

# Changes in Treatment Outcomes of Gastric Cancer Surgery Over 45 Years at A Single Institution

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**Purpose:** Although many studies have demonstrated improvements in short-and long-term outcomes of gastric cancer surgery, changes in long-term survival over time are not well-established. This study was conducted to evaluate changes in host, tumor, and treatment factors in patients treated at a single institution over a period of 45-yr. **Patients and Methods:** We retrospectively evaluated 9282 patients with gastric cancer from 1955 to 1999, and divided the 45-yr into 4 time frames based on published articles: 1955 to 1962 (n = 228), 1963 to 1972 (n = 891), 1973 to 1988 (n = 2789), and 1989 to 1999 (n = 5374). **Results:** Remarkable changes were noted in host, tumor, treatment factors, and prognosis. Among host factors, patients of more advanced age were identified in the 4th period and mean age shifted from 49 to 55 yrs. Among tumor factors, early gastric cancers and upper body tumors increased up to 32% and from 7% to 13%, respectively. An increase in the annual number of patients (from 29 to 649), gastrectomies (from 14 to 600), rate of resection (from 50% to 90%), rate of curative resection (up to 92%), and proportion of total gastrectomy (from 8% to 29%) was noted. Operative mortality was reduced from 6.1% to 0.7%. The overall 5-yr survival rate significantly increased from 22% to 65%. **Conclusion:** Treatment results of gastric cancer surgery have improved remarkably over the 45-year period. Increase of early stage gastric cancer with early diagnosis considerably influenced the improved survival of patients with gastric cancer.

**Key Words:** Gastric cancer, surgery, treatment results

## INTRODUCTION

Although the results of gastric cancer treatment

have considerably improved with improved prognosis due to early diagnosis, radical operation, and the development of adjuvant therapy, patients with gastric cancer still have poor prognosis.<sup>1,2</sup> During the past 5 decades, progress in oncology, treatment modality and strategy for gastric cancer patients has been noted. Recently, treatment methods, especially surgical approaches, have been tailored to patient and tumor characteristics.<sup>3</sup>

At our institute, standardization of surgical treatment for gastric cancer, i.e. en bloc extended regional lymph node dissection, was first achieved in 1983. Since then, we adopted the surgical treatment policy of D2 resection for early gastric cancer (EGC) and D2 or more extended resection for advanced gastric cancer (AGC).<sup>4</sup> For patients with advanced gastric cancers, adjuvant chemotherapy has usually been used, and neoadjuvant chemotherapy is used on some patients with locally advanced cancers. Nowadays, various surgical approaches are being practiced, including conventional surgery, function preserving surgery, and minimally invasive surgery such as laparoscopic surgery and less extensive lymph node dissection.

This study was conducted to evaluate changes of host, tumor, and treatment factors in patients treated at a single institution over a 45-yr period and their effect on prognosis in a high prevalence area.

## PATIENTS AND METHODS

We evaluated the clinicopathologic features and

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prognosis of 9282 patients with gastric cancer who received surgical intervention from 1955 to 1999. Because medical records from 1955 to 1985 were not available, the clinicopathologic features of patients with gastric cancer treated between 1955 and 1986 were obtained from the earlier publications of the institution. Two articles published in 1964 evaluated 228 patients who underwent surgical intervention out of 401 total patients admitted for gastric cancer.<sup>5,6</sup> Two articles published in 1975 and in 1991 included 891 and 2789 patients, respectively.<sup>4,7,8</sup> Medical records of 5374 patients with gastric cancer treated from 1987 to 1999 were reviewed. Fortunately, there was no overlap in study period among the previous papers allowing us to divide the 45-yr interval into 4 periods: 1955 to 1962 as the 1st period (n = 228); 1963 to 1972 as the 2nd period (n = 891); 1973 to 1988 as the 3rd period (n = 2789); and 1989 to 1999 as the 4th period (n = 5374). In the 3rd period, tumor node metastasis (TNM) stages were classified according to the American Joint Committee for Cancer Staging and End Result Reporting which was published in 1977.<sup>9</sup> For survival comparison at each TNM stage, TNM staging of the 4th period was also based on the same TNM staging system published in 1977.

