

Quantitation of Gastric Intestinal Metaplasia by Morphometry in Japanese Patients

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With the aid of an image processor, the length of the intestinal metaplasia (IM) was recorded in 33 gastrectomy specimens (23 with early gastric cancer and 10 with gastric peptic ulcer). A total of 1917 sections were analyzed. The length of the areas with IM and the total length of the muscularis mucosa were measured in individual sections. The resulting ratio (length of IM/length of muscularis mucosa) was noted as the intestinal metaplasia index (IMI), as an expression of the extension of IM in the specimens. The IMI was influenced by the age of the patient and by the histologic type of the tumor: a higher IMI was found among older patients and among patients with adenocarcinoma of intestinal type. A comparison with a similar study done in gastrectomy specimens from Swedish patients indicates that despite the latter group being older, and the tumors being more advanced, the IM was much more extended in the gastric mucosa of the Japanese patients with gastric adenocarcinomas of intestinal type. From the results it is suggested that extended IM in the gastric mucosa may have some bearing on the histogenesis of gastric carcinomas, particularly adenocarcinomas of intestinal type.

Key words: Gastric mucosa — Intestinal metaplasia — Quantification

Despite a worldwide decline in incidence of gastric carcinoma, this tumor localization remains the most frequent in the Japanese population,^{1,2)} though the reasons for this remain obscure. The histogenesis of the gastric carcinoma is still a matter of debate. Several alterations of the gastric mucosa have been found to antedate gastric adenocarcinomas, such as chronic (atrophic) gastritis,^{3,4)} intestinal metaplasia,⁵⁻⁷⁾ dysplasia^{8,9)} and intramucosal cysts.^{10,11)} One of them, intestinal metaplasia (IM), has received a great deal of attention in recent years. Despite the interest in IM as a lesion antedating gastric carcinoma, little effort has been made to quantitate the distribution of IM in the gastric mucosa. Some studies have been concerned with non-quantitative descriptions of the quality of the mucosa in gastric biopsies⁴⁾ or at autopsy.^{12,13)} Others are concerned with semi-quantitative estimates of enzymatic mucosal changes occurring in IM at the luminal aspect of the gastric mucosa.^{6,14)}

Recently we applied morphometric¹⁵⁾ and image analysis¹⁶⁾ methods to assess IM in gastrectomy specimens. This was done in order to obtain objective and reproducible results¹⁷⁾ which, in the future, will permit us to compare populations with disparate incidence of gastric carcinoma. So far, no quantitative studies have been carried out to demonstrate that populations with a high frequency of gastric adenocarcinoma have more extended mucosal areas with IM than populations with a low frequency of gastric carcinoma. In the present work, morphometry was applied to assess the length of the

gastric mucosa occupied by IM, in relation to the total length of the mucosa in gastrectomy specimens. The results were compared with similar studies carried out in specimens from Swedish nationals (unpublished data).

MATERIALS AND METHODS

From the files of the Departments of Pathology, National Cancer Center and Cancer Institute, Tokyo, 33 consecutive gastrectomy specimens having either early gastric cancer (23 cases) or benign gastric ulcer (10 cases) were analyzed. After removal, the specimens had been fixed in 10% neutral formalin for three days. After fixation, the specimens were cut into blocks measuring up to 4.5 cm in length, as illustrated in Fig. 1. The specimens were stained with hematoxylin and eosin.

Special attention was paid to the gastric mucosa occupied by intestinal metaplasia (easily recognized by the presence of medium-size vacuolated gastric cells,¹⁸⁾ by cells with brush border and/or by Paneth cells. The length of IM was assessed by the aid of an Olympus VIP 21 CH colour video image processor (Ikegami) connected to a NEC PC 8011 computer. The apparatus consists of a digitizer table connected to an electronic pen (stylus). The length of the muscularis mucosa (corresponding to the length of the area occupied by IM) was drawn by the stylus on the video screen. Each measurement was transferred to the computer. Subsequently the length of the muscularis mucosa in the whole specimen was recorded for each section. The resulting ratio (length IM/length muscularis mucosa) was recorded as the intestinal metaplasia index (IMI), expressed as percent of gastric mucosa having IM. All preparations were scanned

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using a 12 X objective. The image displayed in the TV monitor had been calibrated to express the length of IM in centimeters.

