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Significance of Splenectomy for Upper Gastric Carcinoma With Invasion to the Greater Curvature

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This study aimed to clarify the significance of splenectomy (Sp) for upper gastric carcinoma with invasion to the greater curvature. The Japan Clinical Oncology Group (JCOG) conducted a phase III randomized clinical trial (JCOG 0110), where the significance of Sp in total gastrectomy (TG) for upper gastric carcinoma without invasion to the greater curvature was not proved because Sp did not contribute to an improved prognosis. From 1992 to 2010, 167 patients underwent TG for carcinoma of the upper stomach, except for patients with carcinoma of the residual stomach. Among them, 60 patients with tumor invasion to the greater curvature of the upper stomach (Gre group) were enrolled. Within the Gre group, the following factors were compared between the Sp group (n = 30) and non-Sp group (n = 30): patient background, postoperative staging, rate of neoadjuvant chemotherapy, surgical outcomes and rates of R0 resection, morbidity, adjuvant chemotherapy, and overall survival (OS). The Gre group patients were relatively younger, and tumor size and the numbers of Borrmann type 4 tumors, circumferential lesions, undifferentiated type lesions, and advanced cases were significantly larger than those in the non-Gre group. There were also significant differences in patient age and organs resected other than the spleen between the Sp group and non-Sp group. There was no significant difference in OS between the 2 groups. The significance of Sp for upper gastric carcinoma with invasion to the greater

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curvature was equivocal because the patients received no survival benefit by undergoing Sp.

Key words: Gastric cancer; Invasion to greater curvature; Prognostic factor; Splenectomy; Upper curvature of the stomach

In Japan, the role of splenectomy (Sp) in total gastrectomy (TG) for carcinoma of the proximal stomach has been discussed since the 1960s. From the 1970s to the 1980s, Sp was reported as a procedure to improve the prognosis.[1,2] However, its significance has not been clear since the 1990s.[3–5] The Japan Clinical Oncology Group (JCOG) conducted a phase III randomized clinical trial (JCOG 0110) to evaluate Sp in TG for proximal gastric cancer in 2017.[6] In this trial, the significance of Sp was denied because the morbidity was high, and Sp did not contribute to an improved prognosis. However, the subjects of the trial were patients with tumors not involving the greater curvature of the stomach. A clinical question remains as to the significance of Sp for patients with tumors involving the greater curvature.

This purpose of this study was to clarify the significance of Sp in patients with upper gastric carcinoma with invasion to the greater curvature.

Materials and Methods

Patients

From 1992 to 2010, 167 patients underwent TG for carcinoma of the upper stomach (except for carcinoma of the residual stomach) at the Division of Gastrointestinal, Endocrine and Pediatric Surgery, Department of Surgery, University of Miyazaki Hospital in Japan. Of these patients, 60 had invasion of the carcinoma to the greater curvature of the upper stomach and were enrolled (Gre group) in this study.

Surgical procedure and adjuvant chemotherapy

Most patients underwent TG and regional lymph node (LN) dissection according to the gastric cancer treatment guideline.[7] Regional dissection of LNs for early gastric cancer included stations 1–6 categorized as D1 or stations 1–9, 11p, and 12a categorized as D1 according to the classification of the Japanese Gastric Cancer Association (JGCA).[8] The dissection for advanced carcinoma included stations 1-12a categorized as D2. The para-aortic LNs of some patients were also dissected. Four patients underwent laparoscopic surgery, and 56 patients underwent laparotomy. Three patients received neoadjuvant chemotherapy with S-1 plus cisplatin (2 courses, S-1 at 80–120 mg/m^2 on days 1–21 and cisplatin at 60 mg/m^2 on day 8) with reference to the S-1 plus cisplatin vs S-1 In RCT In the Treatment for Stomach cancer (SPIRITS trial) in Japan.[9] Since 2007, S-1 has been used as postoperative adjuvant chemotherapy (8 courses, S-1 at 80–120 mg/m^2 on days 1–28) based on the results of the Adjuvant Chemotherapy Trial of S-1 for Gastric Cancer (ACTS-GC trial) in Japan,[10] but prior to this, 5-fluorouracil drugs and taxane drugs were used.