### Statistical analysis

All statistical analyses were performed using Statistical Package for Social Science (SPSS) version 11.0 for Windows (SPSS, Inc, Chicago, IL, USA). Inter-group comparisons of clinicopathological variables were made using the Student's t-test for continuous variables and 2-tailed  $\chi^2$  test for discrete variables.

Follow up of patients in the 4th period was completed until death or the incised date of June 30, 2004. At the time of the last follow up, 214

patients (4.4%) had been lost. The median follow-up interval for patients alive at the incised date was 70 mo (range, 55 - 189 mo). Postoperative mortalities, defined as mortalities occurring within 30 days after operation, occurred in 34 cases (0.7%).

Lost and operative mortality cases were treated as censored data for the analysis of survival rates. Kaplan-Meier method was used for calculating survival rate and difference between the curves was assessed using log-rank test.<sup>10</sup> The accepted level of significance was  $p < 0.05$ .

## RESULTS

### Host & tumor factors

Changes of host and tumor factors are shown in Tables 1 and 2. Although exact statistical analysis was impossible due to lack of exact demographic data in the 1st and 2nd period, among host factors, patients of more advanced age were identified in the 4th period and the mean age was shifted from 49 in the 1st period to 55 in the 4th period. There was also a change in male to female ratio from 3 : 1 to 2 : 1. Among tumor factors, upper body tumors increased from 7% to 13%. Tumors with differentiated histology increased from 36.3% to 39.8% although the histologic types were available for the last 2 periods only. Serosa negative or node negative cancers were found more frequently in the later periods and early gastric cancers increased up to 32.6%, thus tumors treated in the later periods were found at earlier stages.

### Treatment factors & prognosis

Fig. 1 shows annual number of gastrectomies

**Table 1.** Comparisons of Host Factors

	'55 - '62	'63 - '72	'73 - '88	'89 - '99	p value
Age (Mean, yrs)	49	50	54	55	NA
Gender ratio (Male : Female)	3.0 : 1 (NA)	1.9 : 1 (648 : 243)	1.5 : 1 (1690 : 1099)	2.1 : 1 (3621 : 1753)	< 0.001

NA, not available.

**Table 2.** Comparisons of Tumor Factors

	'55 - '62	'63 - '72	'73 - '88	'89 - '99	<i>p</i> value
Analyzed patients (n)	228	568	2,789	4,819	
Location					< 0.001
Lower 1/3	157 (69.5%)	466 (82.0%)	1,732 (62.1%)	2,249 (46.7%)	
Middle 1/3	50 (22.1%)	61 (10.7%)	644 (23.1%)	1,888 (39.2%)	
Upper 1/3	15 (6.6%)	30 (5.3%)	252 (9.0%)	601 (12.5%)	
Whole	4 (1.8%)	11 (1.9%)	161 (5.8%)	81 (1.7%)	
Unknown	2	-	-	-	
Histology					< 0.001
Differentiated	-	-	901 (36.3%)	1,919 (39.8%)	
Undifferentiated	-	-	1,579 (63.7%)	2,900 (60.2%)	
Unknown	-	-	109	-	
Depth of invasion					< 0.001
Serosa (-)	25 (21.9%)	94 (28.3%)	779 (27.7%)	2,519 (59.1%)	
Serosa (+)	89 (78.1%)	238 (71.7%)	1,884 (72.3%)	2,300 (40.9%)	
Unknown	114	232	126	-	
Nodal involvement					< 0.001
Negative	32 (27.9%)	189 (32.2%)	1,260 (47.3%)	2,293 (46.0%)	
Positive	82 (72.1%)	379 (67.8%)	1,403 (52.7%)	2,526 (54.0%)	
Unknown	114	126	-	-	
Stage					
I	-	-	392 (14.6%)	1,385 (28.7%)	
II	-	-	677 (25.2%)	863 (17.9%)	
III	-	-	1,321 (49.2%)	2,182 (45.3%)	
IV	-	-	293 (10.9%)	389 (8.1%)	
Unknown	-	-	106	-	

