JGA Keynote Program
The 2nd International Gastrointestinal Consensus Symposium (IGICS)

GERD Including NERD

February 13, 2009, Tokyo, Japan
www.b-comm.gr.jp/5jga/igics

Guest Editor
Shin’ichi Takahashi, Tokyo

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Outline

The 5th Annual Meeting of the Japanese Gastroenterological Association
JGA Keynote Program
The 2nd International Gastrointestinal Consensus Symposium (IGICS)

Date  February 13 (Fri.), 2009
Time   08:40–17:00
Venue  Keio Plaza Hotel, Tokyo Japan
Topic  Concerning about GERD Including NERD

IGICS Committee Members
JGA International Exchange Committee Members
Shin’ichi Takahashi, Japan (Chairperson of the 2nd IGICS)
Tetsuo Arakawa, Japan
Takashi Joh, Japan
Yoshikazu Kinoshita, Japan
Takayuki Matsumoto, Japan
Yuji Naito, Japan
Koji Takeuchi, Japan

IGICS International Active Members
Ki-Baik Hahm, Korea
Udom Kachintorn, Thailand
Abdul Aziz Rani, Indonesia
Jose D. Sollano, Philippines
Qi Zhu, China
Dear Colleagues,

It is our great pleasure to announce that we will hold the 2nd International Gastrointestinal Consensus Symposium (IGICS) on February 13 (Fri.), 2009 in Tokyo as a JGA Keynote Program in the 5th Annual Meeting of the Japanese Gastroenterological Association (February 12-13, 2009, President: C. Sakamoto).

This symposium began in 2008. The focus of IGICS is to be held as a single-topic conference in which discussions are made on a single topic throughout the conference day. The topic for the 2nd IGICS is “Concerning GERD including NERD”. Although we have numerous GERD patients, and despite its being a common disease globally, we do not know the prevalence of GERD in Asian countries. Moreover, several new issues regarding GERD, such as pathogenic mechanism, diagnostic guideline, therapeutic algorithm and prevention method, have been uncovered, and need to be addressed. In this symposium, we will have 2 special lectures, 1 special talk, 22 oral presentations, and 14 poster presentations. We hope to clarify the reality of these issues from basics to bedside, especially in Asian countries, and to discuss similarities and differences among them.

The intent of this symposium is to foster the academic development of young gastroenterologists from Asian countries and to increase collaboration on an international level. It is our sincere hope that you will be able to attend the symposium, as we believe it will be greatly enriched by your active participation in the discussion. We will provide IGICS awards for several excellent papers presented by young investigators.

We sincerely look forward to seeing you in Tokyo in February 2009.

With kind regards,

Shin’ichi Takahashi
Chairperson of the 2nd IGICS
### Program

**Friday, February 13, 2009**

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Dr. Shin’ichi Takahashi, Kyorin University School of Medicine, Japan
Special Lectures

Special Lecture 1
Chairperson: Tetsuo Arakawa

SP-1
GERD, NERD and Barrett’s Esophagus
K.M. Fock
Changi General Hospital, Singapore

Although gastroesophageal reflux disease (GERD) is less common and milder in endoscopic severity in Asia when compared with US and Europe, there is nevertheless data to suggest the increase in frequency of this disease. This could be due to changing socioeconomic conditions in the region as well as increasing awareness of the condition. Since the publication of the Asia Pacific Consensus in 2004, heartburn has been translated into the local language in Asia and patients and doctors are increasingly aware of the significance of GERD symptoms. Epidemiological data shows that non-erosive reflux disease still constitute the majority of the cases encountered.

NERD is defined as troublesome reflux symptoms in the absence of esophageal mucosal damage on endoscopy, but to translate this definition into clinical practice is easier said than done. This is because heartburn, a cardinal symptom in GERD patients has a high positive predictive value for the diagnosis of GERD but low sensitivity. The first structured questionnaire used in the assessment of GERD has a sensitivity of 92% but a specificity of 19%. More recent questionnaires, such as ReQuest has been internationally validated for use in patients with NERD, have shown high internal consistency and content validity. These structured instruments make symptom recognition in NERD patients more accurate and reproducible.

A positive PPI has been suggested as a test to lend greater confidence to the diagnosis of NERD. This test suffers from two disadvantages: lower response rate of NERD to PPI compared with GERD patients and meta-analysis of PPI test revealed that combined estimates of sensitivity and specificity were 0.78 and 0.54. These values while acceptable are lower than expectations.

