Annals of Surgical Oncology, **8**(5):402–406
Published by Lippincott Williams & Wilkins

Impact of Splenectomy for Lymph Node Dissection on Long-Term Surgical Outcome in Gastric Cancer

Kang Young Lee, MD, Sung Hoon Noh, MD, Woo Jin Hyung, MD, Jun Ho Lee, MD, Ki Hyeok Lah, MD, Seung Ho Choi, MD, and Jin Sik Min, MD, PhD

Background: In the treatment of gastric cancer, splenectomy is performed for effective lymph node dissection around the splenic artery and splenic hilum. The purpose of this study was to clarify the long-term outcome of splenectomy in the treatment of gastric cancer.

Methods: The effect of splenectomy on recurrence and prognosis was examined in a retrospective analysis of 665 patients who had undergone curative total gastrectomy for gastric carcinoma from 1987 to 1996. The risk factors associated with recurrence and prognosis were investigated by univariate and multivariate analysis.

Results: The splenectomy group showed more advanced lesions and a higher recurrence rate than the spleen-preserved group. However, after adjusting for the TNM (tumor, node, metastasis) stage, there was no significant difference in recurrence rate and pattern between the two groups. Logistic regression analysis revealed that gross type, serosal invasion, and nodal metastasis were independent risk factors for recurrence while splenectomy was not. When comparing patients with the same TNM (tumor, node, metastasis) stages, no significant difference in the 5-year survival rates was apparent. Multivariate analysis demonstrated that age, serosal invasion, and nodal metastasis were independent prognostic factors whereas splenectomy was not.

Conclusions: These data suggest that splenectomy for lymph node dissection in gastric cancer is not effective regarding long-term patient prognosis.

Key Words: Splenectomy—Lymph node dissection—Long-term outcome—Gastric cancer.

Extended lymph node dissection is regarded as essential for the treatment of gastric cancer.[1–3] It not only makes the surgical therapy more radical but also provides adequate lymph node staging. In gastric cancer surgery, splenectomy is performed for the purpose of effective lymph node dissection around the splenic artery and splenic hilum; however, the effect of splenectomy on the prognosis has been controversial. The incidence of metastasis to the splenic hilar lymph nodes has been reported to be around 10% in proximal gastric cancer.[4,5] Based on the anatomy of the lymphatics around the stomach, several reports have insisted on the necessity of splenectomy for the treatment of proximal gastric cancer.[6,7] However, some investigators have reported that splenectomy did not increase the survival rate but instead increased the incidence of postoperative complications.[8–10] The aim of this study is to clarify the long-term outcome of splenectomy in gastric cancer surgery in terms of postoperative recurrence and prognosis.

PATIENTS AND METHODS

From January 1987 through December 1996, 3662 patients with gastric adenocarcinoma underwent gastric resection in our department. Among them, 1034 patients underwent total gastrectomy. Of those patients treated with total gastrectomy, excluded from this study were: 185 patients who underwent noncurative resection, 136 patients who underwent combined resection of organs other than the spleen, 41 patients who had cancer in the distal one third of the stomach, and 7 patients who had direct invasion to the spleen. A total of 665 patients who

Received November 10, 2000; accepted December 5, 2000.

From the Department of Surgery (KYL, SHN WJH, JHL, KHL, SHC, JSM) and Cancer Metastasis Research Center (SHN, WJH, JHL), Yonsei University College of Medicine, Seoul, Korea.

Address correspondence and reprint requests to: Sung Hoon Noh, MD, Department of Surgery, Yonsei University College of Medicine, CPO Box 8044, Seoul, Korea; Fax: 82-2-313-8289; E-mail: sunghoonn@yumc.yonsei.ac.kr.

had cancers in the upper, the midbody, or the whole of the stomach were enrolled in the study. Of those 665 patients, 173 patients (26.0%) underwent total gastrectomy without splenectomy (spleen-preserved group) and 492 patients (74.0%) underwent splenectomy (splenectomy group) for the purpose of lymph node dissection. D2 or more extended lymph node dissections were usually performed; lymph nodes along the upper border of the pancreas to the posterior gastric artery were dissected in the spleen-preserved group. The standard reconstruction was Roux-en-Y esophagojejunostomy. The number of retrieved lymph nodes exceeded 15 in all patients. Tumors were staged according to the International Union Against Cancer (UICC) staging system.[11]