Methods

First, the 167 patients who underwent TG were classified into 2 groups: the Gre group (n = 60) and non-Gre group (n = 107). The authors compared patient backgrounds and overall survival (OS) between the 2 groups. Next, the Gre group patients were subclassified into 2 groups: the Sp group (n = 30) and non-Sp group (n = 30). The authors compared the following factors between these 2 groups: age, sex, mean tumor size, macroscopic type according to the Borrmann classification, tumor location, histopathologic type, pathologic T and N factors, stage, rate of neoadjuvant chemotherapy, surgical outcomes, rate of R0 resection, morbidity, rate of adjuvant chemotherapy, and OS. The tumor information and diagnosis were according to the JGCA classification,[8] and postoperative complications were classified using the Clavien-Dindo grading system,[11] where grade III or higher represents morbidity.

Statistical analysis

Clinical parameters are expressed as the number (%) or mean ± SD. Comparisons between groups were made using the χ^2 test for categorical variables and the Student *t*-test for continuous variables. Survival was analysed using the Kaplan-Meier method, and the log-rank test was used to determine the differences between the 2 groups. The cutoff for definition of a subgroup was determined by a

Table 1 Clinicopathologic characteristics of patients with (Gre) and without (non-Gre) tumors involving the greater curvature

Variable	Gre (n = 60)	Non-Gre (n = 107)	*P* value
Age (years, mean ± SD)	61.0 ± 13.6	66.7 ± 10.1	0.0026
Sex			0.4196
Male	39	76	
Female	21	31	
Size of tumor (mm, mean ± SD)	93.4 ± 48.2	56.5 ± 24.6	<0.0001
Borrmann type			<0.0001
Type 4	29 (48.3%)	15 (14.0%)	
Other	31 (51.7%)	92 (86.0%)	
Section			<0.0001
Circ	38 (63.3%)	0	
Histologic type			0.0001
Differentiated (tub)	14 (23.3%)	58 (54.2%)	
Undifferentiated (por, sig, muc)	46 (76.7%)	49 (45.8%)	
Pathologic depth of invasion[a]			<0.0001
T1	8	28	
T2	1	12	
T3	7	38	
T4	44	29	
Pathologic nodal stage[a]			<0.0001
N0	14	51	
N1	7	21	
N2	17	25	
N3	22	10	
Stage[a]			0.0001
I	9	36	
II	5	28	
III	29	25	
IV	17	18	
Preoperative chemotherapy	3 (5.0%)	4 (3.7%)	0.6963
Postoperative chemotherapy	33 (55.0%)	46 (43.0%)	0.1359

Circ, circumferential lesion; muc, mucinous adenocarcinoma; por, poorly differentiated adenocarcinoma; sig, signet ring cell carcinoma; tub, tubular adenocarcinoma. Statistically significant difference is shown in the underlined entries.

[a]*Japanese Classification of Gastric Carcinoma*, 14th edition.[8]

receiver operating characteristic analysis. The independent prognostic factors were determined by multivariate analysis using a Cox proportional hazards model. All P values were based on a 2-sided test, and $P < 0.05$ was considered statistically significant. Statistical analyses were performed using JMP 11 (SAS Institute Inc, Cary, North Carolina).

Results

Clinicopathologic characteristics

The clinicopathologic characteristics of the Gre group (n = 60) and non-Gre group (n = 107) are summarized in Table 1. The Gre group included patients who were younger (61.0 versus 66.7 years, $P = 0.0026$) with larger tumors (93.4 versus 56.5 mm, $P < 0.0001$); larger numbers of Borrmann type 4 tumors (48.3% versus 14.0%, $P < 0.0001$), circumferential lesions (63.3% versus 0.0%, $P < 0.0001$), lesions of undifferentiated type (76.7% versus 45.8%, $P = 0.0001$), and lesions with deeper invasion to the wall ($P < 0.0001$); more LN metastases ($P < 0.0001$); and more advanced stage cases ($P = 0.0001$) than the non-Gre group.