Ambulatory pH studies were initially thought to be diagnostic in NERD patients. However, study shows that only 45% of NERD patients have a positive pH study. Ambulatory pH-impedance monitoring has been used in NERD patients who have persistent symptoms. At least two initial studies have shown pH-impedance studies could identify about 40% NERD patients as suffering from reflux disease based on impedance/pH criteria.

Dilated intercellular spaces in esophageal biopsy was seen under electron microscopy. As EM is expensive and difficult to perform, light microscopy has been investigated as a possible diagnostic criteria for NERD. DIS was found in 68-100% of NERD patients and in 14-30% depending on whether EM or LM was used.

Another endoscopic technique, Narrow Band Imaging (“NBI”) endoscopy which could provide clearer visualization of squamoco-

Special Lecture 2
Chairperson: Yoshikazu Kinoshita

SP-2
Research on Acid-Peptic Diseases in Asia: What Lies beyond the Horizon?
Francis K.L. Chan
Department of Gastroenterology & Hepatology, The Chinese University of Hong Kong

For decades, research on acid-peptic diseases in Asia had been limited by the narrow disease spectrum and inadequate resources of the region. The true magnitude of many important clinical observations could not be evaluated because of a lack of large-scale, systematic data collection. Investigator-initiated clinical trials for assessing treatment strategies were uncommon. As a consequence, many Asian countries have adopted clinical practice recommendations from western countries. However, there is emerging evidence that some of these western guidelines may not be applicable in Asia. Recently, the outcomes of several landmark Asian studies not only changed the regional clinical practice but also rewrote certain recommendations in western countries. With increasing westernization of acid-peptic diseases in Asia, conditions such as gastroesophageal reflux disease, nonsteroidal anti-inflammatory drug-induced gastrointestinal toxicity, and H. pylori-negative idiopathic ulcers are increasingly recognized. Acid-peptic research in Asia is likely to make an impact on global clinical practice. To meet this exciting challenge, we need to identify common goals on important research questions, establish multi-national systematic data collection, and train our fellows to conduct clinical trials according to international standards.
Oral Sessions

Oral Session 1: Epidemiology
Chairpersons: Takashi Joh, Abdul Aziz Rani

O-1-1
Impact of Relationship between H. pylori Infection and Reflex Esophagitis in Japan
Takashi Kawai, Mokinori Kataoka, Tetsuya Yamagishi, Kenji Yagi, Kohei Kawakami, Yoshihiro Sakai, Fuminori Moriyasu, Yu Takagi, Tatsuya Aoki

1Endoscopy Centre, Tokyo Medical University Hospital, Tokyo, 24th Department of Internal Medicine, Tokyo Medical University, Tokyo, 3rd Department of surgery, Tokyo Medical University, Tokyo, Japan

Introduction: H. pylori infection rate has been reported to be high in people over the age of 40, but has been decreasing among younger people. H. pylori infection has also been negatively associated with reflex esophagitis (RE). We examined the H. pylori infection rate and correlation of H. pylori infection with RE.

Methods: The subjects were 418 patients who received upper gastrointestinal endoscopy (UGIE) and had their serum IgG H. pylori antibody examined during a health check. The mean age of the patients was 39.2±8.3 (range 22-58 years). We investigated UGIE findings reference to RE (LA classification: A, B, C, D).

Result: Total H. pylori infection rate was 33.5% (140/418). Infection rates were 15.7% in the age 20-29, 28.0% in the age 30-39, 34.3% in the age 40-49 and 69.1% in the age 50-59. The percentage of RE among those subjects with H. pylori-negative was 23.4% (22.9% in age 20-29, 31.7% in age 30-39, 32.4% in age 40-49 and 41.7% in age 50-59), which was significantly higher than the percentage (12.1%) of RE among those with H. pylori-positive (0% in age 20-29, 16.7% in age 30-39, 12.2% in age 40-49 and 10.5% in age 50-59). In H. pylori-negative patients severity of RE didn’t become worse inspite of ageing, on the other hand in H. pylori-positive patients severity of RE became worse with ageing

Conclusion: In this study increase in RE was recognized with H. pylori-negative patients. On the other hand, it is possible that H. pylori infection influence on advance of severity of RE.