RESULTS

Histological examination The histological examination of the 33 gastrectomies revealed early gastric cancer in 23 specimens and peptic gastric ulcer in the remaining 10. Of the 23 adenocarcinomas, 14 were classified as of intestinal type and the remaining 9 as of diffuse type.

Number of slides available for review A total of 1917 sections were cut from the 33 specimens (mean number of sections/case = 58.1 sections; range 42–102 sections). In specimens having carcinoma of intestinal type, the mean number of sections was 57.2 (range 42–102), for those of diffuse type, 72.3 sections (range 45–102), and for those with peptic gastric ulcer, 46.5 sections (range 43–66 sections).

Age and sex Table I shows that the mean age in the 14 cases with early gastric cancer of intestinal type was 61.2 years (range 30–77 years), in the 9 cases of early gastric cancer of diffuse type, 51.8 (range 39–59 years), and in the 10 cases with peptic ulcer, 45.4 years (range 28–61 years). The difference between patients with early gastric

cancer of intestinal type and the other group of patients was significant ($P < 0.001$).

In patients having adenocarcinomas of intestinal type, 11 were males and 3 females, in those with diffuse type, 6 were males and 2 females and in those with benign ulcers, 7 were males and 3 females.

IMI The results are presented in Table I. Specimens having adenocarcinoma of intestinal type or diffuse type or with peptic ulcer had a wide variation in the IMI. Specimens with adenocarcinoma of intestinal type had a mean IMI of 54.4% (range 5.66%–99.73%), specimens with adenocarcinoma of diffuse type, a mean IMI of 25.5% (range 2.44%–66.19%) and those with peptic ulcer disease, a mean IMI of 15.7% (range 0%–67.17%).

IMI above 50% was found in 1 out of 9 specimens (11.1%) with adenocarcinoma of diffuse type, in 2 out of 10 (20%) with a peptic ulcer and in as many as 8 out of 14 (57.1%) of those with adenocarcinoma of intestinal type.

IMI and age The number of cases was too small to study possible difference in the extension of IMI in various age groups. From the table, however, it may be deduced that five older patients with a mean age of 66.6 years had a high IMI (above 70%), while 15 younger patients with a mean age of 49.1 years had low IMI (below 20%).

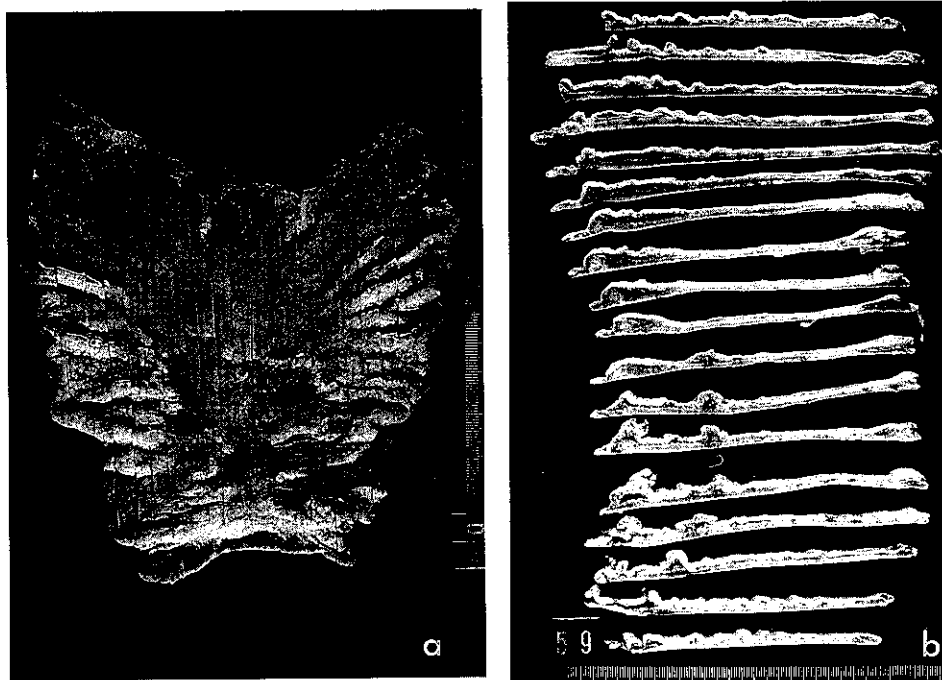


Fig. 1. (a) Gastrectomy specimen showing longitudinal sectioning of the specimen. (b) Tissue samples obtained from the same specimen for histological examination.

