



Early Gastric Cancer: Results in a General Hospital in Japan

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One hundred and forty patients underwent surgical treatment for early gastric cancer. Cumulative and age-corrected cumulative 5-year survival rates were 87.5% and 96.2%, respectively. Cumulative and age-corrected 10-year survival rates were 68.5% and 88.3%, respectively. When cancerous tissue did not remain in the resectional stumps and no regional lymph node was metastasized, the survival was almost equal to that of the general population. Resection of the secondary lymph nodes is considered beneficial, since 13.9% of cases had metastasized lymph nodes in our series. The 5-year survival of 90% is a realistic figure for early gastric cancer, attainable in a general hospital which does not specialize in cancer research.

Early gastric cancer (EGC), sometimes called superficial spreading carcinoma or carcinoma in situ, is defined as a lesion in which cancerous invasion is confined to the mucosa (m) or mucosa and submucosa (sm) regardless of the regional lymph node metastasis. Since the Japanese Endoscopic Society established this definition in 1962, the detection rate of EGC has increased steadily. Currently, EGC comprises about 20 to 30% of all cases of gastric cancer in Japan [1, 2]. Mass survey of upper gastrointestinal barium study and routine endoscopic biopsy of suspicious lesions contributed to this high detection rate. Although many excellent 5-year survival rates exceeding 90% were reported in Japan [1-4], they were mostly from university hospitals and institutes oriented to cancer research. There are few reports in English literature of the surgical results of EGC from Japanese general

hospitals. In this report, we compared our long-term results in Hiroshima Red Cross and Atomic Bomb Hospital, which is a typical general hospital in Japan, with results of other hospitals in Japan and other nations. The aim is to see whether the 5-year survival of 90% is an attainable value in a general hospital. In addition, the factors that might have prognostic importance were also evaluated. Throughout this report, the General Rules for Gastric Cancer Study in Surgery and Pathology [5] was utilized for description and classification of the variables.

Methods and Materials

Between 1967 and 1979, there were 819 patients operated on for gastric malignancy, including 2 cases of gastric sarcoma. One hundred and forty patients were histologically diagnosed as having EGC, representing 17.1% of all surgically treated patients including those undergoing palliative procedures and exploratory laparotomies. When only patients operated on for cure are considered, these 140 patients constitute 22.6%. The clinical charts and pathology reports of the 140 patients were reviewed. The age and sex of the patient, location, macroscopic and histological type of the lesion, metastasis in regional lymph nodes and distant sites, depth of invasion, operation performed, and the presence of cancerous tissue in the resectional stumps were scrutinized. According to the General Rules, regional lymph nodes were divided into 15 groups. Each group was classified either primary, secondary, or tertiary, depending on the location of the cancerous lesion in the stomach and the proximity of the nodal group to the lesion. When the cancerous tissue was detected within 5 mm of the

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oral or anal edge on histological specimen, the cancer was assumed to have been left in the stump. The operation was judged to be noncurative in such a case [ow(+) or aw(+)]. Present status of the patients was obtained from census-register certificates, patients' charts, family members, or physicians who had seen the patients when they died.

Of the 140 patients, 137 were subdivided into 4 categories as follows: category A, 8 patients with positive stumps [ow(+) or aw(+)], regardless of the nodal metastasis; category B, 113 patients with negative stumps and lymph nodes (n0); category C, 10 patients with negative stumps but with metastases in primary lymph nodes (n1); and category D, 6 patients with negative stumps but with metastases in secondary lymph nodes (n2). In our series, no patient had metastasized tertiary lymph nodes, and no grossly metastasized node was left unresected. Cumulative and age-corrected cumulative survival rates were calculated for the entire group and for each category. The standard chi-squared test was utilized to evaluate the relationship of each factor.

Results

The ages ranged from 24 to 82 years, with a mean of 57.9 years. Eighty-four patients were men and 56 women (1.5:1). Including one double early cancer case, 81 lesions (57.9%) were seen in the middle third of the stomach; fifty-seven (40.7%) were seen in the anal third; only 3 lesions were in the cephalic third. Cancers on the lesser curvature were the most common (65, 46.4%), followed by those on the posterior wall (42, 30.0%). Descriptions of the macroscopic appearance of the resected specimen were available in 116 lesions. Twelve of them were described as advanced cancers (Borrmann I, II, III, or IV) [6] and had been considered so until the histology reports revealed the early cancerous lesion. Type IIc was the most common (38 of 116, 32.8%), followed by the type IIc + III (21 of 116, 18.1%). As a whole, 91 of the 112 lesions (81.3%) were classified as depressed lesions (IIc, IIc + IIa, IIc + III, IIa + IIb, III + IIc, III, Bor II, Bor III). Twenty-one lesions (18.8%) were classified as elevated (I, IIa, I + IIa, IIa + IIb, Bor I). Twenty-eight lesions were either judged as unclassified, or simply not described.

