



Cancer of the Stomach: A Review of Two Hospitals in Korea and Japan

Young Jae Mok, M.D.,¹ Bum Whan Koo, M.D.,¹ Chung Woong Whang, M.D.,¹ Sae Min Kim, M.D.,¹ Keiichi Maruyama, M.D.,² Mitsuru Sasako, M.D.,² and Taira Kinoshita, M.D.²

¹Department of Surgery, Korea University Hospital, Seoul, Korea, and ²Gastric Surgery Division, National Cancer Center Hospital, Tokyo, Japan

The records of 525 patients with primary adenocarcinoma of the stomach treated at Korea University Hospital (K.U.H.), Seoul, Korea, and 1,932 patients treated at National Cancer Center Hospital (N.C.C.), Tokyo, Japan, over a 7-year period were reviewed to study biologic characteristics and treatment results in the two hospitals. More than 70% of the patients were 41 to 70 years old in both hospitals, though K.U.H. had more younger patients and N.C.C. had more older patients. Comparison in regard to clinicopathologic features showed significant differences in type of cancer, tumor size, depth of invasion, lymph node metastasis, stage, and histologic type. Such a difference mostly was due to a greater frequency of early gastric cancer in N.C.C. patients (51.2%) than in K.U.H. patients (19.0%). Patients of K.U.H. were more likely to have advanced cancer, large invasive tumors, a higher percentage of lymph node metastasis, a higher stage, and more undifferentiated tumors. The 5-year survival rate of all resected cases was 69.5% in N.C.C. and 54.2% in K.U.H. ($p > 0.05$). Those factors which showed a significant difference in clinicopathologic features did not affect the survival difference between the two hospitals except in stage IIIb and signet-ring-cell cancer. The 5-year survival rate for stage IIIb was 18.0% in K.U.H. and 36.8% in N.C.C. It would seem that survival difference in stage IIIb related to extensive lymph node dissection in N.C.C. Survival difference in signet-ring-cell gastric cancer (31.2% in K.U.H. and 91.0% in N.C.C.) was related to the fact that 79.1% of signet-ring-cell gastric cancer patients in N.C.C. had early gastric cancer. This present study once again demonstrates the importance of early detection in the treatment of gastric cancer and suggests that gastric cancer of two countries is not different.

Gastric cancer is a major cause of death in many countries, even though there has been a significant decline in its incidence. Survival rates after surgery of gastric carcinoma reported from Japan are superior to those reported in the Western literature [1, 2]. Several studies [3-7] have demonstrated beyond doubt that the prognosis of gastric cancer is related to early detection. However, difference in prognosis has led to the view that Japanese gastric cancer is biologically different and that the radical surgery performed in Japan is more effective than that in the Western world, even though Japanese surgeons stress the improvement in survival resulted from an organized approach to gastric cancer surgery, as expressed in "The General Rules

of the Japanese Research Society for Gastric Cancer" (JRSGC) [8] and from extensive lymph node dissection.

Gastric cancer is the leading cause of death in Korea and Japan. Therefore, we reviewed the experience of patients treated for primary gastric cancer retrospectively at Korea University Hospital (K.U.H.), Seoul, Korea, and the National Cancer Center Hospital (N.C.C.), Tokyo, Japan, to determine whether there is any difference in biological behavior and treatment results between two hospitals.

Materials and Methods

All patients who were treated surgically for primary gastric adenocarcinoma over a 7-year period from 1983 to 1990 at the K.U.H. ($n = 603$) or the N.C.C. ($n = 2052$) were reviewed. Of these, 525 cases were resectable in the K.U.H. (ratio of resection; 87.1%) and 1932 cases were in the N.C.C. (ratio of resection; 94.2%). These resectable cases were based on this analysis because histologic confirmation was essential.

We reviewed all available information, which included age, sex, type of cancer, tumor location, tumor size, TNM stage, histologic type, operative procedure, and survival. The tumors were divided by location as follows: Upper or proximal third of the stomach, middle third, and lower or distal third. This distribution was based on the site where the major portion of the tumor mass was located. Grossly advanced carcinomas of the stomach were classified as one of four types proposed by Borrmann [9]. Type I is circumscribed, solitary, polypoid carcinoma without ulceration (polypoid type); type II, an ulcerated carcinoma with wall-like marginal elevation and sharply defined borders (ulcerating type); type III, a partially ulcerated carcinoma with marginal elevation and partial diffuse spread (ulcerofungating type); and type IV, a diffuse carcinoma. The UICC-TNM staging systems [10] were used for clinical and pathology-related descriptions at the K.U.H. and the general rules of the JRSGC [8] were used at the N.C.C.