Table 2 Clinicopathologic characteristics of the patients with (Sp) and without (non-Sp) splenectomy in the cases involving the greater curvature

Variable	Sp (n = 30)	Non-Sp (n = 30)	*P* value
Age (years, mean ± SD)	56.9 ± 14.8	65.1 ± 11.1	0.0188
Sex			0.7866
Male	19	20	
Female	11	10	
Size of tumor (mm, mean ± SD)	88.0 ± 48.9	98.7 ± 47.7	0.3928
Borrmann type			0.1965
Type 4	12 (40.0%)	17 (56.7%)	
Other	18 (60.0%)	13 (43.3%)	
Section			0.1080
Circ	16 (53.3%)	22 (73.3%)	
Histologic type			0.5416
Differentiated (tub)	6 (20.0%)	8 (26.7%)	
Undifferentiated (por, sig, muc)	24 (80.0%)	22 (73.3%)	
Pathologic depth of invasion[†]			0.1766
T1	4	4	
T2	0	1	
T3	6	1	
T4	20	24	
Pathologic nodal stage[†]			0.6116
N0	7	7	
N1	2	5	
N2	10	7	
N3	11	11	
Stage[a]			0.6364
I	4	5	
II	2	3	
III	17	12	
IV	7	10	
Preoperative chemotherapy	3 (10.0%)	0	0.0756
Postoperative chemotherapy	15 (50.0%)	18 (60.0%)	0.4363

Circ, circumferential lesion; muc, mucinous adenocarcinoma; por, poorly differentiated adenocarcinoma; sig, signet ring cell carcinoma; tub, tubular adenocarcinoma. Statistically significant difference is shown in the underlined entries.

[a]*Japanese Classification of Gastric Carcinoma*, 14th edition.[8]

The clinicopathologic characteristics of the Sp group and non-Sp group are summarized in Table 2. There was a significant difference in age between the Sp group and non-Sp group (56.9 versus 65.1 years, $P = 0.0188$).

Table 3 Surgical factors and short-term outcome of the patients with (Sp) and without (non-Sp) splenectomy in the cases involving the greater curvature

Variable	Sp (n = 30)	Non-Sp (n = 30)	*P* value
Operation time (min, mean ± SD)	472.9 ± 187.8	421.2 ± 172.1	0.3057
Blood loss (mL, mean ± SD)	1129.6 ± 595.7	946.1 ± 989.7	0.4264
Number of dissected lymph nodes (mean ± SD)	33.7 ± 16.6	31.8 ± 13.8	0.6433
Number of metastatic lymph nodes (mean ± SD)	9.0 ± 9.0	10.4 ± 11.2	0.5873
Other organ resection	15 (50%)	3 (10.0%)	0.0007
Esophagus/pancreas/colon/diaphragm/liver		9/6/2/2/1 (duplicate)	
Residual tumor[a]			0.2532
R0/	22	16	
R1	1	1	
R2	7	13	
Complication (Clavien-Dindo ≧ III)[b]	11 (36.7%)	5 (16.7%)	0.0798
Anastomotic leakage	5 (16.7%)	1 (3.3%)	0.0852
Pancreatic fistula	2 (6.7%)	0	0.1503
Abscess	7 (23.3%)	2 (6.7%)	0.0706
Pulmonary complications	7 (23.3%)	1 (3.3%)	0.0227
Ileus	1 (3.3%)	3 (10.0%)	0.3006
Hospital death	2 (6.7%)	0	0.1503

Statistically significant difference is shown in the underlined entries.

[a]*Japanese Classification of Gastric Carcinoma*, 14th edition.[8]

[b]Classification of surgical complications.[11]

Surgical outcomes

Surgical outcomes compared between the Sp group and non-Sp group are summarized in Table 3. There was a significant difference between the Sp group and non-Sp group in organs resected other than the spleen (50.0% versus 10.0%, $P = 0.0007$). There was no significant difference between the 2 groups in the number of LNs dissected (33.7 ± 16.6 versus 31.8 ± 13.8, $P = 0.6433$). Grade III or higher morbidity was 36.7% (11/30) in the Sp group and 16.7% (5/30) in the non-Sp group, but the difference was not significant ($P = 0.0798$). The rate of anastomotic leakage was 16.7% (5/30) in the Sp group and 3.3% (1/30) in the non-Sp group, also with no significant difference ($P = 0.0852$).

