics and CY. The clinicopathologic characteristics of the 116 patients with CY1 are provided in Table I. There were 13 patients (11%) with serosa-negative tumors and 89 patients (77%) with macroscopic infiltrative type including type 3 and type 4. Seventeen patients who had an unresectable tumor underwent gastrojejunostomy ($n = 7$), enterostomy ($n = 3$), exploratory laparotomy ($n = 4$), or staging laparoscopy ($n = 3$). R1 resection attributable to CY1 was performed in 56 patients. The median numbers of harvested lymph nodes in patients who underwent D0, D1, and D2 or more lymph node dissection were 16, 30, and 45, respectively. The patients who underwent R1 resection were 10 patients with minimal peritoneal metastasis and one patient with hepatic metastases that were completely resected simultaneously.

Table II gives the CY details of the 116 CY1 patients. Seventeen patients (15%) had negative cytology at Douglas' pouch but positive cytology at the other 2 cavities. Eighty-eight patients (75.9%) received postoperative chemotherapy, mainly a fluoropyrimidine-based regimen, and 28 patients did not receive any chemotherapy.

Survival. The overall 1-, 2-, and 5-year survival rates for the CY1 patients were 43.9%, 22.9%, and 6.2%, respectively, with the median survival time (MST) of 11 months (Fig 2, *A*). The overall 2-year survival rates for the patients with positive cytology at 1, 2, and 3 cavities were 41.9%, 35.8%, and 15%, with the MSTs of 17, 18, and 9 months, respectively ($P < .01$, Fig 2, *B*).

The results of the univariate and multivariate analyses to identify prognostic factor for CY1 patients are shown in Table III. The significant prognostic factors identified by the univariate analysis were the depth of tumor invasion, lymph node metastasis, peritoneal metastasis, number of CY-positive cavities, macroscopic type, gastric resection, residual tumor, and postoperative chemotherapy. The multivariate analysis demonstrated that the lymph node metastasis, macroscopic type, residual tumor, and postoperative chemotherapy were significant and independent prognosticators.

Table I. Clinicopathologic characteristics of the 116 gastric cancer patients with positive peritoneal cytology

Variable	n *(% or range)*
Age	
Median (range)	64 (29–86)
Sex	
Male	79 (68)
Female	37 (32)
Depth of tumor invasion	
T1b (SM)	3 (3)
T2 (MP)	2 (2)
T3 (SS)	8 (7)
T4a (SE)	71 (61)
T4b (SI)	32 (27)
Lymph node metastasis	
N0	9 (8)
≥N1	107 (92)
Hepatic metastasis	
H0	109 (94)
H1	7 (6)
Peritoneal metastasis	
P0	54 (47)
P1	62 (53)
Macroscopic type	
Type 0	9 (8)
Type 1	4 (3)
Type 2	14 (12)
Type 3	46 (40)
Type 4	43 (37)
Histologic type	
Differentiated	39 (34)
Undifferentiated	77 (66)
Operative procedure	
Total gastrectomy	62 (53)
Distal gastrectomy	37 (32)
Not resected	17 (15)
Lymph node dissection*	
D0	22 (22)
D1	28 (28)
≥D2	49 (50)
Residual tumor	
R1	56 (48)
R2	60 (52)
Postoperative chemotherapy	
Yes	88 (76)
No	28 (24)

*Resected case.

