

Digestive Endoscopy and Gastrointestinal Oncology Division

Introduction

The Digestive Endoscopy and Gastrointestinal Oncology Division covers a range of research fields: endoscopic diagnosis and treatment, chemotherapy, and palliative care for patients with head and neck, esophageal, gastric, and colorectal cancer. Much of the research is carried out as prospective studies, either at single institutions or in collaboration with other institutions. The division's research mainly focuses on the development of new instruments in endoscopic diagnosis, new endoscopic treatment and new anti-cancer agents as well as new combinations with/without radiation therapy.

Research Activities in Digestive Endoscopy

A new instrument, narrow band imaging system (NBI), combined with magnifying endoscopy, has had a major impact in the field of endoscopic diagnosis. This system can visualize a unique image that emphasizes the capillary pattern and the structure of mucosal surfaces. Significant contributions to the clinical development of this system have been made by our division with support from a Grant for Scientific Research Expenses from Japan's Health and Welfare Program. This system is now indicated for diagnosis of head and neck, esophageal, and colorectal cancers. In 2006, three articles were published by our division that clarified its usefulness in differential diagnosis between neoplastic and non-neoplastic lesions with high rates of accuracy (6, 7, 8). These progresses also provided earlier detection of cancers, particularly in depressed-type early colorectal cancers (9-13). Based on these promising results, prospective multi-institutional studies are now under way in

the fields of head and neck, esophagus and colorectal cancer to confirm the efficacy of this system in screening examinations. Carcinogenesis of the head and neck and esophageal carcinoma is another target in this research field, in collaboration with the National Cancer Center Research Institute (14).

Endoscopic submucosal dissection (ESD) is now routinely indicated for early gastric cancer. A nationwide survey of endoscopic resection, including conventional EMR and ESD, was carried out in 2006. It revealed the advantages of ESD in lower recurrent rate with a 3-year survival rate of 99.2% (15). ESD is now being applied to the treatment of early colorectal cancers (16, 17). There have been some new developments in endoscopic treatments for esophageal cancer. Salvage EMR and photodynamic therapy (PDT) for local residual/recurrent tumors after chemoradiotherapy are now performed, and a prospective study to evaluate feasibility and efficacy of salvage PDT is now under way.

Research Activities in Gastrointestinal Oncology

There are numerous ongoing prospective clinical trials in the oncology field, which are mainly targeted for IND registration trials. The final results of several studies were published in 2006 (18-21). Of note, one biological study in an international phase II study of gefitinib for gastric cancer revealed that pAkt may play a critical role in response to gefitinib therapy (22). Another nationwide prospective study of chemotherapy and radiotherapy for gastric lymphoma, which was led by our institution, revealed that Epstein-Barr virus involvement is a predictive factor for

resistance to chemoradiotherapy (83). Two review articles regarding chemotherapy for advanced gastric cancer, particularly in disparities between Japan and Western countries, have been published in high quality journals (23, 24).

Translational research is another challenging field in therapeutic development. To investigate the possibility of HER2 targeted agents in the treatment of gastric cancer, HER2 expression in surgically resected specimens and biopsy samples was analyzed by immunohistochemistry and fluorescence in situ hybridization (81). This retrospective study revealed a HER2 overexpression rate of around 20%, which is considered to be comparable to that in breast cancer. Based on these results, an international randomized controlled trial, evaluating the efficacy of trastuzumab for advanced gastric cancer, has been initiated. An array-based analysis to investigate predictive markers for chemoradiotherapy in patients with esophageal cancer was also published (25). This study suggested possible candidate genes that can predict patients' prognoses. This was followed by an ongoing prospective confirmatory study in patients with stage II-III esophageal cancer treated with chemoradiotherapy.

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