Table 1 shows the histological features of the cases. Forty-four lesions (30.7%) were confined in the mucosa and 97 (69.3%) invaded the submucosa. Regional lymph node metastasis was found in 19 patients (13.9%). Ten of them were limited in the primary lymph nodes (n1) and 9 involved the secondary nodes (n2). Metastasis in the tertiary nodes was not found. For the remaining 3 patients, com-

Table 1. Histological features in 140 patients with early gastric cancer.

Depth of invasion ^a		Nodal metastasis		Histological type ^b	
m	43	n0	118	Sig	53
sm	97	n1	10	Tub 2	45
		n2	9	Tub 1	14
		n?	3	Por	14
				Pap	10
				Muc	4

^am: mucosa; sm: submucosa.

^bSig: signet-ring cell carcinoma. Tub 2: moderately differentiated tubular adenocarcinoma. Tub 1: well-differentiated tubular adenocarcinoma. Por: poorly differentiated adenocarcinoma. Pap: papillary adenocarcinoma. Muc: mucinous adenocarcinoma.

ment on the regional lymph nodes were not made in 2, and in 1 patient, nodal status was unknown because only a polypectomy was performed and no histological evaluation of the lymph node was made. Signet-ring cell carcinoma was the most common (53, 37.9%).

Gross liver metastasis was not found in any patient. Peritoneal dissemination was suspected in 1 patient. This patient died 6 years after the operation and the cause of death could not be clarified. All of the patients' profile, macroscopic and microscopic features of the lesions were similar to those in other reports of EGC [7].

Seventy-three partial or subtotal gastrectomies were performed after the Billroth II method (52.1%). Fifty-eight Billroth I partial gastrectomies were done (41.4%). Total gastrectomy was performed on 7 patients, cardiac resection on 1, and polypectomy on 1. The choice of operative method depended on the location of the lesion and the surgeon's preference. Resection of the regional lymph nodes became more popular in recent years (Fig. 1). After 1973, an additional 3 or 4 groups of nodes, including at least some secondary nodes, were removed routinely in each case, as well as lymph nodes along the lesser and greater curvatures.

Cumulative and age-corrected cumulative survival curves are shown in Fig. 2. Cumulative 5-year survival was 87.5%, and 96.2% when age-corrected. Ten-year survivals were 68.5% and 88.3%, respectively. Cumulative survival curves of the 4 categories are shown in Fig. 3.

Causes of death are summarized in Tables 2 and 3. In category A, 7 of the 8 patients died during the follow-up period. Four died of recurrent disease. Causes of the other 3 deaths were either unrelated to the gastric cancer or unknown. In category B, 18

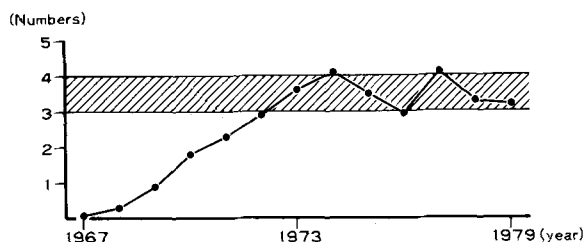


Fig. 1. Number of resected lymph node groups per patient, except those on the lesser and the greater curvatures.

of the 113 died. Cancer recurrence was suspected in only 1 patient, who died 7.8 years later with cutaneous nodules suggesting skin metastasis. No histological evidence could be obtained. Three of the 18 patients died of other malignancies (Table 3). The first died of pancreatic carcinoma 13 years after the initial operation. The second died of cerebral glioma 11.3 years later. The last died of coexisting lung cancer about 6 months after the surgery for gastric cancer. In category C, 4 of the 5 deaths were due to cancer recurrence. In category D, one of the 3 deaths was also due to recurrence. The causes of the remaining 2 deaths were not elucidated.