The 2-year overall survival rates of the 43 patients with type 4 tumors and the 73 other patients were 5.3% and 32.3%, with MSTs of 9 and 14 months, respectively ($P < .01$, Fig 3, *A*). Among the patients with type 4 tumors, there was

Table II. Peritoneal lavage cytology details of the CY1 patients

	Douglas' pouch	*Right subhepatic cavity*	*Left subphrenic cavity*	*No. of patients (%)*
Positive at 3 cavities				
	+	+	+	77 (67)
Positive at 2 cavities				
	+	+	−	7 (6)
	+	−	+	9 (8)
	−	+	+	5 (4)
Positive at 1 cavity				
	+	−	−	6 (5)
	−	+	−	4 (3)
	−	−	+	8 (7)
Positive number at each cavity	99 (85%)	93 (80%)	99 (85%)	

CY1, Positive peritoneal lavage cytology; +, positive; −, negative.

no significant difference in survival between the 16 patients with R1 resection and the 27 patients with R2 resection, with MSTs of 11 and 8 months, respectively ($P = .10$, Fig 3, *B*). There was no substantial difference in clinicopathologic characteristics between these 2 groups except for the operative procedure and peritoneal metastasis; however, in light of the limited sample size, we conducted an analysis of the post-hoc power of this subgroup considering the risk of type II error. Given the effect size of 0.5 with the sample size of 43, we obtained the power of 0.71 at $\alpha = 0.05$.

CY stratified by T and N stage. To assess the potential risk of positive peritoneal cytology, we stratified the patients' CY status by T and N stage in patients without overt metastasis who underwent R0 or R1 resection. A total of 890 patients were extracted from the 1,039 patients who underwent CY at 3 cavities. We divided these patients into 4 groups, based on the validation study of endoscopic ultrasound by Power et al[9] (Table IV).

The incidence of CY1 in patients with T3–4 and/or N+ disease and those with T1–2N0 disease were 10% and 0.4%, respectively. Two patients with T1–2N0 disease had positive cytology at only the left subphrenic cavity. They died of other diseases 21 and 59 months after gastrectomy, one without chemotherapy and the other with chemotherapy, respectively.

DISCUSSION

CY1 rates in patients with gastric cancer ranging from 11 to 27% have been reported.[6,7,10-14] The present study's CY1 rate of 11% was relatively low, even though the patients underwent CY at 3 cavities; however, our figure is not simply comparable with other studies because of the difference in the patients' backgrounds. When we subclassified patients according to the depth of tumor invasion, the CY1 rate in the patients with serosa-invading tumors was 40% (data not shown), which is greater than those of the previous studies.[6,11]

According to the Japanese Classification of Gastric Carcinoma, CY should be performed immediately after laparotomy in patients with gastric carcinoma excluding those with a T1 tumor. Ascites is aspirated for CY if present; otherwise, physiologic normal saline of 100 mL is instilled in the abdominal cavity and aspirated from Douglas' pouch.[1] In the present study, however, 17 of the 116 CY1 patients (15%) had negative CY at Douglas' pouch but positive CY at other cavities. In particular, 12 patients had positive CY at only one cavity, either the right subhepatic cavity or the left subphrenic cavity. Homma et al[15] performed CY at 4 cavities: the left subphrenic cavity, right subhepatic cavity, Douglas' pouch, and inside the omental bursa, and they reported that CY at Douglas' pouch was negative in 11 of 62 CY1 patients (17.8%), which is comparable with our present findings. One possible explanation for our false-negative rate of approximately 15% at Douglas' pouch alone may be that the number of viable cells in the abdominal cavity was too small to be detected; alternatively, free cancer cells were in the peritoneum but not at Douglas' pouch.[15] Free cancer cells are thought to accumulate first at Douglas' pouch, which is located at the bottom of the peritoneal cavity. However, when the number of free cancer cells is small, these cells may accumulate in any of these cavities at random. This hypothesis was supported by our finding that the positive rate of only one cavity was approx. 5% for each cavity, with no significant difference among the 3 cavities (Table II).