The patients were followed up closely until December 31, 1999; the median length of follow-up was 75 months (range 1–153 months). At the time of the last follow-up, 109 patients (63.0%) had survived in the spleen-preserved group and 242 (49.2%) had survived in the splenectomy group. Determination of recurrence was made by clinical and radiological examination or by operation. The main patterns of recurrence were recorded as the first site of detectable failure at the time of diagnosis; patients were divided into three groups: locoregional, peritoneal, and hematogenous recurrence. Among the 237 patients who had postoperative recurrence, exact sites of failure were unknown for 25 patients due to incomplete data. The clinicopathological features, postoperative recurrence, and 5-year survival rates were compared between the spleen-preserved and splenectomy groups.

TABLE 1. *Clinicopathological characteristics of the patients who underwent total gastrectomy*

Characteristic	Splenectomy (N = 492)	Spleen-preserved (N = 173)	*P* value
Sex			.851
Male	326 (66.3)	116 (67.4)	
Female	166 (33.7)	56 (32.6)	
Age (mean, years)	52.0 ± 11.7	53.7 ± 11.4	.091
Tumor size (cm)	5.9 ± 3.5	4.8 ± 3.0	<.001
Tumor location			<.001
Upper third	215 (43.7)	50 (28.9)	
Middle third	236 (48.0)	115 (66.5)	
Whole	41 (8.3)	8 (4.6)	
Gross type			<.001
Superficial	61 (12.4)	60 (34.9)	
Localized	103 (20.9)	30 (17.4)	
Infiltrative or diffuse	328 (66.7)	82 (47.7)	
Histology			.048
Differentiated	128 (26.1)	58 (34.1)	
Undifferentiated	362 (73.9)	112 (65.9)	
Depth of invasion			<.001
T1	62 (12.6)	60 (34.7)	
T2	79 (16.1)	33 (19.1)	
T3	336 (68.3)	63 (36.4)	
T4	15 (3.0)	17 (9.8)	
Lymph node metastasis			<.001
N0	167 (33.9)	91 (52.6)	
N1	149 (30.3)	37 (21.4)	
N2	81 (16.5)	27 (15.6)	
N3	94 (19.3)	18 (10.4)	
Retrieved nodes (mean)	44.3 ± 16.8	41.5 ± 16.5	.065
Metastatic LN ratio	0.18 ± 0.24	0.12 ± 0.21	.007
Recurrence	190 (38.6)	39 (22.5)	<.001
Operative mortality	3 (0.6)	0	

Values in parentheses are percentages.

Statistical Analysis

All statistical analyses were conducted using the statistical program SPSS 9.0 for Windows (SPSS, Chicago, Illinois). The clinicopathological variables were analyzed using the two-tailed χ^2 test and the Student's *t*-test. The risk factors influencing recurrence were determined using logistic regression analysis. Cumulative survival rates were calculated by the Kaplan-Meier method. The significance of the differences in survival was determined by the log-rank test. Multivariate analysis for prognosis of patients was conducted using Cox's proportional hazard model. A *P*-value of $<.05$ was considered statistically significant.

RESULTS

Comparison of the Clinicopathological Features

Clinicopathological data on the 173 (26.0%) spleen-preserved patients and the 492 (74.0%) splenectomized patients are shown in Table 1. There were significant differences between the two groups regarding tumor size, tumor location, gross appearance, histological type, depth of invasion, and status of lymph node metastasis. Patients who underwent splenectomy showed more advanced lesions.

The mean number of retrieved lymph nodes was 41.5 in the spleen-preserved group and 44.3 in the splenectomy group ($P = .065$). The metastatic lymph node ratio (ratio between positive and retrieved lymph nodes) was 0.12 in the spleen-preserved group and 0.18 in the splenectomy group ($P = .007$). There was no operative mortality in the spleen-preserved group; however, there were three cases (0.6%) in the splenectomy group.