Location of the primary cancer or its gross and histological type did not affect lymph node metastasis. Only invasion of the submucosal layer significantly raised the rate of nodal involvement (Table 4).

Discussion

The follow-up of the patients was difficult in the present series. Five patients were lost to follow-up and in 8 patients the causes of death could not be clarified. Our cumulative survival data were calculated taking all these cases into account, following the method shown in the General Rules and related literature [8]. Our survival data are compared with those of other authors (Table 5). Our results are slightly inferior to the reports from the university hospitals or other cancer research institutes in Japan, while still better than those of European authors. It seems apparent that the adoption of the General Rules helped to promote our results. All regional lymph nodes are meticulously numbered, so that we are able to identify numerically the nodes that must be removed or that we are removing. In addition, as the curability of the operation is defined in 4 grades from absolutely noncurative to absolutely curative, the goal to be aimed at and its achievability are clearly known for each operation. The General Rules are widely accepted throughout Ja-

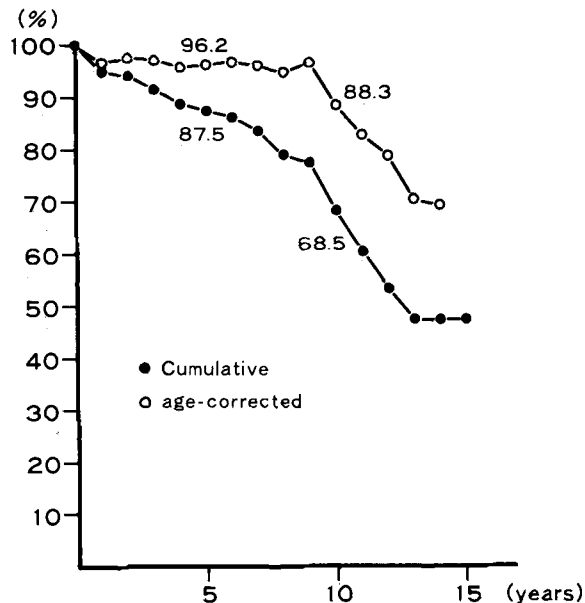


Fig. 2. Cumulative and age-corrected survival curves of the total 140 patients.

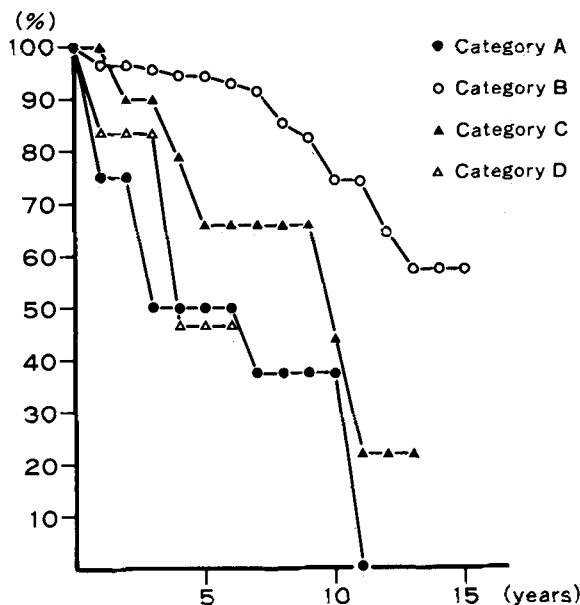


Fig. 3. Cumulative survival curves of the 4 categories. Category A: ow(+) or aw(+); category B: ow(-), aw(-), n0; category C: ow(-), aw(-), n1; and category D: ow(-), aw(-), n2.

pan and help to compare the results of surgery among different hospitals.

When we analyzed the results of each category, the small patient number in categories A, C, and D, and incomplete documentation of the causes of death in some cases prevented the meticulous statistical evaluation. In category A, the deleterious

Table 2. Death from cancer recurrence in 137 patients with early gastric cancer.

Category	No. of deaths during follow-up	No. of documented ca. recurrence	Years after operation
A	7/8	4/7	1.0–10.4 (mean 5.2)
B	18/113	1/18	7.8
C	5/10	4/5	1.3–10.6 (mean 4.9)
D	3/6	1/3	3.8

Table 3. Other malignancies in category B.