O-1-2
Characteristics of Erosive Esophagitis in Patients Taking Low-Dose Aspirin
Takatsugu Yamamoto, Koichiro Abe, Kengo Hattori, Taro Ishii, Yasushi Kuyama

Department of Internal Medicine, Teikyo University School of Medicine, Tokyo, Japan

Introduction: Low-dose aspirin (LDA) is widely used for prophylactic purpose against atherothrombotic diseases. This medicine is also a risk for gastrointestinal mucosal injury. Recent reports suggest that erosive esophagitis develops frequently in LDA users. However, clinical information remains insufficient regarding Japanese population. We conducted the present study to investigate the prevalence of erosive esophagitis in patients taking LDA.

Methods: From all patients undergoing esophagogastroduodenoscopy at our institute from January 2005 through December 2006, 530 patients (295 males and 235 females) having taken LDA more than one month prior to the examinations were selected as study subjects. The endoscopic findings were retrospectively reviewed to evaluate the presence or absence of erosive esophagitis. The Los Angeles classification was used for evaluating severity of esophagitis.

Result: Erosive esophagitis was found in 42 patients (7.9%, 22 males and 20 females). Of these, 36 had mild esophagitis (Grade A and B) and 6 did severe esophagitis (Grade C and D). Four of 6 with severe esophagitis were female and 4 were older elderly patients over 75 years. Concomitant administration of proton pump inhibitors was confirmed in 216 patients (40.7%).

Conclusion: Among the present subjects, the prevalence of erosive esophagitis seems not so high as reported earlier. One possible reason for the difference is co-administration of acid suppressants. It was interesting that the rate of severe esophagitis seemed higher in older elderly patients than younger subjects.

O-1-3
Epidemiologic Study of Gastroesophageal Reflux Disease Symptoms in South China
Xiong Lishou, Chen Minhu, Lin Jinkun, Hu Pinjin

Department of Gastroenterology, the First Affiliated Hospital, SunYat-sen University, Guangzhou, China

Introduction: Data on the epidemiology of gastroesophageal reflux disease (GERD) in South China are rare. It’s estimated that up to 50%-70% of patients with typical symptoms of GERD have a normal endoscopy (non-erosive reflux disease, NERD). This study
was intended to assess the population-based prevalence of GERD symptoms in South China and its impact on health-related quality of life, and to explore the stratification and symptom characteristics of the consecutive patients with non-erosive reflux disease (NERD) in clinic.

Methods: A face-to-face interview was carried out in South China using a validated Chinese version Reflux Disease Questionnaire to assess the prevalence of GERD symptoms. Random clustered sampling of permanent inhabitants aged 18 to 90 years was carried out under stratification of urban and suburban areas. The impact of GERD symptoms on health-related quality of life was evaluated using the Chinese version of SF-36. Then, the patients with typical heartburn and/or acid regurgitation symptoms were enrolled to fill out a questionnaire and undertaken an upper gastrointestinal endoscopy, followed by ambulatory 24-h esophageal pH monitoring.

Result: (1) A total of 3338 residents (male 1468, female 1870) were investigated. Mean age among the responders was 42.6±16.4yr. Response rate was 95%. The prevalence of heartburn and/or acid eructation at least weekly episodes was 6.2%. The age-and-gender adjusted point prevalence of GERD symptoms in South China is 2.3%(95%CI, 1.8%, 2.8%) according to the definition in this study. There was no difference in prevalence between male (2.6%) and female (2.4%). There was no significant association between age and prevalence of GERD symptoms. Body mass index was not associated with GERD symptoms. The suburban inhabitants reported more GERD symptoms. As compared with the general population, subjects with GERD symptoms experienced considerable impairment in health-related quality of life. (2) Eighty-two consecutive NERD patients were collected. Abnormal (NERD pH+) and normal (NERD pH-) 24-h pH test were found in 24 (29.3%) and 58 (70.7%) patients, respectively. Among the 42 NERD pH+ patients who reported heartburn symptoms during monitoring, SI was positive in 19 (45.2%) patients and negative in 23 (54.8%) patients. There were no significant differences of the prevalence of other upper gastrointestinal symptoms except acid regurgitation between NERD pH+ and NERD pH- groups.

Conclusion: The prevalence of GERD symptoms in South China was much lower than that reported in the western countries. It had a negative impact on health-related quality of life. NERD may be a heterogeneous disease, but the proportion of NERD patients with pathological acid reflux was relatively lower than that reported in western countries.