We have performed CY at 3 different cavities based on the hypothesis that the number of positive cavities may reflect the total amount of

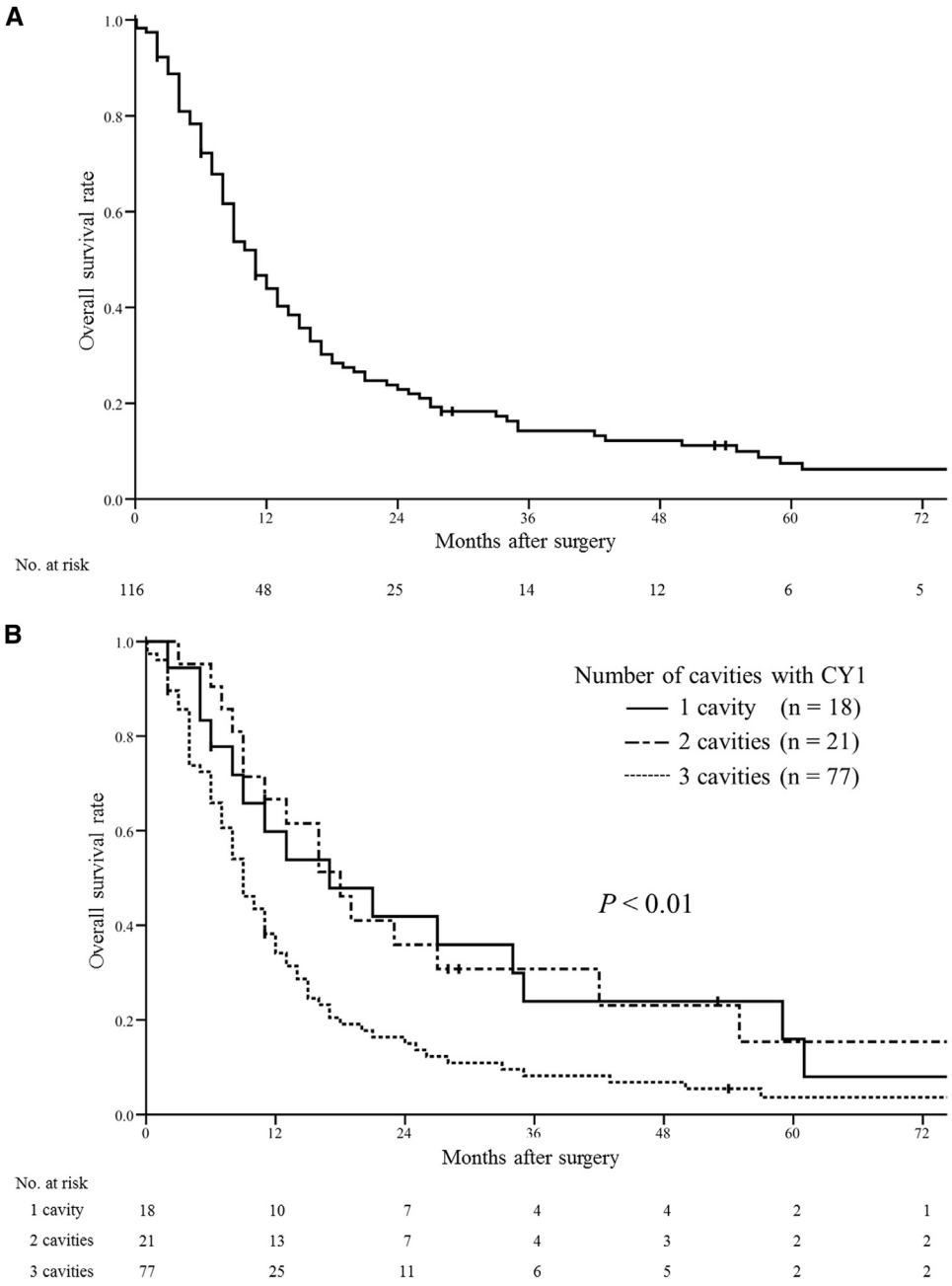

Fig 2. (*A*) The survival curve for the 116 CY1 patients. (*B*) The survival curves according to the number of positive cavities.