Operative Procedures

Gastric resection consisted of removal of gross evidence of malignant disease by total or subtotal removal of the stomach,

Offprint requests: Young Jae Mok, M.D., Department of Surgery, Korea University Hospital, 80 Guro-Dong, Guro-Ku, Seoul 152-050, Korea.

Table 1. Age distribution of patients with primary gastric cancer resected.^a

Age	Korea University Hospital (n = 525)		National Cancer Center (n = 1932)	
	No. of cases	%	No. of cases	%
≤30	17	3.2%	15	0.8%
31–40	61	11.6%	113	5.8%
41–50	132	25.2%	334	17.3%
51–60	161	30.7%	537	27.8%
61–70	137	26.1%	563	29.1%
>70	17	3.2%	370	19.2%
Total	525	100%	1932	100%

^a*p* < 0.05.

the greater and lesser omentum, and the neighboring regional lymph node. The type of resection (total or distal subtotal) was selected according to the location of the tumor. Distal subtotal gastrectomy was performed in 76.8% of the K.U.H. patients and 67.6% of the N.C.C. patients. Total gastrectomy was performed in 21.7% of the K.U.H. and 28.3% of the N.C.C. patients.

The lymph node dissection at the K.U.H. was performed with R₂ resection, which included en bloc dissection of the N₁ and N₂ nodes as defined by the UICC TNM classification [10]. At the N.C.C., the standard procedure was R₂ or R₃ resection, which included the N₁, N₂, and N₃ nodes as defined by the general rules of the JRSGC [8].

Statistical Analysis

The survival rates were calculated by the method of Kaplan-Meier [11], and univariate analyses comparing two hospitals were performed using the log-rank statistic. The chi-square test was used to compare different frequencies of clinicopathologic factors between two hospitals. A *p* value of less than 0.05 was considered to be significant. Computations were carried out using the statistical package SAS (Statistical Analysis System).

Results

The age distribution of the patients with primary gastric cancer who underwent resection is shown in Table 1. A peak incidence of gastric cancer at K.U.H. was noted in the 51–60-year-old group (30.7%) followed by the 61–70-year-old group (26.1%). In the N.C.C., a highest incidence was noted in the 61–70-year-old group (29.1%) followed by the 51–60-year-old group (27.8%). More than 70% of primary gastric cancer was found in 41–70-year-olds in both hospitals. However, patients under 40 years old comprised 14.8% of the K.U.H. and 6.6% of N.C.C., while patients over 70 years of age comprised 3.2% and 19.2% of the K.U.H. and the N.C.C., respectively. There was a statistically significant difference in the age distribution between two hospitals. The male-to-female ratio was 2.01:1 in the K.U.H. and 2.23:1 in the N.C.C. (Table 2).

Clinicopathologic Factors

The clinicopathologic characteristics of 525 patients of the K.U.H. and 1932 patients of the N.C.C. who had gastric

resection were compared (Table 2). Significant differences were present in the factors of age, type of cancer, tumor size, depth of invasion, lymph node metastasis, and histologic type. Early gastric cancer was found in 51.2% of the N.C.C., whereas 19.0% of the K.U.H. patients had early gastric cancer. This discrepancy of proportion of the early gastric cancer revealed substantial differences between the two hospitals. Patients of the K.U.H. were more likely to have advanced cancer, large invasive tumor, a higher percentage of lymph node metastasis, a higher stage (stage IIIa and IIIb), and more undifferentiated tumor than those of the N.C.C.

The most common location of the tumor was the lower third (51.4%) in the K.U.H. and the middle third (42.6%) in the N.C.C. There was no significant difference in the location of the tumor. In the K.U.H., poorly differentiated adenocarcinoma was the most common type (45.0%). Predominant histologic types in the N.C.C. were well-differentiated (27.2%), moderately differentiated (24.3%), and poorly differentiated adenocarcinoma (27.7%). Signet-ring-cell cancer constituted 9.3% of the K.U.H. and 15.1% of the N.C.C. patients. This discrepancy in regard to histologic type may be attributable to a difference in the incidence of early gastric cancer vs advanced cancer between two hospitals—that is, more early gastric cancer in the N.C.C. and more advanced cancer in the K.U.H. The operative procedure which was most frequently performed was distal gastrectomy: 76.8% in the K.U.H. and 67.6% in the N.C.C. The frequency of operative procedure did not differ significantly among the two hospitals.

