Gastric Cancer
—Prevention and Early Diagnosis—

Abstract: The morbidity rate of gastric cancer in Japan has gradually decreased and with the increase in number of early gastric cancer, post-therapeutic results have greatly improved. The factors responsible for these phenomena include the decreased incidence of gastric cancer as a result of primary prevention and early detection by secondary prevention. In terms of dietary factors, salt promotes carcinogenesis, whereas green and yellow vegetables, fruit, and green tea suppress it. It is important for the prophylaxis of carcinogenesis to consume abundant fresh vegetables and fruits and to avoid hyperchloric diet. Helicobacter pylori has been implicated in cancer cell proliferation after cancerization. The significance of mass examination for early detection is attracting much attention, but it is not economically feasible in many countries. Occult blood reaction, tumor markers, and a forward endoscope with a small diameter are superior to mass examination in making the diagnosis in terms of specificity, and they are more economical. The kind and characteristics of typical early gastric cancer cases and important points in diagnosis are outlined for the protruding type (0-I, 0-IIa), depressed type (0-IIc, 0-III), and flat type (0-IIb). In the treatment of early gastric cancer, surgical procedures for reduction, such as endoscopic mucosal resection (EMR) and partial resection of the stomach under laparoscopic observation, may be used, contributing to an improved quality of life for the patient.

Key words: Gastric cancer; Cancer prevention; Early diagnosis; Early treatment

Introduction
The incidence of gastric cancer is the highest among cancers of various organs in Japan, with approximately 100,000 people per year suffering from this form of cancer. As a result of the increased incidence of early gastric cancer and advances in therapeutic methods, the survival rate has improved, and the mortality rate associated with gastric cancer is now lower than that associated with lung cancer. The reasons for this decreased morbidity have been thought...
to include changes in the Japanese diet and methods of food preservation. Attention is being paid to the correlation between gastric cancer and *Helicobacter pylori* as well as to the secondary prevention of cancer.

In treating early gastric cancer cases, EMR laparoscopic partial resection of the stomach, and other procedures have been employed, contributing to improvement in patients’ post-operative quality of life (QOL). The prevention and early diagnosis of gastric cancer are important for QOL as well as patient outcome. If secondary cancer could be prevented post-operatively, the eradication of gastric cancer would be a distinct possibility. This article outlines the prevention and early diagnosis of gastric cancer.

### Prevention of Gastric Cancer

#### 1. Primary prevention

The procedures for gastric cancer prevention can be divided into primary and secondary types. As a result of a case-control study (CCT) of gastric cancer and a cohort study of gastric cancer patients, diet and methods of food preservation have been attracting attention as means of primary prevention. It is noteworthy that a high salt diet is correlated with gastric cancer, whereas salt itself is not carcinogenic. High concentrations of salt have been considered to disrupt the mucosal layer of the stomach to promote mucosal cell damage from gastric fluid and to cause inflammation that promotes carcinogenesis. Basic studies have revealed that vitamin C, carotenoids, and other components of green and yellow vegetables, fruit, and green tea exert an inhibitory effect on carcinogenesis via their antioxidative action.

In terms of methods of food preservation, the prevalence of refrigerators has increased the consumption of fresh vegetables and fruits. Furthermore, the indirect influences of decreased consumption of salty foods and protection of the gastric mucosa by increased consumption of cow’s milk have been considered to be related to the primary prevention of gastric cancer.

### Table 1 Preventive Factors and Risk Factors for Gastric Cancer, Which Are Related to Diet

<table>
<thead>
<tr>
<th>Preventive factors</th>
<th>Risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Certain factors</strong></td>
<td>Vegetables and fruits</td>
</tr>
<tr>
<td>The prevalence of refrigerators</td>
<td></td>
</tr>
<tr>
<td><strong>Almost certain factors</strong></td>
<td>Vitamin C</td>
</tr>
<tr>
<td><strong>Possible factors</strong></td>
<td>Starch</td>
</tr>
<tr>
<td></td>
<td>Grilled fish</td>
</tr>
<tr>
<td><strong>Inadequate evidence</strong></td>
<td>Fish</td>
</tr>
<tr>
<td></td>
<td>Selenium</td>
</tr>
<tr>
<td></td>
<td>Garlic</td>
</tr>
<tr>
<td></td>
<td>Cow’s milk</td>
</tr>
</tbody>
</table>

lation of the risk of cancer in the cardiac part of the stomach with cigarette smoking appears to be particularly high.6) It is therefore important for the prevention of gastric cancer to ingest plenty of fresh vegetables and fruits, particularly those with carotenoids and vitamin C, and to avoid the ingestion of salty foods and a hyperchloric diet (Table 1).

It is noteworthy that a correlation exists between *H. pylori* and the occurrence of gastric cancer, because *H. pylori* is involved in the development of chronic atrophic gastritis and the initial stage of gastric mucosal damage. *H. pylori* infection is present in 90% and 32% of differentiated and undifferentiated gastric cancer cases, respectively.7) Subsequent studies, however, have indicated that *H. pylori* may promote the proliferation of cancerized gastric cancer cells, based on the concept that *H. pylori* exerts a carcinogenic effect by inducing carcinogenic substances or DNA impairment of gastric mucosal epithelial cells.8) Therefore, the eradication of *H. pylori* has been thought to be effective in patients in whom the possibilities of secondary prevention of cancer and residual gastric cancer developing after gastrectomy are indicated.9)

2. Secondary prevention (early detection)

Secondary prevention means (mass) examination of cancer. X-ray photography is mainly used in mass examinations for gastric cancer, and many other medical resources have been employed. Odds ratios for mass examination of the stomach are approximately 0.3–0.6, suggesting that the mortality rate is slightly decreased by secondary prevention. Secondary prevention is generally not well suited for other countries because of its high cost. In the present situation in which the morbidity rate is decreasing annually, secondary prevention is being reconsidered.