free cancer cells in the entire abdominal cavity and eventually influence the survival of CY1 patients. Miyashiro et al[14] reported a similar finding, ie, that the survival of advanced gastric cancer patients was associated with the number of cancer cells per slide examined during CY. In the present study, the patients with positive cytology at 3 cavities had greater poorer survival; however, there was no significant difference in survival between those with positive cytology at one cavity and those at 2 cavities. Homma et al[15] reported similar results: the survival of patients with 1 or 2 positive cavities was greater than those with 3 or more positive cavities. These results may indicate that the amount of free cancer cells in the entire abdominal cavity is still limited in patients with positive cytology in up to 2 cavities. The number of positive cavities, however, was not selected as an independent prognostic factor in the present study's multivariate analysis. A possible explanation is that the impact

Table III. Univariate and multivariate analyses for various prognostic factors

Variables	n	*MST, mo*	*Univariate* P *value*	*Multivariate* *HR (95% CI)*	P *value*
Age, y					
<65	58	11			
≥65	58	11	.42		
Sex					
Male	79	11			
Female	37	11	.62		
Depth of tumor invasion					
T1, T2, T3	13	24		1.00	
T4	103	9	.04	1.10 (0.55–2.22)	.78
Lymph nodes metastasis					
N0	8	25		1.00	
≥N1	108	10	.04	2.80 (1.27–6.18)	.01
Hepatic metastasis					
H0	109	11			
H1	7	7	.10		
Peritoneal metastasis					
P0	54	15		1.00	
P1	62	9	<.01	1.17 (0.70–1.97)	.55
Number of CY-positive cavity					
1, 2 cavities	39	17		1.00	
3 cavities	77	9	<.01	1.33 (0.86–2.07)	.20
Macroscopic type					
Type 0, 1, 2, 3	73	14		1.00	
Type 4	43	9	<.01	1.81 (1.19–2.78)	<.01
Histologic type					
Differentiated	39	11			
Undifferentiated	77	11	.73		
Gastric resection					
Resected	99	12		1.00	
Not resected	17	6	<.01	1.21 (0.68–2.16)	.52
Residual tumor					
R1	56	17		1.00	
R2	60	8	<.01	3.02 (1.95–4.68)	<.01
Postoperative chemotherapy					
Yes	88	13		1.00	
No	28	7	<.02	3.16 (1.98–5.14)	<.01

CI, Confidence interval; *CY*, peritoneal lavage cytology; *HR*, hazard ratio; *MST*, median survival time.

of the number of positive cavities on survival was offset by a greater impact of postoperative chemotherapy, which was selected as an independent prognostic factor. Nevertheless, we consider that different treatment strategies according to the number of positive cavities might be warranted.

We also found that the macroscopic type and residual tumor status were independent prognostic factors in the present patient series. Combining these 2 factors, no significant difference in survival was observed between the CY1 patients with type 4 tumors who underwent R1 or R2 resection. In contrast, there was a difference in survival between the CY1 patients with nontype 4 tumors who underwent R1 or R2 resection (MST, 25 vs 9 months; $P < .01$; data not shown). The effectiveness of palliative gastric resection is still controversial.[16] Some studies demonstrated a survival benefit of palliative gastrectomy for patients with one metastatic site,[17,18] but Kodera et al[19] reported that there was no prognostic difference in CY1 patients with type 4 tumors irrespective of gastrectomy. In our opinion, gastrectomy for patients with type 4 tumors should be avoided when overt peritoneal metastasis or positive peritoneal cytology is proven. In our previous series, 22 patients with a type 4 tumor have undergone staging laparoscopy to date. Of these