Survival Rates

Postoperative survival curves for patients who underwent resection are shown in Figure 1. The 5-year survival rate was 69.5% for those of the N.C.C. and 54.2% for those of the K.U.H. (*p* > 0.05). The 5-year survival rate in terms of clinicopathologic variables for K.U.H. and the N.C.C. is presented in Table 3. Significant differences in stage IIIb and signet-ring-cell cancer are shown in Table 3 and Figure 2.

In the case of early gastric cancer, the 5-year survival rate was 86.2% for the K.U.H. and 94.1% for the N.C.C. patients. There was no difference in the 5-year survival rate according to type of cancer. Postoperative survival rates according to each stage are shown in Figure 2. A significant survival difference was present only in stage IIIb. The 5-year survival rate in stage IIIb was 18.0% in the K.U.H. and 36.8% in the N.C.C. Patients with the differentiated type showed better 5-year survival rate than those with the undifferentiated type in both hospitals. However, signet-ring-cell cancer had a significant difference in the 5-year survival rate: 31.2% in the K.U.H. and 91.0% in the N.C.C. It appears that the survival difference in signet-ring-cell cancer is due mainly to a greater frequency of signet-ring-cell cancer among the early gastric cancer patients of the N.C.C. Of the total of 1932 patients who underwent resection for primary gastric carcinoma at N.C.C., 292 patients (15.1%) had signet ring cell cancer. Among the 990 patients with early gastric cancer at the N.C.C., 231 patients had signet ring cell. Therefore, early gastric cancer was present in 79.1% (231/292) of the patients with signet-ring-cell gastric cancer in the N.C.C.

Table 2. Clinicopathologic features of all primary cancer resected.

Variable	Korea University Hospital (%) (n = 525)	National Cancer Center (%) (n = 1932)	p value ^a
Age, year (average)	19–87 (53.3 ± 11.6)	20–89 (59.5 ± 11.9)	p < 0.05
Sex			
Men	351 (66.9%)	1335 (69.1%)	
Women	174 (33.1%)	597 (30.9%)	NS
Type of cancer			
Early gastric cancer	100 (19.0%)	990 (51.2%)	
Borrmann I	13 (2.5%)	36 (1.9%)	
Borrmann II	115 (21.9%)	256 (13.3%)	
Borrmann III	241 (45.9%)	479 (24.8%)	
Borrmann IV	56 (10.7%)	154 (8.0%)	p < 0.01
Location of tumor			
Upper 1/3	46 (8.8%)	383 (19.8%)	
Middle 1/3	209 (39.8%)	823 (42.6%)	
Lower 1/3	270 (51.4%)	723 (37.4%)	NS
Tumor size			
T < 4 cm	185 (35.2%)	1156 (59.8%)	
4 cm ≤ T < 8 cm	250 (47.6%)	498 (25.8%)	
T ≥ 8 cm	90 (17.2%)	278 (14.4%)	p < 0.01
Depth of invasion			
T1	100 (19.0%)	990 (51.2%)	
T2	88 (16.8%)	305 (15.8%)	
T3	266 (50.7%)	447 (23.2%)	
T4	71 (13.5%)	190 (9.8%)	p < 0.01
Lymph node metastasis			
N0	195 (37.1%)	1120 (58.0%)	
N1	158 (30.1%)	303 (15.7%)	
N2	121 (23.1%)	318 (16.4%)	p < 0.01
Distant metastasis			
M0	460 (87.6%)	1688 (87.4%)	
M1	65 (12.4%)	244 (12.6%)	NS
Stage (UICC, 1987)			
Stage Ia	86 (16.4%)	886 (45.9%)	
Stage Ib	61 (11.6%)	205 (10.6%)	
Stage II	87 (16.6%)	195 (10.1%)	
Stage IIIa	113 (21.5%)	161 (8.3%)	
Stage IIIb	88 (16.8%)	152 (7.9%)	
Stage IV	90 (17.1%)	332 (17.2%)	p < 0.01
Histologic type			
Well differentiated	40 (7.6%)	525 (27.2%)	
Moderately differentiated	174 (33.1%)	470 (24.3%)	
Poorly differentiated	236 (45.0%)	536 (27.7%)	
Signet-ring-cell	49 (9.3%)	292 (15.1%)	
Papillary	0	58 (3.0%)	
Mucinous	20 (3.8%)	49 (2.5%)	p < 0.01
Operative procedure			
Distal gastrectomy	403 (76.8%)	1306 (67.6%)	
Total gastrectomy	114 (21.7%)	546 (28.3%)	
Proximal gastrectomy	1 (0.2%)	49 (2.5%)	
Partial gastrectomy	7 (1.3%)	31 (1.6%)	NS

^aBased on chi-square test. NS indicates not significant.