Cancer	Years after operation
Pancreas carcinoma	13.0
Cerebral glioma	11.3
Lung carcinoma	0.5

effects of positive stumps are obvious from the survival curve and the death-cause analysis. In 1 patient in category B, the resected specimen of the first partial gastrectomy revealed cancerous tissue in the oral edge. An additional remnant total gastrectomy was performed 1 week later. This patient is alive today, about 7 years after the operation, without signs of recurrence. There was only one case of recurrence (cutaneous metastasis) documented in category B. Therefore, gross type, histological type, or depth of invasion did not affect the prognosis per se in our series, when there was no lymph node metastasis. In Japanese literature, many authors reported recurrent cases in patients who would have been classified as category B in our report [4, 13–17]. Liver metastasis from hematogenous dissemination seemed to be frequent in such cases. No conventional parameter is yet available to predict in which patient of category B a recurrent disease will develop in future.

The only parameter that affected the lymph node metastasis was the depth of invasion (1/43, 2.3% of m and 18/97, 18.6% of sm, $p < 0.01$). Gross pathological and histological type or the location of the cancer did not affect the nodal involvement. Survival curves of the m and sm cancers, however, showed no statistically significant difference.

The role of extended lymph node extirpation is less well established in EGC compared with that of advanced gastric cancer [18–20]. In our series, the difference in the extent of nodal extirpation failed to show any significant difference in survival in categories C and D, perhaps because of the small number of cases. In one large series, Hayashida et al. reported a better prognosis in the EGC cases

Table 4. Depth of invasion and nodal involvement in 140 patients with early gastric cancer.

Depth	n0	n1	n2	n?
m	41	0	1	1
sm	77	10	8	2

$p < 0.01$.

Table 5. Survival rates from literature of patients with early gastric cancer.

Author	5-year (%)		10-year (%)	
	Cumulative	Age-corrected	Cumulative	Age-corrected
Kaneko et al. [1]	90.0	95.9	87.1	101.5
Okui and Suzuki [4]	89.3	99.8	79.4	98.0
Murakami [9]	89.6		72.6	
Present series	87.5	96.2	68.5	88.3
Gentsch et al. [10]	74.0	87.2		
Gebhardt et al. [11]	69.0	82.0		
Fielding et al. [12]	57.8	70.4		

when the extent (primary, secondary, or tertiary) of resected lymph nodes exceeded the extent of metastasized lymph nodes [7]. According to the General Rules, these operations are absolutely curative, if the resectional stumps and the distant sites are free from cancer. In other words, when several primary nodes have metastases, the operation could be absolutely curative only when primary and secondary nodes are resected. Consequently, in many cases of EGC, secondary nodes are resected frequently in an effort to attain an absolutely curative operation, because the judgment of negative lymph node cannot be made through inspection and palpation only. Sakakibara et al. stated that resection of secondary nodes should be routinely carried out in EGC cases [21]. Our impression is that at least some of our patients were benefited from the resection of apparently metastasis-free lymph nodes.

We did not find any preferred organ for metastasis. Four of our 10 recurrent cases died more than 5 years after the initial operations. Recurrence occurred even after 10 years in 2 instances. These late recurrent cases preclude the assumption that the lapse of a 5-year period guarantees the cure of the disease. Postoperative chemotherapy was not provided in a standardized manner, even when provided, so it is unclear whether chemotherapy was effective in delaying recurrence in this study.

Our 3 cases of synchronous and metachronous cancers in other organs may support the idea of an increased tendency of EGC patients to develop another cancer in their later lives. Similar cases were reported by Matsusaka et al. [17] and Sakamoto et al. [22]. However, a larger number of such cases are necessary to elucidate whether this is statistically significant as compared with the general population.

Résumé

Cent quarante malades ont été traités chirurgicalement pour cancer précoce de l'estomac.

Les taux de survie à 5 ans non corrigés et corrigés en fonction de l'âge se sont élevés respectivement à 87,5% et 96,2%.

Le taux de survie a été le même que celui concernant la population en général dès lors que l'éradication du cancer avait été complète et que les ganglions régionaux n'étaient pas envahis. La résection des ganglions est bénéfique puisqu'aussi bien 13,9% des ganglions étaient envahis dans cette série.

Un taux de survie à 5 ans de 90% peut être obtenu en cas de cancer gastrique précoce même dans un hôpital général sans vocation oncologique spécifique.