Comparison of the Incidence, Pattern, and Risk Factors of Recurrence

Postoperative recurrences were diagnosed in 22.5% of the spleen-preserved group and 38.6% of the splenectomy group ($P < .001$). When a comparison of the recurrence rates was made, after adjustment for TNM (tumor, node, metastasis) stage, no significant differ-

ences were found in the recurrence rates between the two groups (Table 2). Among the patients diagnosed as having recurrences, loco-regional recurrences occupied 20.6% of the recurrences in the spleen-preserved group and 18.2% of those in the splenectomy group ($P > .05$). The incidence of distant metastasis was similar in the two groups. There was no significant difference in recurrence pattern between the two groups (Table 4).

Logistic regression analysis revealed that gross type, serosal invasion, and nodal metastasis were independently correlated with postoperative recurrence. Splenectomy was not an independent risk factor for postoperative recurrence (Table 3).

TABLE 3. *Logistic regression analysis of independent risk factors for recurrence*

Variable	RR	95% CI	*P* value*
Age (<55 vs. ≥55)	1.08	0.74–1.59	.677
Sex (male vs. female)	1.13	0.76–1.67	.553
Histologic type (differentiated vs. undifferentiated)	1.33	0.84–2.12	.221
Location (mid-body vs. upper body or whole stomach)	1.34	0.92–1.94	.128
Gross type (superficial or localized vs. infiltrative or diffuse)	2.18	1.40–3.38	.001
Size (<5 cm vs. ≥5 cm)	1.06	0.70–1.61	.776
Serosal invasion (absence vs. presence)	3.96	2.29–6.83	< .0001
Nodal metastasis (absence vs. presence)	3.06	1.94–4.81	< .0001
Splenectomy (no vs. yes)	1.45	0.91–2.31	.118

RR, relative risk; CI, confidence interval.
* By logistic regression analysis.

Comparison of the Prognosis

The 5-year survival rate was 52.9% for patients in the splenectomy group and 64.8% for patients in the spleen-preserved group ($P < .001$). There were no significant differences between the survival rates at each stage for the patients who underwent total gastrectomy with or without splenectomy (Table 5).

Univariate analyses revealed that age, tumor size, location, gross type, histological type, serosal invasion, nodal metastasis, and splenectomy significantly affected survival rates. Multivariate analysis showed that age, serosal invasion, and nodal metastasis were independent prognostic factors while splenectomy was not (Table 6).

DISCUSSION

In treatment of gastric cancer, distal pancreatectomy was often performed along with total gastrectomy to facilitate dissection of the lymph nodes along the splenic artery and splenic hilum. Currently, distal pancreatectomy is not recommended for gastric cancer patients without direct invasion of the pancreas because this procedure does not increase the survival rate, but it does increase the early and late postoperative complications.[12–14]

Many surgeons tend to perform the pancreas-preserving total gastrectomy for the treatment of proximal gastric cancer because of the efficacy of radical resection, the low incidence of postoperative complications, and the high survival rates. The cancerous involvement of the lymph nodes along the splenic artery or splenic hilum has been reported to be about 10% each in proximal gastric cancer.[4,5] Lymph node metastasis in gastric cancer has a strong correlation with the depth of tumor invasion. In early gastric cancer, splenectomy should not be performed because lymph node metastasis is not found in the splenic hilum; the 5-year survival rate of patients with early gastric cancer is significantly higher in the spleen-preserved group.[15] However, in advanced gastric cancer, the effect of splenectomy on the prognosis is controversial. In the present study, no survival benefit from splenectomy at any stage was found, and splenectomy was not an independent prognostic factor in patients who had undergone total gastrectomy.

TABLE 2. *Recurrence rate of the splenectomy and the spleen-preserved groups*

Stage	Splenectomy (N = 492)	Spleen-preserved (N = 173)	*P* value
I	4.3 (4/94)	0.0 (0/77)	.128
II	33.0 (36/109)	25.0 (7/28)	.497
III	48.9 (92/188)	33.3 (13/39)	.081
IV	57.4 (58/101)	65.5 (19/29)	.527

Values in parentheses are numbers of recurrences/numbers of total patients.