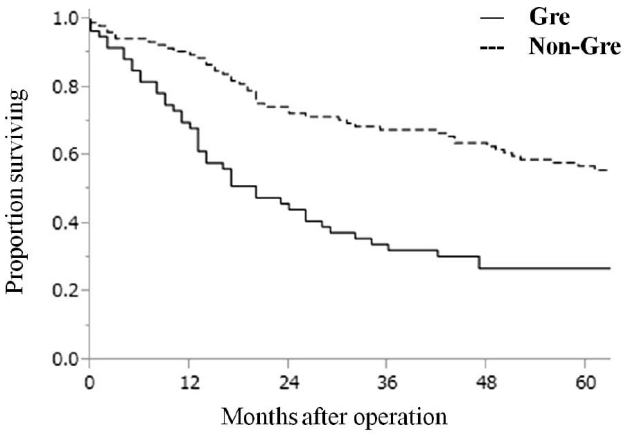

Fig. 1 Survival curve for patients with gastric carcinoma involving the greater curvature (Gre, continuous line) and not involving the greater curvature (non-Gre, broken line). Survival between the 2 groups was significantly different (5-year overall survival: Gre 27.0% versus non-Gre 57.0%, $P < 0.0001$).

Survival analyses

The rate of 5-year OS was significantly different between the Gre group (27.0%) and the non-Gre group (57.0%; $P < 0.0001$; Fig. 1). Within the Gre group, the rate of 5-year OS was not significantly different between the Sp group (30.0%) and the non-Sp group (24.3%; $P = 0.9140$; Fig. 2).

Univariate and multivariate analyses of prognostic factors

Factors associated with the OS were evaluated by univariate and multivariate analyses. A univariate analysis showed that age ≧70 years [hazard ratio (HR): 2.16; $P = 0.0184$], Borrmann type 4 (HR: 1.93; $P = 0.0340$), deeper invasion than the submucosal layer (≧T2, HR: 5.77; $P = 0.0006$), vessel invasion (positive, HR: 3.83; $P = 0.0048$), pathologic nodal stage (≧N2, HR: 2.99; $P = 0.0010$), metastases of LN 10 (positive, HR: 3.41; $P = 0.0047$), stage ≧III (HR: 4.44; $P = 0.0002$), organ resected other than the spleen (present, HR: 2.64; $P = 0.0036$), and residual tumor (R1/R2, HR: 4.00; $P < 0.0001$) were signifi-

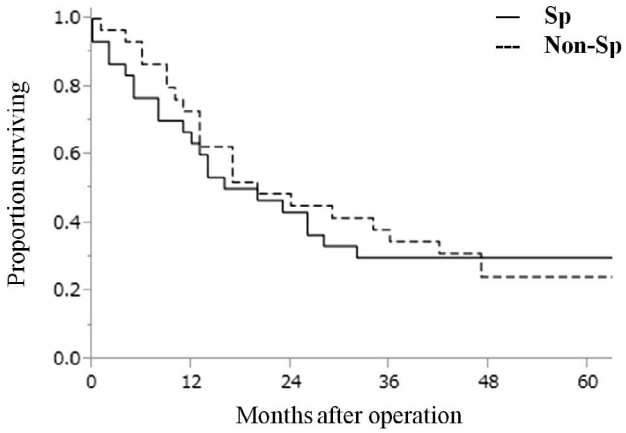

Fig. 2 Survival curve for patients with (Sp, continuous line) and without (non-Sp, broken line) splenectomy in the cases of gastric carcinoma involving the greater curvature. Survival between the 2 groups was not significantly different (5-year overall survival: Sp 30.0% versus non-Sp 24.3%, $P = 0.9140$).

cant variables influencing unfavorable OS (Table 4). Among them, metastases of LN 10 (positive, HR: 3.65; $P = 0.0066$), organ resected other than the spleen (present, HR: 2.72; $P = 0.0093$), and residual tumor (R1/R2, HR: 5.73; $P < 0.0001$) remained as independent risk factors for OS in a subsequent multivariate analysis (Table 5).

Table 4 Univariate analysis of adverse prognostic factors of the 60 patients with gastric carcinoma involving the greater curvature

Prognostic factors	HR	95% CI	*P* value
Age (≧70 years)	2.16	1.14–3.97	0.0184
Sex (male)	1.65	0.88–3.27	0.1188
Size of tumor (≧120 mm)	1.80	0.90–3.40	0.0943
Borrmann type (type 4)	1.93	1.05–3.60	0.0340
Histologic type [undifferentiated (por, sig, muc)]	1.54	0.78–3.43	0.2246
Pathologic depth of invasion [≧T2 (MP)][a]	5.77	1.95–25.17	0.0006
Vessel invasion (positive)	3.83	1.45–13.56	0.0048
Pathologic nodal stage (≧N2)[a]	2.99	1.54–6.31	0.0010
Metastasis of lymph node 10[a] (positive)	3.41	1.51–7.00	0.0047
Stage ≧III[a]	4.44	1.95–12.08	0.0002
Preoperative chemotherapy (absent)	1.18	0.36–7.25	0.8141
Postoperative chemotherapy (absent)	1.26	0.46–0.69	0.4628
Operation time (≧400 min)	1.40	0.73–2.65	0.3076
Blood loss (≧1300 mL)	1.73	0.82–3.41	0.1447
Other organ resection (present)	2.64	1.39–4.88	0.0036
Residual tumor (R1/R2)[a]	4.00	2.10–7.64	<0.0001
Complication (Clavien-Dindo ≧ III)[b]	1.56	0.79–2.91	0.1918