Discussion

There is now strong evidence that gastric cancer may occur in different biologic forms, that there are changing patterns of disease, and that diagnostic and therapeutic strategies may influence the long-term results. It is these features which produce the apparent differences between East and West and which hold the key to future advances in management [12].

Several studies have been published concerning the biological behavior in gastric cancer. As early as 1954, MacDonald and Kotin [13] reported biologic predeterminism in gastric carcinoma. They suggested that biologic predeterminism, rather than the time or type of surgical treatment, governs end results

in gastric carcinoma and that early gastric cancers are selected naturally with the result of their slow growth and long duration of symptoms. ReMine et al. [14] suggested that although the balance between host resistance and tumor aggression is an important factor in the outcome in any patient who has a malignant lesion, “biologic predeterminism” is not the only factor that influences prognosis. Lauren [15] observed that gastric carcinoma could be distinguished into two main types—“intestinal” and “diffuse”—and assumed that they, at least to some extent, are caused by different etiologic factors. Munoz et al. [16] reported that the intestinal type was predominant in areas at high risk for stomach cancer, while the diffuse type was

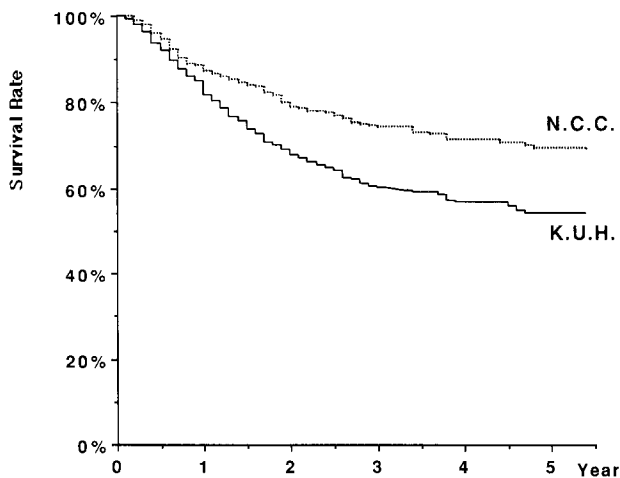


Fig. 1. Survival rate for gastric carcinoma resected.

more frequent in the low-risk areas, and they suggested that these two types of cancer might be of different etiology. However, epidemiological studies [17, 18] demonstrated that migration from a high- to a low-risk country is followed by a decreased mortality from gastric cancer and suggested that the gastric cancers in high- and low-risk areas may be similar. Moreover, Kubo [19] has found that there was no significant difference in histologic appearance of gastric carcinoma both in different countries and at different times in an international comparative study of gastric carcinoma.

In this study, we found that there were significant differences in gastric cancer specific for age, type of cancer, tumor size, depth of invasion, lymph node metastasis, stage, and histologic type between two hospitals. However, it would seem that the difference in the comparison of clinicopathologic features is mostly due to a greater frequency of early gastric cancer in the N.C.C. It is interesting that the patients of both hospitals were operated upon with almost same operative procedures.

It is the most striking feature of this series that several factors which showed a significant difference in comparative study in regard to clinicopathologic features did not affect survival except in stage IIIb and signet-ring-cell cancer. In our study, the 5-year survival rate in stage IIIb, which includes T4N1M0 and T3N2M0 in which extensive lymph node dissection may be most effective treatment, showed statistical significance. Such a difference in stage IIIb may be attributed to the wide lymph node dissection in the N.C.C. Several studies [20–22] have suggested that extensive lymph node dissection is more effective for improving survival for all patients except those with early gastric cancer. The role of extensive lymph node dissection needs, of course, to be further examined in a large study between two hospitals. The higher survival rate of signet-ring-cell cancer was considered to be due to the greater proportion of cases of early gastric cancer among signet-ring-cell cancer in the N.C.C., as already mentioned.

This paper has described biological behavior and treatment results in an effort to determine whether there was any difference in gastric cancer between Korea and Japan. It appears that differences are due mainly to a greater frequency of patients presenting with early gastric cancer in Japan. In conclusion, the

Table 3. 5-year survival rate in terms of clinicopathologic variables.