0-1-4
The Prevalence of Gastroesophageal Reflux Disease in Outpatients in China and the Characteristics of Reflux Symptoms in Patients with GERD
Junying Xu, Xuelian Xiang, Xiaohua Hou
Department of Gastroenterology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China

Introduction: The reflux disease questionnaire (RDQ) is a short, patient-completed instrument; using to diagnose gastroesophageal reflux disease (GERD) in primary care. The aim of this study was to investigate the prevalence of GERD in outpatients of department of gastroenterology according to RDQ in China and evaluate the characteristics of reflux symptoms in patients with GERD.

Methods: A face-to-face interview was carried out in 1636 outpatients of GI department aged 13 to 91 years in three hospitals in Wuhan, Hubei Province using a validated Chinese version RDQ and other items recording the demographic characteristics to assess the prevalence of GERD. Subjects were defined as having GERD according to the RDQ score (> 12).

Result: The prevalence of GERD in outpatients was 10.8% (176 of 1636). There was no difference in prevalence between male (11.0%) and female (10.5%), the prevalence in elder patients (age > 60 yr.) was higher than in younger (14.6% vs. 9.8%, p < 0.05). Among GERD symptoms, heartburn and acid reflux were very common symptoms, the prevalence of acid reflux, heartburn, substernal pain and regurgitation was 85.8%, 78.4%, 63.1% and 57.4% respectively. The frequency of reflux symptoms was more important in diagnosis of GERD than the severity of symptoms, in GERD patients, the symptoms score according to frequency was significantly higher than that according to severity (9.4±2.6, vs. 7.2±2.6, p = 0.001).

Conclusion: There is a high prevalence of GERD in outpatients of GI department. Heartburn and acid reflux are most common symptoms in GERD patients. The frequency of reflux symptoms is more important than the severity of symptoms in diagnosis GERD.

0-1-5
Heavy Smoker and Using of Non Steroidal Anti-Inflammatory Drugs (NSAIDs) Are Independent Risk Factor for Erosive Reflux Esophagitis among Indonesian Patients Undergoing Upper Gastrointestinal Endoscopic Examination
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Background: It is presently not fully understood which risk factors contribute to the occurrence of erosive reflux esophagitis among Indonesian patients. The aim of this study was to analyze the spectrum and risk factors of erosive reflux esophagitis based on presenting endoscopic findings.

Methods: Patients from gastroenterology clinic who had undergone upper gastrointestinal endoscopy were recruited into a case-control study. A total of 45 patients with and 90 patients without endoscopically diagnosed erosive reflux esophagitis were categorized as case and control subjects. Using multivariate logistic regressions for statistical analysis, the presence of erosive reflux esophageal served as outcome variable. Demographic characteristics, body mass index, using of non steroidal anti inflammatory drugs (NSAIDs) and medication that decreasing lower esophageal sphincter, consumption of alcohol and cigarettes, and the presence of hiatus hernia server as predictor variables.
**Results:** We evaluated 135 patients which had done gastrointestinal endoscopy, 48 % were male and 52 % were female, with mean age was 43.7 year (SD ± 14.13) and mean body mass index (BMI) was 22.48 kilograms (SD ± 4.10). From 45 patients with erosive reflux esophagitis, we found grade A 20.7 %, grade B 8.1 %, grade C 2.2% and grade D 2.2%. Age ≥ 45 years, male, hiatus hernia, consumption of alcohol, body mass index ≥ 25 kilograms were no significant. We found heavy smoker (OR 11.52 95%CI 3.78-35.10) and using of NSAIDs (OR 3.89 95%CI 1.44-10.53) as independent risk factors.

**Conclusions:** Heavy smoker and using of non steroidal anti inflammatory drugs (NSAIDs) were associated as a strong risk for developing erosive reflux esophagitis.

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**O-1-6**

**A Prospective Multicenter Study on the Prevalence and Symptoms of Erosive Reflux Esophagitis in Secondary and Tertiary Hospitals in Korea**

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**Introduction:** Recent studies suggest that erosive esophagitis (EE) is increasing in Asia. The aims of this study were to determine the prevalence of EE among outpatients visiting gastroenterology clinics of secondary and tertiary hospitals in Korea, and to analyze their symptoms.