performed for gastric cancer, which increased gradually over the past 45-yr. After 1990, more than 300 cases of gastrectomies were performed and more than 500 gastrectomies have been performed since 1997. Along with the increase in the number of gastrectomies, overall resection and curative resection rate were markedly increased during the last 2 periods. Most recently, the overall resection rate was 89.7% and the curative resection rate was 91.9%. The mortality rate of resected cases in the 1st period was 6.1% whereas

it was 0.7% in the 4th period. The follow-up rate for each period was also increased, reaching 95.6% in the 4th period. Although statistical comparison among the periods for survival rates was limited due to a lack of available data in the 3 periods, 5-yr survival rates increased gradually from 22.2% to 64.5%. Survival after curative resection in the 4th period was 70.2% whereas those in the 3rd period were 12.4% for 1973 to 1982 and 30.4% for 1983 to 1988. Relatively accurate stage-by-stage comparison could be performed between the 3rd

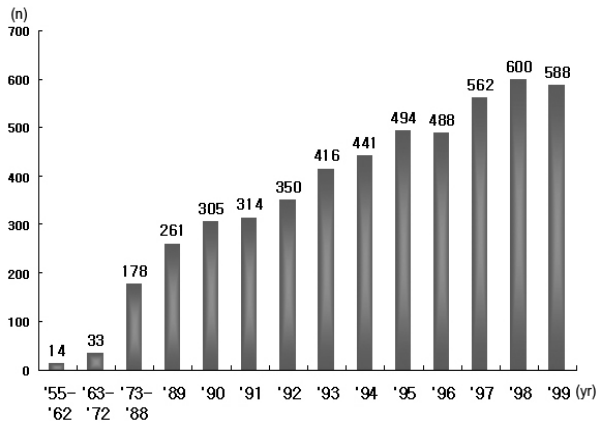


Fig. 1 Annual number of gastrectomies for gastric cancer from 1955 to 1999.

and 4th periods. Survival differences were noted in stages I, II, III, and IV between the 2 periods (Table 4).

## DISCUSSION

The main findings of the present study are an increased proportion of patients with early gastric cancer, increased incidence of total gastrectomy along with an increase of proximal lesions, and decreased mortality related to gastrectomy. In conjunction with these changes, the prognosis of patients with gastric cancer has improved.

Table 3. Comparisons of Treatment Factors

	'55 - '62	'63 - '72	'73 - '88	'89 - '99	<i>p</i> value
Operated patients (n)	228	891	2,789	5,374	-
Resected patients (n)	114 (50.0%)	568 (55.9%)	2,085 (74.8%)	4,819 (89.7%)	< 0.001
Curative resection	-	-	1,769 (84.8%)	4,430 (91.9%)	
Noncurative resection	-	-	316 (15.2%)	389 (8.1%)	
Type of resection					
Subtotal	103 (90.4%)	534 (94.0%)	1,608 (77.1%)	3,416 (70.9%)	
Total	11 (9.6%)	34 (6.0%)	477 (22.9%)	1,403 (29.1%)	
Bypass surgery	85 (37.3%)	206 (32.0%)	464 (16.6%)	289 (5.4%)	-
Exploration only	29 (12.7%)	117 (13.1%)	240 (8.6%)	266 (4.9%)	-
Mortality after gastrectomy	7 (6.1%)	-	-	34 (0.7%)	< 0.001

Table 4. Comparisons of Prognosis and Follow-Up Rates

	'55 - '62	'63 - '72	'73 - '88	'89 - '99	<i>p</i> value
Analyzed patients (n)	228	891	2,789	5,374	-
Follow-up rate (%)	56.1	63.4	76.6	95.6	< 0.001
Overall 5-yr survival (%)	22.2	23.5	22.6	64.5	-
5-yr survival after curative resection (%)			31.1 (73-'82) 55.4 ('83-'88)	70.2	-
5-yr survival by stage (%)					-
I	-	-	91.6	94.2	
II	-	-	71.2	73.4	
III	-	-	19.8	44.7	
IV	-	-	0.7	11.1	

In the present study, major changes were observed with respect to tumor factors. The changes of tumor factors during the last 45 yrs originated mainly from early detection. In the later years, the earlier stage gastric cancers were increased. As the incidence of early gastric cancer increased, node negative cancers were also increased. These changes appear to have contributed to the recent improved prognosis.