Table I. The Age of 33 Japanese Patients and the Intestinal Metaplasia Index (IMI) Obtained by Morphometry in Gastrectomy Specimens^{a)}

	Intestinal type ca.		Diffuse type ca.		Gastric ulcer	
	Age	IMI	Age	IMI	Age	IMI
	30	5.66	39	4.84	28	0.40
	53	15.56	40	40.13	36	18.68
	55	12.18	45	68.19	40	26.87
	59	88.67	53	48.43	40	—
	60	67.26	55	2.44	41	—
	62	69.68	57	51.20	46	59.62
	64	34.89	58	3.22	52	67.70
	65	99.73	59	9.03	54	8.97
	65	79.71	66	10.95	56	—
	65	42.48			61	0.18
	66	60.13				
	67	91.51				
	69	34.36				
	77	81.38				
Mean	61.2	54.4	51.8	25.5	45.4	15.7
(range)	(30-77)	(5.66-99.73)	(39-66)	(2.44-68.19)	(28-61)	(0-67.70)

a) Fourteen having early gastric cancer of intestinal type, 9 with cancer of diffuse type and 10 with peptic gastric ulcer.

DISCUSSION

Two parameters have been reported in the literature to influence the presence of gastric IM: the age of the patient and the histological type of the carcinoma. In fact, IM has been found to increase with increasing age,¹⁹⁾ and to be more often present in specimens with adenocarcinoma of intestinal type.⁵⁾ In those studies, however, the extension of IM was not given or was roughly estimated by semi-quantitative assessment.

By means of morphometry, we have confirmed that IM is highest in specimens containing adenocarcinoma of intestinal type rather than in specimens having adenocarcinoma of diffuse type or with peptic ulcer disease. However, when correlating the IMI with the age of the patient, it was found that patients with adenocarcinoma of intestinal type were older than patients in the other two groups. It is noteworthy that the highest IMI (i.e. above 70%) for the total material was found in older patients (mean 66.6 years) while low IMI (i.e. below 20%) was found in younger patients (mean 49.1 years). Thus, not only the histological tumor type but particularly the age, influenced the IMI in the present material.

In a recent study on the extension of IM in gastrectomy specimens in Swedish patients (unpublished data) we found that the mean IMI in adenocarcinoma of intestinal type was 45.5% (range 15.1-79.3%), in adenocarcinomas of diffuse type, 9.3% (range 2.2-10.1%),

and in gastric ulcers, 29.3 (range 14.6-69.9%). The mean age of Swedish patients with adenocarcinoma of intestinal type was 68.3 (range 34-80 years), for adenocarcinoma of diffuse type, 58.0 years (range 45-68 years), and for peptic ulcer, 59.0 years (43-75 years). Thus, both in the Swedish and in the Japanese material, patients with adenocarcinoma of intestinal type were 10 years older (mean) than the those with diffuse type adenocarcinoma, suggesting that age strongly influences the IMI. Notwithstanding, Japanese patients with adenocarcinoma of intestinal type have higher IMI than those from the Scandinavian patients with the same type of tumor. This is in spite of the fact that the Scandinavian patients were older, their tumors more advanced and the number of sections obtained per gastrectomy specimen somewhat higher than in the Japanese material. Thus, IM is more widespread in the gastric mucosa of Japanese with intestinal-type cancer than among Swedes with the same type of tumor.

In the present work we have studied IM in general. However, IM in the gastric mucosa may be subdivided histologically into complete and incomplete types,¹⁴⁾ the former having goblet cells, absorptive cells and/or Paneth cells and the latter only goblet cells. It has been claimed¹⁴⁾ that the incomplete-type IM is more often associated to gastric carcinoma.

By the method applied herein, it has not been possible to record morphometrically the two types of IM. In a

future study we will apply histochemistry¹⁵⁾ to achieve a reliable morphometric assessment of the various types of IM. This will permit us to study in more detail the topographic distribution and the possible significance of complete and incomplete IM in gastric carcinogenesis.

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