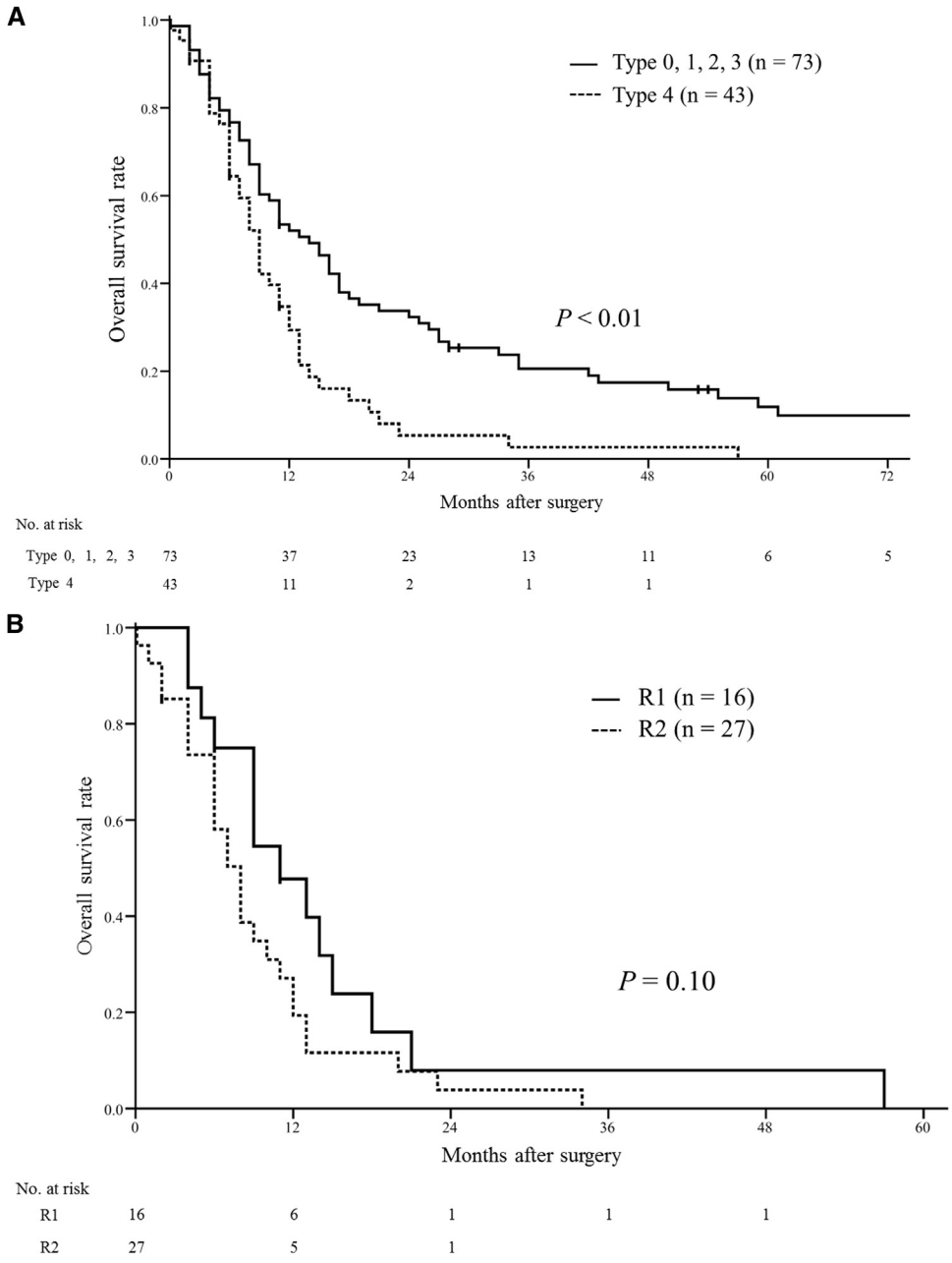

Fig 3. (*A*) The survival curves of the 43 patients with type 4 tumors and the 73 other patients. (*B*) The survival curves of the patients with type 4 tumor who underwent R1 and R2 resections.

patients, 10 (45.4%) were found to have overt or occult peritoneal disease (Sakamoto K, et al. ,2013; unpublished data). This information provided by CY is therefore essential for determining the therapeutic strategy in patients with type 4 gastric cancer, and staging laparoscopy should be performed first for this disease.