CI, confidence interval; HR, hazard ratio; muc, mucinous adenocarcinoma; por, poorly differentiated adenocarcinoma; sig, signet ring cell carcinoma. Statistically significant difference is shown in the underlined entries.

[a]*Japanese Classification of Gastric Carcinoma*, 14th edition.[8]

[b]Classification of surgical complications.[11]

Table 5 Multivariate analysis of adverse prognostic factors of the 60 patients with gastric carcinoma involving the greater curvature

Prognostic factors	HR	95% CI	*P* value
Age (≧70 years)	1.94	0.98–3.78	0.0554
Borrmann type (type 4)	1.05	0.49–2.20	0.8979
Pathologic depth of invasion [≧T2 (MP)][a]	1.46	0.14–13.50	0.7462
Vessel invasion (positive)	3.02	0.67–16.62	0.1548
Pathologic nodal stage (≧N2)[a]	1.10	0.36–2.82	0.8495
Metastasis of lymph node 10[a] (positive)	3.65	1.47–8.63	0.0066
Stage ≧III[a]	2.00	0.42–11.04	0.3806
Other organ resection (present)	2.72	1.29–5.77	0.0093
Residual tumor (R1/R2)[a]	5.73	2.65–12.73	<0.0001

CI, confidence interval; HR, hazard ratio. Statistically significant difference is shown in the underlined entries.

[a]*Japanese Classification of Gastric Carcinoma*, 14th edition.[8]

Survival analyses related to prognostic factors

The graphs in Fig. 3 show the 5-year OS for each of the factors of metastases of LN 10 LNs, organ resected other than the spleen and residual tumor (Fig. 3a–3c). There were significant differences between the 2 options for each factor. Subsequently, the significance of Sp was examined in each of the good prognosis groups (Fig. 3d–3f) and the poor prognosis groups (Fig. 3g–3i). In the R1/R2 patients (n = 22), the non-Sp group showed a significantly better prognosis than the Sp group (Fig. 3i; 5-year OS 7.1% versus 0.0%; $P = 0.0496$). In the patients with metastases of LN 10 (n = 9), the prognosis was very poor regardless of whether Sp was performed (Fig. 3g). In the good prognosis group, there was no significant differences in OS between the Sp group and the non-Sp group.

Discussion

The incidence of the splenic hilar LNs metastases, defined as station 10 according to the JGCA classification,[8] in patients with proximal gastric cancer is reported to be high. Approximate incidences of 9–12% have been reported for all gastric carcinomas[3–5] and of 10–26% for advanced proximal gastric carcinoma and carcinoma involving the greater curvature.[12,13] Therefore, the standard procedure for advanced proximal gastric carcinoma is D2 TG with Sp in Japan. However, Sp is not recommended in the National Comprehensive Can-