**Methods:** From May to July 2003, outpatients undergoing their first upper gastrointestinal endoscopies after visiting gastroenterology clinics in Korea was enrolled. Prevalence of EE was calculated from their endoscopic findings and symptoms were analyzed from the validated symptom questionnaire.

**Results:** Among 4462 cases from 24 hospitals, 523 (11.7%) had EE. Among 879 cases with predominant typical GERD symptoms, EE was diagnosed in 146 (16.6%). Among 558 cases having predominant typical GERD symptoms with a frequency of at least twice a week or with a significant impact on their daily lives, EE was found in 107 (19.2%). EE was positively associated with male gender, old aged (≥65 years) female, predominant typical GERD symptoms at least twice a week, and the numbers of typical GERD symptoms. Severity of GERD symptoms was not associated with higher prevalence of EE. The most common typical and atypical GERD symptoms in cases with EE were regurgitation and epigastric soreness, respectively.

**Conclusions:** The prevalence of EE among outpatients visiting gastroenterology clinics in Korea was 11.7%. Independent factors associated with increased prevalence of EE were male gender, old age females, number of typical GERD symptoms, and frequent typical GERD symptoms.

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**O-2-1**

**Involvement of NK-1 Receptor in the Development of Chronic Dyspeptic Symptoms in a Rat Chronic Acid Reflux Esophagitis Model**

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**Introduction:** We previously reported that a rat with reflux esophagitis (RE) decreased their voluntary movement, which could be a measure of chronic visceral symptoms. However, what mediates these symptoms is still unknown, and pain related neuropeptides or their receptors in esophageal mucosa are possibly related to generation of symptoms of esophagitis. In this study, we investigated the role of NK-1 as a mediator of the esophageal symptoms.

**Methods:** Eight-week aged male Wistar rats were used in this study. Chronic acid RE was experimentally induced by ligation of the transitional region between the forestomach and the glandular portion; duodenal stenosis was achieved by wrapping the duodenum. Degree or severity of esophageal symptoms was evaluated by assessing the voluntary movements, which were monitored by infrared sensor system for 10 days. NK-1 receptor antagonist, L-732,138, was administered every day (15, 50mg/kg/ twice daily, sc) and change of the voluntary movement was assessed. Ten days after the operation, rats were sacrificed to examine the esophageal mucosa. NK-1 receptor and Tachykinin-1 (precursor gene of Substance P) mRNA were detected by real-time RT-PCR. NK-1 receptor protein expression was examined by Western blotting.

**Result:** Esophageal erosions and/or ulcers were found in all the rats with RE at day 10, and not seen in sham operated rats. Expression of NK-1 protein and mRNA in esophageal mucosa was significantly increased both at erosive and non-erosive site. Tachykinin-1 mRNA expression at non-erosive esophageal mucosa was significantly increased in esophagitis rats. Voluntary movement of the esophagitis model rats was significantly lower than that of the sham-operated rats at day 10. The voluntary movement of esophagitis rats was significantly increased by administration of L-732,138.

**Conclusion:** Generation of dyspeptic symptoms of reflux esophagitis may be mediated by NK-1 receptor and related neuropeptides.
**O-2-2**

**Interaction between Reflux Esophagitis and Bronchial Asthma in Rats**

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**Introduction:** Several studies reported a strong association between reflux esophagitis (RE) and bronchial asthma (BA). The precise mechanisms of interaction between RE and BA are uncertain, possibly due to lack of animal models.

We established a novel rat model and examined pathogenic interaction of RE and BA.

**Methods:** RE and BA were induced in Brown-Norway rats by ligating the transitional region between the forestomach and the glandular portion and wrapping the duodenum near the pylorus, and by ovalbumin (OVA) sensitization and challenge with OVA aerosol. Rats were divided into four groups: control, RE, BA, and RE+BA. OVA-induced airway inflammation was assessed by the number of infiltrating cells and cytokine levels in bronchoalveolar lavage fluid (BALF). Esophageal lesion index, histology and expression of cytokine mRNA, as determined by real-time RT-PCR, were also examined.

**Result:** Significant increases in the number of cells, especially eosinophils, and IL13 but not IFN-gamma concentration in BALF were observed in the RE+BA group compared with the BA group. These enhancements of OVA-induced airway inflammation were prevented by treatment with rabeprazole. Although the esophagitis lesion index in the RE+BA group did not differ from that in the RO group, eosinophilic infiltration in the esophageal submucosa and levels of mRNA expression of cytokines such as IL5, IL10, IL13, and RANTES were significantly increased.