It is also important to select patients who benefit from CY at 3 cavities. Power et al[9] demonstrated that the negative predictive value of low-risk endoscopic ultrasound (T1–2N0) for occult peritoneal disease was 96%, and they concluded that laparoscopy can be avoided in these patients. Similarly, the present study's patients with T1–2N0 disease had a very low risk of positive peritoneal cytology in at least one cavity. Considering cost-effectiveness, CY at 3 cavities should be carried out only for patients with T3–4 and/or N+ disease. Using these criteria, CY at 3 cavities would be avoided in 554 (53%) of the 1,039 patients in this study. Our previous investigation demonstrated that positive ascites on

Table IV. Peritoneal lavage cytology stratified by T and N stage in 890 patients without overt metastasis who underwent R0 or R1 resection

	CY1	*CY0*	*Total*
T3–4 and/or N+	34	303	337
T1–2N0	2	551	553
Total	36	854	890

CY0, Negative peritoneal cytology; *CY1*, positive peritoneal lavage cytology.

computed tomography predicted the positive peritoneal cytology with 40% sensitivity and 97% specificity.[20] Stratification by endoscopic ultrasound and computed tomography may aid in the selection of patients who do not require CY at 3 cavities or staging laparoscopy.

The present study has some limitations. First, this was a retrospective investigation with patients treated at a single institution during a 25-year period (1987–2012), and the diagnostic modalities, operative procedures, and pre- and postoperative adjuvant therapy varied during this study period, which might cause inevitable selection bias. In addition, it is uncertain whether the false-negative rate of 15% at Douglas' pouch has clinical significance. This may reflect only the overdiagnosis of cytological examination or contamination of the collected specimens. However, few studies have examined CY at multiple cavities in consecutive patients with gastric cancer, and the results of this study may provide useful information for decision making in the treatment of CY1 patients. The development of novel chemotherapeutic regimens such as intraperitoneal chemotherapy is a challenge for the future.[21] Finally, the sample size, especially in our subgroup of patients with type 4 tumors (n = 43), was too small to exclude the risk of type II error. The estimated power of 0.71 was insufficient to detect the difference if present between 16 patients with R1 resection and 27 patients with R2 resection. The results of this subgroup analysis are unreliable at this point, and further investigation is required.

In conclusion, CY at 3 cavities might be useful to decrease the false-negative rate. Although the survival of the CY1 patients was poor, those with 1 or 2 positive cavities had better survival than those with 3 positive cavities. The prognoses of the CY1 patients with type 4 tumors were extremely poor even when an R1 resection was performed; however, palliative gastrectomy for these patients is still controversial.