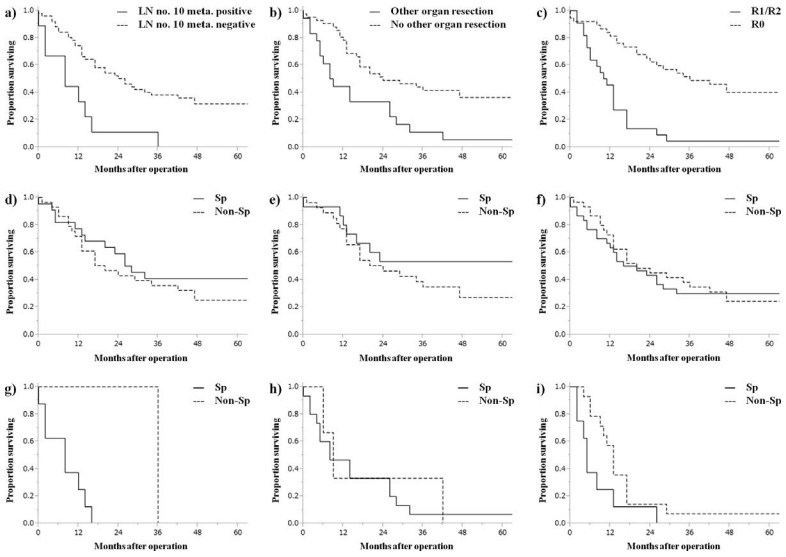

Fig. 3 Survival curves for patients with (continuous line) and without (broken line) adverse prognostic factors (a, lymph node no. 10 metastasis; b, other organ resection; c, residual tumor). Survival between the 2 groups in each graph was significantly different (5-year overall survival: LN 10 metastasis positive 0.0% versus negative 31.8%, $P = 0.0012$; other organ resection 5.6% versus no other organ resection 36.4%, $P = 0.0016$; R1/R2 4.6% versus R0 40.2%, $P < 0.0001$). Survival curves for patients with (Sp, continuous line) and without (non-Sp, broken line) splenectomy in the cases without adverse prognostic factors (d, LN 10 metastasis negative; e, no other organ resection; f, R0). Survival between the 2 groups in each graph was not significantly different (5-year overall survival: d, Sp 40.9% versus non-Sp 25.1%, $P = 0.4612$; e, Sp 53.3% versus non-Sp 27.1%, $P = 0.3060$; f, Sp 40.9% versus non-Sp 40.2%, $P = 0.6544$). Survival curves for patients with (Sp, continuous line) and without (non-Sp, broken line) splenectomy in the cases with adverse prognostic factors (g, lymph node 10 metastasis positive; h, other organ resection; i, R1/R2). Survival between the 2 groups in R1/R2 cases was significantly different (5-year overall survival: Sp 0.0% versus non-Sp 7.1%, $P = 0.0496$). Other survival between the 2 groups in each graph was not significantly different (5-year overall survival: g, Sp 0.0% versus non-Sp 0.0%, $P = 0.1701$; h, Sp 6.7% versus non-Sp 0.0%, $P = 0.5387$).

cer Network guideline[14] due to the high morbidity and the low effect of LN 10 dissection shown by some randomized controlled trials and meta-analyses.[4,5,15,16] One answer to this argument was found in the results of the JCOG 0110 trial.

In this trial, patients with tumor invasion to the greater curvature and with macroscopic LN metastases in the splenic hilum or along the splenic artery were excluded because many surgeons who participated in the trial judged that such tumors should be resected en bloc by Sp. Patients with Borrmann type 4 tumors were also excluded because their prognosis was poor regardless of any operation. In our study, the authors targeted patients who were excluded from the JCOG 0110 trial. Although there are few reports limited to Gre patients, 1 report shows exactly the same tendency as our study in the clinicopathologic characteristics of the Gre patients.[17] The tendency is toward larger tumors, more Borrmann type 4 tumors, more undifferentiated type tumors, deeper invasion to the wall, and more LN metastases, which result in more advanced stages. The fact that tumor exists in the greater curvature might mean that it is already associated with many disadvantageous factors at the time of diagnosis. In the surgical outcomes in the Gre group, grade III or higher postoperative complications occurred in 11 (36.7%) patients. There was no notable difference in the morbidity rate, but it was higher in the Gre group ($P = 0.0798$). The severe complications in the Gre group included anastomotic leakage (n = 5, 16.7%), peritoneal abscess (n = 7, 23.3%), pulmonary complications (n = 7, 23.3%), and pancreatic fistula (n = 2, 6.7%). Although postoperative bleeding and pancreatic fistula are reported as Sp-related major complications in many reports,[3,4,6,11] there were no patients with bleeding and few with pancreatic fistula only. There might be some patients who had anastomotic leakage due to pancreatic fistula. Regarding the prognostic factors, the finding that there was no utility of Sp in the 2 groups with and without metastases LN 10 sug-