**Conclusion:** We established a novel rat model of RE and BA, and found significant interactions of the two diseases. This model thus appears to be useful for examining the association between gastroesophageal reflux disease and bronchial asthma.

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**O-2-3**

**Role of TRPV1 Expression Associated with Nerve Growth Factor in the Esophageal Visceral Sensitivity**

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**Introduction:** Recently, acid–sensing receptors such as a transient receptor potential vanilloid receptor subtype 1 (TRPV1) have been proposed to contribute to the occurrence of acid-related symptoms in gastroesophageal reflux disease including non-erosive reflux disease (NERD). In addition, neuropeptides such as substance P and CGRP are well known to be involved in the pain perception in various organs. It has been also reported that nerve growth factor (NGF), which is produced by inflammatory cells or mast cells, increase the expression of TRPV1 and neuropeptides in the dorsal root ganglion (DRG). The aim of the present study was to determine interaction between acid-sensing nociceptors and neuropeptides in the esophageal mucosa and DRG in rats.

**Methods:** Under pentobarbital anesthesia, 6 Fr catheter with balloon was orally inserted into the esophagus of Wister rats, and hydrochloric acid (HCl, pH1.0) or physiological saline was injected through the lateral hole of catheter and was pooled into the lower esophagus by inflating the balloon at stomach for ten minutes. Some rats were administered TRPV1 antagonist (capsazepine) intravenously before HCl infusion. Three hour later, TRPV1, NGF and substance P contents in both esophageal mucosa and DRG were assessed by real-time RT-PCR, western blotting and ELISA.

**Result:** TRPV1 mRNA and protein level in both the esophageal mucosa and DRG were significantly increased in HCl group compared with control group. NGF and substance P protein level in both the esophageal mucosa and DRG were also significantly increased in HCl group compared with control group. Increased substance P level, but not NGF level, was significantly inhibited by the pretreatment with capsazepine.

**Conclusion:** These results suggest that the increased expression of TRPV1 and substance P is associated with NGF produced by acid exposure to the esophageal mucosa.
Introduction: Human esophageal epithelium is always exposed to physical stimuli or acid that sometimes cause inflammation of mucosa. Transient receptor potential vanilloid 1 (TRPV1) is a sensory neuron–specific ion channel activated by capsaicin, heat and protons. Reaently it has been reported that TRPV1 is expressed in esophageal mucosa and their activation is involved in GERD or NERD and to examine its diagnostic and clinical impact.

Methods: TRPV1 protein of HET-1A was determined by Western blot analysis using biotin-labelled cystein and anti-HNE monoclonal antibody, HNE-modified proteins were determined by Western blot analysis and immunoreactivity. Interleukin-8 (IL-8) production in HET-1A cells stimulated with capsaicin.

Result: TRPV1 was expressed on the membrane of HET-1A. TRPV1 protein was recognized on 100KD by Western blot. Capsaicin induced IL-8 production from HET-1A in a dose dependent manner, and its production was diminished with antagonists of TRPV1, capsaizepine and ruthenium red. Intracellular ROS levels and ROS- and HNE-modified proteins were increased after the stimulation with capsaicin. Moreover, preincubation with synthetic HNE enhanced IL-8 production in HET-1A cells stimulated with capsaicin.

Conclusion: TRPV1 is expressed in not only sensory nerve of esophageal mucosa but also esophageal epithelium. TRPV1 on esophageal epithelium cells has the function of chemokine production, and that function might be regulated by ROS via the post-translational modification of TRPV1.

Introduction: It is unclear which mechanisms play a predominant role in the pathogenesis of noncardiac chest pain (NCCP). A high-frequency intraluminal ultrasound (HFIUS) is considered to be the most effective technique to evaluate esophageal longitudinal muscle. The aim of this study was to evaluate the esophageal muscle and peristaltic contraction using conventional HFIUS in NCCP patients, and to examine its diagnostic and clinical impact.

Methods: Fifty-eight patients with NCCP and 16 asymptomatic controls were enrolled. The upper gastrointestinal evaluations including endoscopy, manometry, and 24-h esophageal pH monitoring were assessed. NCCP patients were classified into two groups, as gastroesophageal reflux disease (GERD)-associated NCCP and non GERD-associated NCCP according to erosive esophagitis by endoscopy and/or pathologic acid exposure by 24-h pH monitoring. We recorded muscle thickness and cross sectional area (CSA) at 3 cm and 9 cm above LES during baseline rest and peak contraction, and evaluated the esophageal contractility by wet swallowing using HFIUS.