As possible substitutes for X-ray photography of the stomach, screening and other procedures using occult blood reaction, tumor markers, and forward endoscopes with a small diameter are considered to be excellent in terms of sensibility and specificity and to be more economical.

**Diagnosis of Early Gastric Cancer**

The diagnosis of early gastric cancer is based on close examination of a high-risk group, which includes cancer medical examination. The definitive diagnosis of gastric cancer has conventionally been made by endoscopy and biopsy, as well as X-ray photography of the stomach, which is the main examination. Owing to the prevalence of forward endoscopes with a small diameter and electron scopes, the number of institutions in which endoscopic examination is the first choice even in the stage of screening is increasing. The incidence of early gastric cancer tends to increase annually and exceeds 70% in institutions where it is high. Morphologically, the incidence of type I early gastric cancer is decreasing, whereas those of type IIa, small gastric cancer (10 mm in size), Borrmann 4 type, and multiple cancers are tending to increase. Therefore, much attention should be paid to these cancer types on medical examination. Ultrasonic endoscopic examination may be employed to examine mural invasion and mural lymph node metastasis, while macroendoscopic examination may be used to predict histological type.

Representative types of early gastric cancer, their characteristics, and important points in diagnosis are described below.

1. **Protruded type of early gastric cancer (0-I, 0-IIa)**

While it is not difficult to diagnose distinctly protruded lesions (type I), greater attention is needed for only slightly protruded type IIa lesions, as they are likely to be obscured because of hyperextension. The contrast method using pigment dispersion is useful for making the diagnosis, and the following points should be examined: (1) Presence or absence of frequent occurrence, (2) elevation of lesions, (3)
size and thickness, (4) superficial properties (presence/absence of central depression, properties and size of constituent granules, and color tone), and (5) properties of the peripheral mucosa. Lesions of 2 cm or more in size are commonly malignant and show an irregular surface. They are nodular and show uneven rubor. Hemorrhage may be occasionally associated with the lesions. Lesions must be differentiated from gastric adenoma, polyp, takoibo (varioliform) erosion, intestinal metaplasia, and hyperplastic changes, but most cases of gastric adenoma are 2 cm or less in size, and the superficial granules are irregular. Most of them do not show difference in size, and have a faded color.

Adenoma has conventionally been included in the category “atypical epithelial lesion”. Many adenoma cases coexist with cancers, although adenoma is fundamentally benign. In other words, EMR and other procedures are needed for the following lesions, because it is highly likely that they will be malignant: lesions with a high proportion of protruded components, which correspond to type I early gastric cancer; lesions whose center shows a coarse structure, depressed and destructed foci, lesions of 2 cm or more in size, and lesions that show morphological changes during observation of the course. When a lesion is diagnosed as group III on biopsy, it should be carefully observed every 3–6 months.

2. Depressed type of early gastric cancer (0-IIc and 0-III)

Ulcers are associated with some type IIc lesions (UI) and not others. The incidence of UI is high. If deformation of the stomach wall, convergence of mucosal folds, and white moss are observed at the depressed site, the lesion can be diagnosed. Mucosal folds invaded with cancer are slightly more depressed than the non-cancerous mucosa, and show a moth-eaten appearance. The following findings are also observed at the end of the afferent side of the convergence of mucosal folds: discontinuity or rupture, stair-like depression, tapering off (thinning), clavate enlargement, and others. The stump of the mucosal folds is depressed inward. Of these malignant findings, the moth-eaten appearance is considered to be most reliable. The depressed site in the center frequently shows changes in which small granules with rubor, erosion with white moss, and slight bleeding coexist. When an open ulcer is associated with the depressed type, the diagnosis is difficult to make, since the histological inflammatory reaction of the ulcer obscures malignant findings and characteristic malignant findings are scarce. In such cases, the presence/absence of malignant findings needs to be confirmed at a site of peripheral mucosa distant from the ulcer.

3. Flat type of early gastric cancer (0-IIb)

Type IIb lesions are classified as single (a lesion without another lesion) or combined (a lesion accompanying another lesion). The former is difficult to diagnose, and diagnosis is made only after slight rubor, a faded color, erosion, and the depressed surface of the mucosa have been observed and an accurate biopsy has been conducted. Lesions that are difficult to differentiate from gastritis are divided according to color tone into those mainly showing rubor and those mainly showing a faded color. The former type are frequently poorly demarcated, while the latter are commonly clear. In terms of histological type, the incidence of undifferentiated cancer tends to be high in the type mainly showing a faded color, while that of differentiated adenocarcinoma is high in the type mainly showing rubor. It is important in making the diagnosis to be careful to notice X-ray photographic and endoscopic findings of only slight deformation and minute abnormal findings on the mucosal surface, which include small granular protrusions and depressed sites.

Conclusions

Among the mucosally invaded cancers (m
cancers), the following are the current indications for EMR; differentiated protruded or flat type of 2 cm or less in size; depressed type of 1 cm or less in size; and undifferentiated type of 5 mm or less in size, with which UI is not associated (−). In the case of surgery for submucosally invaded cancers (sm cancers), gastrectomy with laparoscopy conducted as a supplementary procedure and pylorus-preserving gastrectomy omitting lymph node dissection can be employed. The early diagnosis of gastric cancer is significant in that the patient’s outcome and QOL may be markedly improved by minimal surgical invasion. Primary prevention as a prophylactic measure to counteract secondary cancer may be expected from the aspect of prophylaxis of relapse and the occurrence of double cancers.

REFERENCES