gested that both preventive dissection and therapeutic dissection of LN 10 had no significance. Also, the improved long-term prognosis in the non-Sp group suggested that the spleen should be preserved systematically in patients in whom R0 resection cannot be performed. Watanabe *et al*[17] reported 421 patients who underwent TG with Sp. In their study, the significance of Sp for the Gre group was examined based on the LN dissection effect index (*i.e.*, a benefit index calculated using the incidence of each LN metastases and the OS of patients with metastases of each of the LN stations). The study concluded that the significance of Sp might be limited to patients under 65 years old, those without invasion to the serosal layer of the wall, and those with Borrmann type 4 tumors. In the Gre group, there are cases in which the tumor locates only in the greater curvature and the tumor locates extensively including the greater curvature. Because the limitation of our study is small sample size, it is difficult to examine the details, but the significance of Sp for the patients with main tumors located only in the greater curvature is also interesting in addition to the factors suggested by Watanabe *et al*.[17] Furthermore, there is room for discussion about combination preoperative or postoperative chemotherapy and Sp.

Various reasons have been proposed for why Sp has not contributed to an improved prognosis thus far. Aihara *et al*[18] reported that the number of LN 10 was small,[19,20] LN recurrence itself in the non-Sp group was rare (approximately 1%), and patients with LN 10 metastases are highly likely to develop peritoneal dissemination of multiple LN metastases irrespective of the operative method. In the subanalysis of the JCOG 0110 trial,[6] the prognosis was good in the patients without infection-related complications, especially pancreatic fistula, abdominal abscess, anastomotic leakage, and pneumonia, in both the Sp and Non-Sp groups. Therefore, the significance is particularly impaired in the Sp group with high morbidity.

In contrast, many reports on laparoscopic spleen-preserving splenic hilar lymphadenectomy (SPL) have been made in the last few years. Although SPL was reported from the 1980s to 1990s,[21,22] it has been recognized as insufficient compared with Sp. With the progress of laparoscopic surgery, the usefulness of SPL has begun to receive attention again. Hosogi *et al*[23] reviewed short-term outcomes of laparoscopic SPL and found operation times of 162–359 minutes, blood loss of 42–201 g, morbidity (Clavien-Dindo grade II or more) of 0–19%, and mortality of 0–0.6%. They commented that the indication of laparoscopic SPL should be considered prudently, but it can be an acceptable technique when performed by highly skilled surgeons. Although the significance of Sp may be limited, if the more secure SPL procedure that makes use of magnified visual effects becomes possible, the increased significance of SPL can be expected rather than that of Sp.

In recent years, the rapid spread of laparoscopic surgery, including robotic surgery and individualized and limited minimally invasive surgery such as sentinel LN navigation surgery, has been evaluated. Meanwhile, for advanced gastric cancer, multidisciplinary treatment combining chemotherapy including molecularly targeted drugs with surgical treatment is expected.[24–27] To develop the best treatment plan for advanced gastric cancer, surgical procedures or chemotherapy regimens should be selected by considering radical curability versus complications of surgery and response rate versus adverse events of chemotherapy. Regarding surgical procedures, the results of randomized phase III trials by JCOG have recently been clarified one after another. In the JCOG 0705 trial,[28] the usefulness of gastrectomy for unresectable advanced gastric cancer for the purpose of tumor reduction was denied, and in the JCOG 1001 trial,[29] the significance of omental bursectomy for resectable gastric cancer with invasion to the subserosal or serosal layer of the wall was also denied. The results of the JCOG 0110 trial are as described above.[6] The factors from Sp or SPL that can provide benefit should be discussed in the future, but improvements in chemotherapy are expected for factors that cannot improve the prognosis by surgery. It is important to perform safe surgery considering the potential severe complications, and a planned spleen-preserving surgery for upper gastric carcinoma with invasion to the greater curvature may be effective in improving long-term prognosis.

Conclusion

The significance of Sp for upper gastric carcinoma with invasion to the greater curvature was equivocal because the patients received no survival benefit by undergoing Sp. Because of the limitations of small sample size and the single institution nature of this study, further prospective multi-institutional joint research will be necessary to clarify whether Sp is worthwhile in the treatment

of upper gastric carcinoma with invasion to the greater curvature.

Acknowledgments

The protocol for this research project has been approved by the Human Ethics Review Board of the University of Miyazaki Hospital, and it conforms to the provisions of the Declaration of Helsinki with approval O-0154. Informed consent for data collection was obtained from the patients using the opt-out procedure. Patient data were retrieved from the departmental database. The authors declare no conflict of interest for this article. Takahiro Nishida contributed to the surgery, follow-up care, and writing of the manuscript. Atsushi Nanashima critically reviewed the manuscript.

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