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ENDOSCOPIC MANAGEMENT
OF GASTROINTESTINAL CANCER
AND PRECANCEROUS CONDITIONS
In the last two decades digestive endoscopy has played a pivotal role in the management of gastrointestinal tumors; in more recent years the development of advanced imaging technologies and new devices for endoluminal therapy has markedly expanded both diagnostic and therapeutic indications for endoscopy in gastroenterological oncology.

Prevention of gastrointestinal tumors is today feasible by colonoscopy-based screening programs and follow-up of precancerous conditions, with a significant positive impact on cancer-related mortality. Advanced imaging technologies identify neoplasia at a very early stage and may give real time histology (optical biopsy).

New technologically-advanced devices and materials allow endoluminal therapy to treat lesions that until few years ago could only be treated by surgery, with significant improvement in hospital costs and patients morbidity, besides a significant cost-saving for the health care system, if routinely adopted in clinical practice outside referral centers. Palliation by endoscopy has a lower complication rate, compared to surgery, and improves the quality of life of patients permitting to start chemo-/radiotherapy earlier than after surgery.

Moreover, the progressive diffusion of ultrasound endoscopy in the last years had a tremendous impact in the clinical management of gastrointestinal neoplasia, allowing a proper selection of patients suitable for curative endoscopic resection, or by-pass procedures not feasible by standard endoscopy.

In this book, unique for its completeness and specificity, we have brought together the world’s top experts and asked them to address all aspects, present and future, of the endoscopic management of digestive tumors, from the advanced diagnostics to therapy, with the aim of providing the reader with the state of the art in the field and future perspectives.

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Gastric cancer remains one of the most common causes of death by cancer worldwide. A mortality rate of gastric cancer is showing a decreasing trend, which depends on the proportion of early stage cancers. Survival of patients with early gastric cancer (EGC) is excellent so early detection is essential to provide a more favorable prognosis. In Japan, approximately 50% of gastric cancer cases currently treated are early stage disease. EGCs that have a negligible risk of lymph node metastasis are treated endoscopically and excellent long-term outcomes of endoscopic submucosal dissection for them have been reported. This chapter addresses endoscopic diagnosis of EGC.

**PREPARATION**

EGC is usually characterized by subtle changes on the mucosal surface, especially in intramucosal cancer. However, most patients with gastric cancer have atrophic gastritis due to *Helicobacter pylori* infection and some of them have much mucus on the surface of the stomach, disturbing a detailed observation. Therefore a thorough preparation is essential to keep good quality in routine esophagogastroduodenoscopy as in colonoscopy. Patients are asked to drink a solution containing 100 mL of water, 4 mL simethicone (Gascon; Kissei Pharmaceutical Co, Matusmoto, Japan), 2 g sodium bicarbonate (Yoshida Pharmaceutical, Tokyo, Japan) and 40,000 IU Pronase MS (Kaken Pharmaceutical Co, Tokyo, Japan) ten minutes prior to esophagogastroduodenoscopy at our unit in the National Cancer Center Hospital.

**DETECTION AND CHARACTERIZATION OF EARLY GASTRIC CANCER**

### White light endoscopy

White light endoscopy (WLE) is the primary modality to detect gastric cancer. During endoscopy, adequate air insufflation is necessary particularly to detect lesions located between folds. Mucus and bubble on the mucosal surface should be completely washed out after administration of water with simethicone. If necessary Pronase MS can be added. EGC is usually detected by a subtle mucosal change such as a reddish or discolored area, slightly depressed or elevated change in the mucosa, or loss of the lucent vascular pattern in white light imaging (Figure 1.1A).

Histological type correlates with the tumor location and endoscopic features. Most differentiated-type EGCs are located in an atrophic area. They are either depressed lesions that are reddish or elevated lesions that are either reddish or discolored. Most undifferentiated-type EGCs are located either in a non-atrophic area or near an
atrophic border. They are usually depressed lesions that are discolored.

**Chromoendoscopy**

0.2% indigo-carmine dye solution enhances contrast where a slight elevation or depression exists by pooling on the depressed mucosal surface. Sometimes it is difficult to detect EGC and recognize its demarcation by WLE only. Chromoendoscopy using indigo-carmine dye enables to identify EGCs better than WLE. Furthermore, it is helpful to visualize the demarcation by highlighting the mucosal pattern (Figure 1.1B). Currently in Japan, chromoendoscopy is routinely used in EGDs not only for preoperative purposes but also for screening.