REFERENCES

1. Japanese Gastric Cancer Association. Japanese classification of gastric carcinoma: 3rd English edition. Gastric Cancer 2011;14:101-12.
2. Edge S, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A, editors. AJCC cancer staging manual. Chicago: Springer; 2010.
3. Tamura S, Fujiwara Y, Kimura Y, Fujita J, Imamura H, Kinuta M, et al. Prognostic information derived from RT-PCR analysis of peritoneal fluid in gastric cancer patients: results from a prospective multicenter clinical trial. J Surg Oncol 2014;109:75-80.
4. Kodera Y, Nakanishi H, Ito S, Yamamura Y, Fujiwara M, Koike M, et al. Prognostic significance of intraperitoneal cancer cells in gastric carcinoma: detection of cytokeratin 20 mRNA in peritoneal washes, in addition to detection of carcinoembryonic antigen. Gastric Cancer 2005;8:142-8.
5. Fujiwara Y, Doki Y, Taniguchi H, Sohma I, Takiguchi S, Miyata H, et al. Genetic detection of free cancer cells in the peritoneal cavity of the patient with gastric cancer: present status and future perspectives. Gastric Cancer 2007;10:197-204.
6. Burke EC, Karpeh MS Jr, Conlon KC, Brennan MF. Peritoneal lavage cytology in gastric cancer: an independent predictor of outcome. Ann Surg Oncol 1998;5:411-5.
7. Chuwa EW, Khin LW, Chan WH, Ong HS, Wong WK. Prognostic significance of peritoneal lavage cytology in gastric cancer in Singapore. Gastric Cancer 2005;8:228-37.
8. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2010 (ver. 3). Gastric Cancer 2011;14:113-23.
9. Power DG, Schattner MA, Gerdes H, Brenner B, Markowitz AJ, Capanu M, et al. Endoscopic ultrasound can improve the selection for laparoscopy in patients with localized gastric cancer. J Am Coll Surg 2009;208:173-8.
10. Lee SD, Ryu KW, Eom BW, Lee JH, Kook MC, Kim YW. Prognostic significance of peritoneal washing cytology in patients with gastric cancer. Br J Surg 2012;99:397-403.
11. Fukagawa T, Katai H, Saka M, Morita S, Sasajima Y, Taniguchi H, et al. Significance of lavage cytology in advanced gastric cancer patients. World J Surg 2010;34:563-8.
12. Euanorasetr C, Lertsithichai P. Prognostic significance of peritoneal washing cytology in Thai patients with gastric adenocarcinoma undergoing curative D2 gastrectomy. Gastric Cancer 2007;10:18-23.
13. La Torre M, Ferri M, Giovagnoli MR, Sforza N, Cosenza G, Giarnieri E, et al. Peritoneal wash cytology in gastric carcinoma. Prognostic significance and therapeutic consequences. Eur J Surg Oncol 2010;36:982-6.
14. Miyashiro I, Takachi K, Doki Y, Ishikawa O, Ohigashi H, Murata K, et al. When is curative gastrectomy justified for gastric cancer with positive peritoneal lavage cytology but negative macroscopic peritoneal implant? World J Surg 2005;29:1131-4.
15. Homma Y, Ushida S, Yamada M, Kobayashi H, Suzuki K. Positive peritoneal washing cytology in multiple cavities can predict poor prognosis of advanced gastric cancer patients. Ann Surg Oncol 2010;17:455-60.
16. Fujitani K, Yang HK, Kurokawa Y, Park do J, Tsujinaka T, Park BJ, et al. Randomized controlled trial comparing gastrectomy plus chemotherapy with chemotherapy alone in advanced gastric cancer with a single non-curable factor: Japan Clinical Oncology Group Study JCOG 0705 and Korea Gastric Cancer Association Study KGCA01. Jpn J Clin Oncol 2008;38:504-6.

17. Hartgrink HH, Putter H, Klein Kranenbarg E, Bonenkamp JJ, van de Velde CJ, Dutch Gastric Cancer Group. Value of palliative resection in gastric cancer. Br J Surg 2002;89: 1438-43.
18. Tokunaga M, Terashima M, Tanizawa Y, Bando E, Kawamura T, Yasui H, et al. Survival benefit of palliative gastrectomy in gastric cancer patients with peritoneal metastasis. World J Surg 2012;36:2637-43.
19. Kodera Y, Yamamura Y, Ito S, Kanemitsu Y, Shimizu Y, Hirai T, et al. Is Borrmann type IV gastric carcinoma a surgical disease? An old problem revisited with reference to the result of peritoneal washing cytology. J Surg Oncol 2001; 78:175-81.
20. Yajima K, Kanda T, Ohashi M, Wakai T, Nakagawa S, Sasamoto R, et al. Clinical and diagnostic significance of preoperative computed tomography findings of ascites in patients with advanced gastric cancer. Am J Surg 2006;192:185-90.
21. Ishigami H, Kitayama J, Kaisaki S, Hidemura A, Kato M, Otani K, et al. Phase II study of weekly intravenous and intraperitoneal paclitaxel combined with S-1 for advanced gastric cancer with peritoneal metastasis. Ann Oncol 2010; 21:67-70.