Variable	Korea University Hospital (n = 525)	National Cancer Center (n = 1932)	p value ^a
Age (year)			
31–40	54.3%	75.1%	
41–50	57.5%	79.5%	
51–60	53.5%	75.0%	
61–70	54.1%	69.3%	NS
Sex			
Men	51.1%	65.9%	
Women	60.8%	68.8%	NS
Type of cancer			
Early gastric cancer	86.2%	94.1%	
Borrmann I	72.0%	64.2%	
Borrmann II	61.0%	52.0%	
Borrmann III	44.0%	51.8%	
Borrmann IV	12.9% ^b	7.4%	NS
Location of tumor			
Upper 1/3	39.9%	55.4%	
Middle 1/3	60.8%	77.6%	
Lower 1/3	50.7%	69.4%	NS
Tumor size			
T < 4 cm	74.8%	87.0%	
4 cm ≤ T < 8 cm	46.8%	65.2%	
T ≥ 8 cm	28.8%	27.8%	NS
Depth of invasion			
T1	86.2%	94.1%	
T2	85.6%	78.7%	
T3	41.4%	34.2%	
T4	8.7%	15.8%	NS
Lymph node metastasis			
N0	85.6%	90.4%	
N1	52.6%	64.0%	
N2	24.4%	37.9%	NS
Histologic type			
Well differentiated	81.1%	84.1%	NS
Moderately differentiated	57.5%	67.9%	NS
Poorly differentiated	48.6%	49.0%	NS
Signet ring cell	31.2%	91.0%	p < 0.01
Mucinous	67.2%	31.0%	NS

^aBased on chi-square test. NS indicates not significant.

^b4-year survival rate; no 5-year survival rate available.

present study of gastric cancer in two countries once again demonstrates the importance of early detection in the treatment of gastric cancer and suggests that gastric cancer of two countries is not different.

Résumé

Les dossiers de 525 patients ayant un adénocarcinome primitif de l'estomac traités à l'Hôpital Universitaire de Corée à Séoul et de 1932 patients traités au Centre National du Cancer à Tokyo, vus sur une période de 7 ans, ont été analysés. Plus de 70% des patients avaient entre 41 et 70 ans bien que l'âge moyen était légèrement plus élevé dans l'Hôpital Japonais. En comparant les deux séries, il y avait des différences significatives en ce qui concerne le type de cancer, la taille de la tumeur, la profondeur de l'envahissement, les métastases lymphatiques, le stade et le type histologique, vraisemblablement dues à une plus grande fréquence de cancer au stade de début dans la population Japonaise (51.2%) par rapport à la population Coréenne (19%). Les patients Coréens avaient plus de tumeurs avancées,

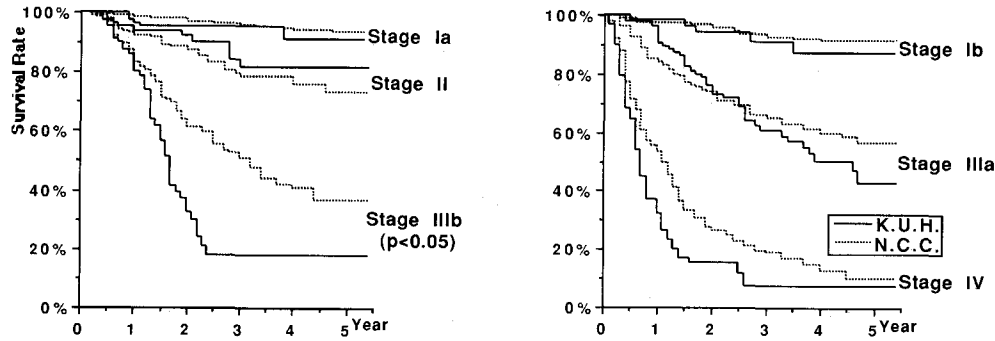


Fig. 2. Survival rate according to TNM staging.

de grande taille, invasives, avec métastases lymphatiques et indifférenciées. La survie à 5 ans était de 69.5% pour les tumeurs résequées au Japon et de 54.2% en Corée ($p > 0.05$). Parmi les différents facteurs clinicopathologiques, seuls le stade IIIb et la présence de cellules en bague à chignon avaient une influence sur la survie. La survie à 5 ans pour les tumeurs de stade IIIb était de 18% en Corée et de 36.8% au Japon. Il semble que cette différence soit due à la dissection plus grande associée au curage lymphatique que l'on préconise au Japon. La différence de survie pour les cancers avec cellules en bague à chignon (31.2% en Corée et 91% au Japon) est due au fait que 79.1% de ces cancers étaient traités au Japon au stade de cancer de début. La présente étude souligne encore une fois l'importance d'une détection et traitement précoces du cancer gastrique et suggère qu'il n'y a pas beaucoup de différences entre les deux pays en dehors des modalités thérapeutiques.