Resumen

El cáncer gástrico temprano, que también ha sido denominado carcinoma de extensión superficial o carcinoma in situ, se define como una lesión en la cual la invasión tumoral se limita a la mucosa o submucosa, sin consideración de las metástasis ganglionares. En la actualidad el cáncer gástrico temprano representa aproximadamente el 20 a 30% de todos los casos de cáncer gástrico en el Japón.

Evaluaciones masivas mediante exámenes radiológicos del tracto gastrointestinal con bario y biopsia endoscópica rutinaria de las lesiones sospechosas han contribuido al logro de esta elevada tasa de detección. Las tasas acumulativas y corregidas para edad de supervivencia a 5 años fueron de 87,5% y 96,2% respectivamente. En ausencia de tejido canceroso residual en el muñón gástrico y de metástasis ganglionares regionales, la supervivencia fue casi igual a la de la población general. La resección de los ganglios linfáticos secundarios es considerada como beneficiosa, puesto que el 13,9% de los casos en nuestra serie presentaba metástasis ganglionares. La supervivencia a cinco años de 90%

para cáncer gástrico temprano es una cifra realista que puede ser lograda en un hospital general no especializado en investigación de cáncer.

References

1. Kaneko, E., Nakamura, T., Umeda, N., Fujino, M., Niwa, H.: Outcome of gastric carcinoma detected by gastric mass survey in Japan. *Gut* 18:626, 1977
2. Kajitani, K., Takagi, K.: Cancer of the stomach at cancer institute hospital, Tokyo. *Gann Monograph on Cancer Research* 22:77, 1979
3. Sakakibara, N., Yahata, M., Ohmura, H., Matsuda, S., Terada, M., Yokobori, N.: Survival results of the early gastric carcinoma from view point of invasion. *J. Clin. Surg. [Japan]* 31:15, 1976
4. Okui, K., Suzuki, M.: Evaluation on the recurrent cases of early gastric carcinoma. *Gastroenterol. Jpn.* 12:357, 1977
5. Japanese Research Society for Gastric Cancer: The General Rules for the Gastric Cancer Study in Surgery and Pathology, 10th ed. Tokyo, Kanehara Shuppan, 1979
6. Borrmann, R.: Geschwulste des Magens und Duodenums. In *Handbuch der Speziellen Pathologischen Anatomie und Histologie*, F. Henke, O. Lubarsch, editors. Berlin, Julius Springer, 1926, pp. IV-L, 864-871
7. Hayashida, T., Kidokoro, T.: End results of early gastric cancer collected from 22 institutions. *Stomach and Intestine [Japan]* 4:1077, 1969
8. Takasugi, T., Sasagawa, M., Yamada, T., Ichikawa, H., Kitaoka, H., Hirota, T.: A Study on end results of early gastric cancer: Analysis with actuarial survival rate. *Stomach and Intestine [Japan]* 12:933, 1977
9. Murakami, T.: Early cancer of the stomach. *World J. Surg.* 3:685, 1979
10. Gentsch, H.H., Groitl, H., Giedl, J.: Results of surgical treatment of early gastric cancer in 113 patients. *World J. Surg.* 5:103, 1981
11. Gebhardt, C., Husemann, P., Gentsch, H.H.: Clinical aspects and therapy of early gastric cancer. *World J. Surg.* 5:721, 1981
12. Fielding, J.W.L., Ellis, D.J., Jones, B.G., Paterson, J., Powell, D.J., Waterhouse, J.A.H., Brooks, V.S.: Natural history of "early" gastric cancer: Results of a 10-year regional survey. *Br. Med. J.* 281:965, 1980
13. Muto, T., Kusama, S., Tochi, K., Kobori, O., Ishikawa, K.: A study on end results of gastric early carcinoma: Analysis with relative survival rate curve. *Stomach and Intestine [Japan]* 5:541, 1970
14. Sano, R., Hirota, E., Shimoda, T., Fujita, K., Koguro, H., Suko, H.: Pathological evaluation of recurrence and mortality in early gastric cancer. *Stomach and Intestine [Japan]* 5:531, 1970
15. Takagi, K., Nakada, K.: Lymph node metastases and surgical results on early gastric cancer. *J. Clin. Surg. [Japan]* 31:19, 1976
16. Iwanaga, T., Furukawa, H., Kosaki, G.: Relapse of early gastric cancer and its prevention. *J. Clin. Surg. [Japan]* 31:29, 1976
17. Matsusaka, T., Kodama, Y., Soejima, K., Miyazaki, M., Yoshimura, K., Sugimachi, K., Inokuchi, K.:

- Recurrence in early gastric cancer: A pathologic evaluation. *Cancer* 46:168, 1980
18. Majima, S., Etani, S., Fujita, Y., Takahashi, T.: Evaluation of extended lymph node dissection for gastric cancer. *Jpn. J. Surg.* 2:1, 1972
 19. Jinnai, D.: Evaluation of extended radical operation for gastric cancer, with regard to lymph node metastasis and follow-up results. *Gann Monograph* 3:225, 1978
 20. Kodama, Y., Sugimachi, K., Soejima, K., Matsusaka, T., Inokuchi, K.: Evaluation of extended lymph node dissection for carcinoma of the stomach. *World J. Surg.* 5:241, 1981
 21. Sakakibara, N., Suzuki, H., Ide, H., Kawada, A., Oshibuchi, H., Kosaka, T., Yabata, M., Sano, Y., Kobayashi, M.: Some problems in surgical operation for early gastric cancer. *Surg. Ther. [Japan]* 33:113, 1975
 22. Sakamoto, K., Akiyama, H., Sakakibara, Y., Kayano, T., Okuyama, S.: Surgical concept and long-term prognosis of early gastric cancer. *Surg. Diag. Treat. [Japan]* 13:37, 1971

Invited Commentary

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The incidence of 17.2% of EGC in relation to all cases of malignant neoplasia of the stomach found in the Hiroshima Red Cross and Atomic Bomb Hospital is lower than the 45.7% [1] obtained in Japan for the diagnosis of EGC. The fact that this is a general hospital explains the finding. Nevertheless, such an incidence of EGC is much higher than most of the incidences published outside Japan [2]. Would this be an indication that gastric cancer in Japan has a different natural history or could this be exclusively due to a better capability of the Japanese doctors in diagnosing the disease at an early stage?

The preponderance of the occurrence of EGC in males in relation to females (1.5:1) in the work by Abe et al. is slightly smaller than the occurrences mentioned in other publications of Japanese case histories, in which the male to female ratio of occurrence was close to 1.9:1 [3]. One also notes the presence of well-differentiated papilliferous tubular adenocarcinoma (Abe et al., Tables 1 and 2) but in a low incidence when compared to other reports from Japan, such as the one by Takasagi and associates [4]. One wonders whether these two latter facts could be related to the existence of other determinant factors of the gastric cancer in the patients treated at the Hiroshima Red Cross and Atomic Bomb Hospital.

One notes in the present paper the admirable spirit of organization and discipline of Japanese medical societies. Even general hospitals are capable of recognizing and following the standards and protocols of staging, surgical therapeutics, and the evaluation of results as proposed by specialized societies. This fact has undoubtedly contributed to

the progress in the treatment of gastric cancer in that country. It has also made possible the pooling of the results from various centers, since the coding of data and the denomination of facts are the same. For this reason, it has become clear that it is very important to try to perform a controlled lymph node cleansing, having as its aim radical surgery in gastric cancer. Results presented by Kodama et al. [5] confirm this fact, for advanced gastric cancer.

As stated in the discussion of the paper by Abe and associates, although the results did not show a significant difference in the survival levels whether or not radical surgery was performed, because of the small number of cases (16), the authors have the feeling that it is essential to perform lymph node resection to attain surgical radicality.

In 8 of the cases histological evidence indicated that tumor remained in the gastric stump. In at least 4 of these there was remission of disease.

The establishment of the margin of safety, free from tumor invasion at least 5 mm from the level of cutting, may become one of the intraoperative difficulties when one treats EGC surgically. It is very useful to determine the limits of the tumor before the operation, by double-contrast X-ray, or, even better, by endoscopy. We know that it is nearly impossible to mark the limits between the neoplastic area and the normal gastric mucosa by palpation through the wall of the stomach. If necessary, the surgeon must perform the direct inspection of the lesion by means of full gastrotomy. Besides, it is advisable to inspect the surgical specimen during the operation by inverting the resected segment before its opening. When the margin of macroscopic safety is less than 2 cm, the surgeon should enlarge the gastric resection in order to ensure the oncological radicality desirable in EGC and to prevent tumoral remission in the remaining stump.

References

1. Maruyama, M.: Detecção precoce do câncer gástrico no Japão. In *Câncer do Estômago e do Intestino*