The overall postoperative recurrence rate was significantly higher in the splenectomy group. However, when a comparison—based on pathological stage—was made between the recurrence rates of the two groups of patients, no significant difference was found. In a patient care evaluation study of stomach cancer initiated by the American College of Surgeons, using data collected from more than 700 tumor registries, the pattern of recurrence was slightly different between the two groups. There was a larger proportion of patients with distant metastases in the group of patients who had undergone splenectomy compared with the patients who had not, the results were 29% and 15.5%, respectively.[16] In this study, recurrence patterns were similar for the groups with and without splenectomy; peritoneal recurrence was most common, followed by hematogenous recurrence. This result was also similar to the recurrence pattern after curative subtotal gastrectomy.[17]

TABLE 4. *Patterns of recurrence of the splenectomy and the spleen-preserved groups*

Pattern	Splenectomy (N = 190)	Spleen-preserved (N = 39)
Locoregional	31 (18.2)	7 (20.6)
Peritoneal recurrence	65 (38.2)	13 (38.2)
Hematogenous	41 (24.1)	6 (17.6)
Combined recurrence	29 (17.1)	6 (17.6)
Extra-abdominal nodes*	4 (2.4)	2 (5.9)
Site unknown	20	5

Values in parentheses are percentages.
* Supraclavicular, inguinal, or axillary lymph nodes.

TABLE 5. *Comparison of 5-year survival rates according to stage*

Stage	Splenectomy	Spleen-preserved	*P* value*
I	89.8	94.6	.471
II	67.9	75.3	.227
III	43.4	46.5	.786
IV	17.4	5.2	.097

* By log-rank test.

TABLE 6. *Multivariate analysis of risk factors for prognosis*

Variable	RR	95% CI	*P* value*
Age (<55 vs. ≥55)	1.43	1.12–1.80	.003
Sex (male vs. female)	1.10	0.86–1.40	.461
Histologic type (differentiated vs. undifferentiated)	1.32	0.98–1.78	.221
Location (mid-body vs. upper body or whole stomach)	1.02	0.80–1.28	.896
Gross type (superficial or localized vs. infiltrative or diffuse)	1.34	1.00–1.79	.051
Size (<5 cm vs. ≥5 cm)	1.25	0.95–1.63	.108
Serosal invasion (absence vs. presence)	2.64	1.82–3.85	< .0001
Nodal metastasis (absence vs. presence)	3.05	2.02–4.23	< .0001
Splenectomy (no vs. yes)	1.07	0.80–1.44	.642

RR, relative risk; CI, confidence interval.
* By Cox's proportional hazard model.

There was no significant difference in the number of retrieved lymph nodes between the two groups. The routine application of D2 or more lymph node dissection has been our institutional policy. In cases of spleen-preserving total gastrectomy, lymph node dissection along the upper border of the pancreas is extended to the posterior gastric artery or approximately 5 cm from the origin of the splenic artery, and the surgeon routinely attempted to remove the lymph nodes at splenic hilum. Statistical evaluation showed no difference in the number of retrieved lymph nodes, because lymph nodes along the splenic artery and the splenic hilum were removed in the spleen-preserved group.

For an accurate investigation regarding the prognostic impact of splenectomy, several important aspects should be considered. In cases of noncurative surgery, recurrence cannot be defined because of the presence of residual tumor and the difficulty in evaluating the effect of splenectomy on the prognosis. Multi-institutional study also has problems such as a lack of standardization in surgical technique and difficulties in surgical quality control.[18] In this study, only patients who had undergone curative total gastrectomy without definite evidence of involvement of splenic hilar lymph nodes were evaluated. In addition, the surgical technique was standardized because all the operations were performed in a single institute, over a relatively short period of time. However, as shown in the comparison of clinicopathological features, the spleen-preserved group exhibited less advanced lesions. There may have been some selection bias on the part of the surgeons when they performed the spleen-preserving total gastrectomy. Therefore, a large-scale, randomized prospective study, using a standardized surgical technique, should be performed for the precise determination of the impact of splenectomy on long-term surgical outcomes.