Resumen

Con el propósito de comparar las características biológicas y los resultados del tratamiento, se revisaron retrospectivamente las historias clínicas de 525 pacientes con adenocarcinoma primario del estómago tratados en el Hospital Universitario de Corea, Seul, y de 1.932 pacientes tratados en el Hospital Centro Nacional de Cáncer de Tokyo, Japón, en un período de 7 años. Más de 70% de los pacientes tenían edades entre los 41 y los 70 años en los dos hospitales, aunque el de Corea tuvo pacientes más jóvenes, y el de Tokyo más añosos. La comparación en cuanto a las características clínicas patológicas demostró diferencias significativas relativas al tipo de cáncer, tamaño del tumor, profundidad de invasión, metástasis ganglionares, estado y tipo histológico. Las diferencias se debieron principalmente a una mayor frecuencia de cáncer gástrico precoz (temprano) en Tokyo (51.2%) que en Seul (19.0%). Los pacientes Coreanos exhibieron una mayor propensión al cáncer avanzado, a los grandes tumores invasivos, a una mayor frecuencia de metástasis ganglionares, a una estadificación de grado más elevado y a una mayor indiferenciación del tumor. La tasa de sobrevida a 5 años de todos los casos resecados fue de 69.5% para Tokyo y de 54.2% para Seul ($p > 0.05$). Aquellos factores que exhibieron diferencias significativas en las características clínicas patológicas, no afectaron la diferencia en las tasas de sobrevida entre los dos hospitales, excepto en los tumores en Estado IIIb y los tumores de células en anillo de sello. La tasa de sobrevida a 5 años en el Estado IIIb fue de

18.0% en Seul y de 36.6% en Tokyo. Parece que la diferencia en sobrevida en el Estado IIIb se relacionó con la extensa disección ganglionar que se practica en el Hospital de Tokyo. La diferencia en la sobrevida en los tumores de células en anillo de sello (31.2% en Seul y 91.0% en Tokyo) apareció relacionada con el hecho de que el 79% de éstos casos eran cánceres precoces. El presente estudio demuestra una vez más la importancia de la detección temprana del cáncer gástrico y sugiere que el cáncer del estómago no es diferente en los dos países.

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Invited Commentary

Louis F. Hollender, M.D., F.A.C.P. (Hon.), F.R.C.P. Engl. (Hon.)

Strasbourg, France

Survival rates for patients with gastric cancer depend on three factors: the width of the gastric resection, the lymph node involvement, and early diagnosis. The concept of whether total gastrectomy should be performed as a general rule or only by necessity is no longer in question: Total gastrectomy with splenectomy should be performed systematically for most gastric cancers. Only small antropyloric lesions can be treated by subtotal resection and even then with a safety margin of 8 to 10 cm. Concerning removal of the tail of the pancreas, most agree that the associated morbidity has not been counterbalanced by a higher survival rate.

Lymph node invasion plays one of the most important roles in prognosis. Only 25% of the patients with lymph node

involvement are still alive after 5 years. Therefore systematic lymphadenectomy involving the 16 chains of lymphatic drainage in three regions (determined by their anatomic proximity to the stomach) is mandatory.

The third major prognostic factor is early diagnosis.

Operations on patients with stage T0 and T1 disease result in 98% survival after 5 years. Repeat gastroscopy with multiple biopsies should be performed at the slightest doubt.

Intraoperative radiotherapy with administration of 25 to 30 Gy is an important contribution to cure, autopsies having proved that local recurrences and intraperitoneal diffusion are frequent. That aspect of treatment is worthwhile discussing.

Even if the large experience of two hospitals—one in Korea and the other one in Japan—confirm as a whole these various findings, their results cannot be compared, as the epidemiology of gastric cancer is not the same in countries where alimentary customs are different. On the other hand, systematic endoscopic examinations in Japan have provided information superior to the follow-up data reported from all other countries. As an aside, it is interesting that the prognosis of the ring cell cancer is better if diagnosed early.