Result: Twenty-four (41%) were diagnosed with GERD-associated NCCP. On manometric examination, esophageal motility disorders were found in 24 patients. Eighteen had ineffective esophageal motility, five had nutcracker esophagus, and one had achalasia. On HFIUS finding, esophageal muscle thickness was observed to be greater in non GERD-associated NCCP group (n=34) than GERD-associated NCCP (n=24) or control (n=16), but there was not significantly different. However, muscle thickness was significantly increased in all five patients with nutcracker esophagus and one patient with achalasia. In one achalasia patient, CSA was more increased than in nutcracker esophagus patients and no peristalsis existed.

Conclusion: Conventional HFIUS can be valuable in patients suspected to be esophageal motility disorder such as achalasia and nutcracker esophagus in NCCP patients, though it may be limittedly helpful to differentiate GERD from NCCP at the clinical setting. Furthermore, prolonged monitoring and automatic analysis on HFIUS may be warranted.
Oral Session 3: Diagnosis
Chairpersons: Motoyasu Kusano, Qi Zhu

O-3-1
Comparison of the Degree of Correlation with Endoscopic Findings between the Frequency Scale for the Symptoms of Gastroesophageal Reflux Disease and the Questionnaire for the Diagnosis of Reflux Esophagitis: A Multicenter Japanese Study

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Introduction: We compared correlation with endoscopic findings of the frequency scale for the symptoms of gastroesophageal reflux disease (FSSG), a written questionnaire developed in Japan, to that for the questionnaire for the diagnosis of reflux esophagitis (QUEST) for the diagnosis of reflux esophagitis.

Methods: We registered 475 patients with untreated upper abdominal symptoms (male/female: 252/223, average age 52.4±17.8 years). Subjects were assessed first with the FSSG and QUEST questionnaires, then by endoscopy, before allocation to a gastric ulcer (GU), duodenal ulcer (DU), gastroesophageal reflux disease (GERD) or functional dyspepsia (FD) group.

Result: On the basis of the endoscopic findings the diagnoses for the 475 subjects were as follows: FD 52.2%, DU 7.6%, GU 7.8%, and GERD 32.4% (Grade N+M 10.1%, Grade A+B 20.2%, Grade C+D 2.3%). There was no difference between the FSSG and QUEST in sensitivity, specificity or accuracy for any condition. The FSSG score rose with increasing endoscopic severity of GERD, but there was no correlation between the QUEST score and endoscopic severity. The FSSG total score was inferior to QUEST in terms of distinguishing GERD from other conditions, but when only the questions relating to reflux symptoms were used, the FSSG was able to distinguish GERD from other conditions as well as QUEST.

Conclusion: The FSSG score reflects the severity of the endoscopic findings of GERD.

O-3-2
Normal Values of 24-Hour Combined Esophageal Multichannel Intraluminal Impedance and pH Monitoring in Chinese Population

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Introduction: There have been no normal values for 24-hour combined esophageal multichannel intraluminal impedance and pH (MII-pH) monitoring in Chinese population. The aim of this study was to define normal range for 24-hour combined esophageal MII-pH monitoring in Chinese population, and compare our impedance parameters to that in western population.

Methods: Healthy volunteers without organic diseases under upper endoscopy and Helicobacter Pylori. infection were recruited, they all underwent 24-h ambulatory combined MII-pH studies. Volunteers with pathologic esophageal acid exposure would be excluded. Gastroesophageal reflux episodes were detected using impedance and characterized by pH as acid, weakly acidic and weakly alkaline, the composition of every reflux episodes was also analyzed as: liquid, mixed and gas. All impedance parameters were given as median (25th, 75th, 95th percentile).