In conclusion, splenectomy in gastric cancer surgery has no influence on the long-term surgical outcome of patients in terms of postoperative recurrence and prognosis for gastric cancer. Therefore, splenectomy for the purpose of lymph node dissection should not be mandatory, and surgeons should consider spleen-preservation in gastric cancer patients who have no definite splenic hilar lymph node enlargement or any direct invasion to the spleen.

REFERENCES

1. Maruyama K, Okabayashi K, Kinoshita T. Progress in gastric cancer surgery in Japan and its limits of radicality. *World J Surg* 1987;11:418–25.
2. Kim JP, Kwon OJ, Oh ST, Yang HK. Results of surgery on 6539 gastric cancer patients and immunochemosurgery as the best treatment of advanced gastric cancer. *Ann Surg* 1992;216:269–79.
3. Roder JD, Bottcher K, Siewert JR, Busch R, Hermanek P, Meyer HJ. Prognostic factors in gastric carcinoma. Results of the German Gastric Carcinoma Study 1992. *Cancer* 1993:72:2089–97.
4. Maehara Y, Moriguchi S, Yoshida M, Takahashi I, Korenaga D, Sugimachi K. Splenectomy does not correlate with length of survival in patients undergoing curative total gastrectomy for gastric carcinoma. *Cancer* 1991;67:3006–9.
5. Maruyama K, Gunven P, Okabayashi K, Sasako M, Kinoshita T. Lymph node metastases of gastric cancer. General pattern in 1931 patients. *Ann Surg* 1989;210:596–602.
6. Toge T, Hamamoto S, Itagaki E, Nakane H, Yajima K, Hattori T. Analysis of suppressor cell activities in spleen cells from gastric cancer patients and the effect of splenectomy on prognosis of gastric cancer. *J Jpn Surg Soc* 1983;84:961–4.
7. Roukos DH. Current advances and changes in treatment strategy

may improve survival and quality of life in patients with potentially curable gastric cancer. *Ann Surg Oncol* 1999;6:46–56.
8. Brady MS, Rogatko A, Dent LL, Shiu MH. Effect of splenectomy on morbidity and survival following curative gastrectomy for carcinoma. *Arch Surg* 1991;126:359–64.
9. Otsuji E, Yamaguchi T, Sawai K, Ohara M, Takahashi T. End results of simultaneous splenectomy in patients undergoing total gastrectomy for gastric carcinoma. *Surgery* 1996;120:40–4.
10. Viste A, Haugstvedt T, Eide GE, Sodreide O. Norwegian stomach cancer trial members. Postoperative complications and mortality after surgery for gastric cancer. *Ann Surg* 1987;207:7–13.
11. Sobin LH, Wittekind CH. *International Union Against Cancer (UICC). TNM Classification of Malignant Tumours*. 5th ed. New York: Wiley 1997;59–62.
12. Bonenkamp JJ, Hermans J, Sasako M, van de Velde CJH. Extended lymph node dissection for gastric cancer. *N Engl J Med* 1999;340:908–14.
13. Cuschieri A, Fayers P, Fielding J, et al. Postoperative morbidity and mortality after D1 and D2 resections for gastric cancer: preliminary results of the MRC randomized controlled surgical trial. *Lancet* 1996;347:995–9.
14. Kitamura K, Nishida S, Ichikawa D, et al. No survival benefit from combined pancreaticosplenectomy and total gastrectomy for gastric cancer. *Br J Surg* 1999;86:119–22.
15. Yoshino K, Yamada Y, Asanuma F, Aizawa K. Splenectomy in cancer gastrectomy: Recommendation of spleen-preserving for early stages. *Int Surg* 1997;82:150–4.
16. Wanebo HJ, Kennedy BJ, Winchester DP, Stewart AK, Fremgen AM. Role of splenectomy in gastric cancer surgery: Adverse effect of elective splenectomy on long-term survival. *J Am Coll Surg* 1997;185:177–84.
17. Yoo CH, Noh SH, Shin DW, Choi SH, Min JS. Recurrence following curative resection for gastric carcinoma. *Br J Surg* 2000;87:236–42.
18. Brennan MF. Lymph node dissection for gastric cancer. *N Engl J Med* 1999;340:956–7.