Depth of tumor invasion, lymph node involvement and distant metastasis are important prognostic factors according to the UICC/AJCC staging system of gastric cancer.<sup>11</sup> Surgery is the only treatment modality offering hope for cure, nevertheless, most patients die from locoregional recurrence or distant metastasis even after curative surgery for advanced stage cancers.<sup>12</sup> Although the incidence of early gastric cancer is increasing, most of the patients are still diagnosed at an advanced stage. Therefore, every attempt should be made to increase early diagnosis.

In this study, we found that the proportion of patients with early gastric cancer is increased up to 32.7% in the 4th period. Currently, gastric cancer in Korea is of the most prevalent cancers, making endoscopic or radiologic examinations more common. Awareness among Koreans has also increased, similar to colorectal or prostate cancer in Western countries.<sup>13,14</sup>

Along with the occurrence of more proximal tumor lesions, the proportion of total gastrectomies has increased. It has been reported that prevalence of morbidity and mortality is higher in total gastrectomy compared to subtotal gastrectomy.<sup>15</sup> The prognosis of the proximal cancer has been reported to be poor for various reasons.<sup>16-18</sup> Increasing numbers of total gastrectomy and the complicated biologic features of proximal gastric cancers, especially esophagogastric junction cancers, require more sophisticated treatment strategies. The suggestions of Siewert et al., to classify the proximal gastric cancers into 3 types according to location and provide different operative options based on their classification may be a reliable treatment strategy for proximal cancers.<sup>19,20</sup>

Another important change observed was decreased prevalence of operative mortality. Although the surgical extent of recent years was more extensive than before, shown by increased

proportion of total gastrectomies, postoperative mortality in the 4th period was decreased to 0.7%. This reflects the progress made in surgery and especially in anesthesia, resulting in improvement of peri- and post-operative management. In addition to technical advances, specialization in gastric cancer treatment at our hospital might have also influenced the lower mortality rate, as noted in other major surgery areas, such as abdominal aortic aneurysm, breast cancer, and colorectal cancer.<sup>21-25</sup>

The present study confirmed previous reports that the prognoses of gastric cancer are improving.<sup>26-30</sup> Overall survival rate of patients has gradually been improved from 22.5% to 64.5%. Survival after curative resection in the 4th period was 70.2%, however, in the 3rd period, it was 12.4% from 1973 to 1982 and 30.4% from 1983 to 1988. The survival improvement resulted mainly from a host factor, i.e. increases of early stage patients, and was reflected in the increase of curative resection rates. Advances in treatment factors also contributed to improved survival. Comparison of survival rates among stages showed higher survival in the 4th period than in the 3rd period. There exists the possibility of the stage migration effect after adopting the systematic lymph node dissection. However, the survival difference in stages II and III might be due to recent advances in surgical treatment, including systematic lymph node dissection and postoperative adjuvant chemotherapy. In the present study, the survival benefit of node negative patients (stages I & II) was evident, which could exclude the stage migration effect.<sup>31,32</sup> Furthermore, with a better follow-up rate in the last 2 periods, comparison of the prognosis in this study should be much more reliable.

A major problem of this study was that records were reviewed for only cases from 1987 to 1999. Data from previous time points were obtained from previously published articles, and, no statistical analysis could be performed on some of the outcome measures. Although this study analyzed limited data from a single center experience in a retrospective way, we found improved outcomes of gastric cancer surgery and improved survival of the gastric cancer patients. We found that the accumulation of treatment

experience with gastric cancer and becoming a large volume hospital had an impact on the improved treatment outcome of gastric cancer patients, but there have been no standardized treatment protocols for each period even though surgery has been relatively standardized.

Early diagnosis and radical surgery with multimodality adjuvant therapy have markedly improved the survival of patients with gastric cancer. Nowadays, various surgical approaches, such as conventional surgery, function preserving surgery, and minimally invasive surgery, are being practiced.<sup>3</sup> Gastric cancer should be considered as a malignancy that requires a multidisciplinary approach by a specialized team. Evaluation of the effect of a highly developed treatment strategy in prospective clinical trial settings is still needed to confirm these observations.

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