Most of the EGCs can be well visualized by chromoendoscopy, however the demarcation of some lesions is still indistinct even after spraying indigo carmine and it is difficult even for expert endoscopist to delineate the margins. Recently, the efficacy of spraying a mixture solution of acetic acid-indigo carmine (6% acetic acid with 0.4% indigo carmine, AIM) was reported to clarify the margin between cancerous and non-cancerous mucosa. The duration of the acetic acid-induced whitening is different between cancerous mucosa and non-cancerous mucosa. In addition, the cancerous area has considerably more mucus than that of the non-cancerous area. A clear contrast between them would become evident by the difference in color and mucus (Figure 1.2). The AIM spraying method was reported as having a higher accuracy in terms of gastric cancer demarcation compared to WLE or chromoendoscopy.

**Narrow banding image magnifying endoscopy**

Narrow band imaging (NBI) is a novel optical image-enhancement modality that highlights the microvascular (MV) architecture and the microsurface (MS) pattern of the gastric superfi-
Early gastric cancer

NBI-ME can distinguish non-cancerous from cancerous lesions. A multicenter randomized controlled trial was conducted comparing on-site diagnostic yield of WLE for small and depressed gastric mucosal cancers with that of NBI-ME. This study showed that the accuracy and specificity of NBI-ME group was significantly higher than with WLE (90.4% vs. 64.8% (P <0.001) and 94.3% vs. 67.9% (P <0.001), respectively). In addition, the combination of NBI-ME with WLE significantly improved performance compared with WLE alone. NBI-ME is also useful to diagnosis superficial mucosa. According to Yao’s vessel plus surface classification system, the characteristic magnifying endoscopy (NBI-ME) findings of EGC are: a clear demarcation line between non-cancerous and cancerous mucosa, and an irregular MV pattern and/or irregular MS pattern within the demarcation line. In the irregular MV pattern, the vessels are closed-looped (polygonal), open-looped, tortuous, branched, or bizarrely shaped, with or without a network, and have a heterogeneous morphology, asymmetrical distribution and irregular arrangement. In irregular MS pattern, the marginal crypt epithelium is an irregular linear/curved/oval/circular/villous structure with a heterogeneous morphology, asymmetrical distribution and irregular arrangement (Figure 1.3).

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lineate the lateral margins of an EGC, including an indistinct one even after indigo carmine spraying. It contributes to optical endoscopic diagnosis and to minimize the number of biopsies. Furthermore, NBI-ME can predict the histological type of EGC to a certain extent based on the vascular pattern inside the lesion. Generally, differentiated-type EGC is suspected with the presence of a fine-network pattern (Figure 1.4A). The network structure is mostly destroyed and shows a corkscrew pattern in undifferentiated-type EGC (Figure 1.4B). Although the MV pattern did not fit in either of these two categories in approximately one third of the cases, this classification can determine the treatment modality for a lesion which has either of two vascular patterns.

NBI-ME enables to make an accurate diagnosis and appropriate judgments for treatment in patients with EGC. However, NBI-ME is less useful in undifferentiated-type EGC to identify the lesion’s lateral margins, because cancer cells invade along the proliferative zone covered with normal epithelium and NBI-ME can’t detect any cancer specific irregular MV or MS pattern in them. Biopsy specimens reaching the muscularis mucosae and 5 mm away from the lesion margin should be taken in order to determine the lateral margins before treatment.

**Prediction of depth of invasion**

Endoscopy is the first choice diagnostic modality for diagnosing gastric cancer, but it can also be helpful in determining the depth of invasion. Endoscopic features such as tumor size larger than 30 mm, remarkable redness, uneven surface, and margin elevation are associated with deeper submucosal cancers in differentiated-type EGC. However endoscopic visualization is somewhat subjective and many endoscopists diagnose based on their own experiences. A simple depth predictive scoring system model to estimate invasion depth of EGC more accurately and objectively is needed. There is very few data of NBI-ME to assist in the prediction of depth of EGC. Further investigation is therefore required to create a consensus for better judgment of EGC invasion depth.

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