Result: Seventy healthy volunteers who met the inclusion criteria were recruited, including 33 cases of male and 37 cases of female. The median number of total reflux episodes over 24 hours in Chinese population is 40 (31,53,75), of which 53.3% were acid(median 22(7,36,54)), 44.7% were weakly acidic (median 16(10,26,40)) and 2% weakly alkaline reflux (median 0(0,1,4)). More than half (52.4%) of gastroesophageal reflux episodes were mixed (median 22(12,31,44), 37.2% were liquid (median 12(6,21,46)) and 10.4% gas reflux (median 4(2,7,11)). Nearly 26.6% of reflux episodes reached 15cm above the lower esophageal sphincter (median 8(2,15,30)). Reflux frequency was common upright but rare recumbent. The bolus clearance time was 9s while acid was chemically cleared in 33s (p=0.000). Male gender was associated with increased number of acid, liquid, mixed and proximal gastroesophageal reflux episodes (p<0.05). Comparison between our data to western data showed the number of total reflux in Chinese population was similar with that in western population.

Conclusion: The number of total reflux episodes in Chinese population was similiar with that in western population. There was difference between genders in impedance parameters, indicating caution of matching gender when doing research. This study provides values of reflux patterns in healthy subjects for comparisons with Chinese GERD patients.
O-3-3
Characteristics of the Refluxate in Non-erosive Reflux Disease (NERD) Patients: A Study Using Intraluminal Impedance Monitoring
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Introduction: It is not known whether the characteristics of the postprandial refluxate in patients with non-erosive reflux disease (NERD) differ from those observed in normal subjects. The aim of this study was to analyze the characteristics of the refluxate in NERD patients by multichannel intraluminal impedance-pH metry (MII-pH).

Methods: The results of MII-pH in 42 NERD patients were compared with the results in 18 healthy volunteers.

Result: Total acid exposed time, mean acid clearance time and mean bolus clearance time were longer in NERD group (p<0.05). Total liquid and mixed reflux episodes were more frequent in NERD group (p=0.002) and only acidic liquid and mixed reflux episodes were more frequent in NERD group (p=0.001). NERD group didn’t show any difference in total gas reflux episodes but the acidic gas reflux was more frequent in NERD group (p<0.001). The proportion of refluxate was similar during acid and nonacid reflux.

Conclusion: The NERD group had more frequent liquid and mixed reflux episodes especially acidic form and more acidic gas reflux. Acid reflux in NERD patients was associated similar proportion of gas reflux compared with healthy volunteers. This suggests a possible mechanism that acidic gas refluxes could bring reflux associated symptom without esophageal erosion.

O-3-4
Is Intercellular Space of Esophagus Reasonable for Diagnosis of GERD?- Electron Microscopic Study in Normal Esophagus
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Introduction: Dilatation of intercellular space (IS) of esophageal epithelial cells is described as an early marker for gastroesophageal reflux disease (GERD). For the measurement of IS, 10 transmission electron microscopy (TEM) photographs and 10 random intercellular transects per photos had been widely accepted without any theoretical criticism. And there were no considerations for the three morphologically different layers of esophageal epithelia. We have evaluated whether IS of normal esophagus differs between layers. And also we have verified the method of IS measurements.

Methods: Esophageal-gastrodudenoscopy was performed in 15 healthy adults without any symptom of GERD, taking two biopsies from esophageal mucosa above 5 cm from the squamocolumnar junction. These tissue samples were handled and managed for TEM, verifying three layers of esophageal mucosa, i.e. stratum corneum, stratum spinosum, and stratum basale. Five digital photomicrographs were taken from each of the three layers by TEM, and IS’s were measured with image analysis program. To measure IS’s, 5, 10, 20, 30, and 40 measurements per photomicrograph were performed by 4 different examiners. Mean value and intra-class correlation coefficient (ICC) were calculated.

Result: Mean IS of lower esophagus irrespective of the epithelial layers was 0.39 ± 0.30 μm. However, when the result was subdivided according to the three layers, mean IS of stratum corneum was 0.62 ± 0.23 μm, stratum spinosum 0.23 ± 0.19 μm, and stratum basale 0.55 ± 0.36 μm, and the difference between layers was statistically significant (p<0.05). On the other hand, ICC of 5, 10, 20, 30, and 40 measurements were 0.688, 0.917, 0.837, 0.790, and 0.765, respectively.

Conclusion: Mean IS values in normal subjects were significantly different between the layers. We suggest that reconsideration of standard method of measuring IS is needed, and that measuring IS at more than 10 loci per photo is recommended to achieve an adequate inter-observer agreement. Further studies on the site and number of taking TEM photos from each of the three layers are required.

O-3-5
Esophageal Epithelial Surface in Patients with GERD: An Electron Microscopic Study
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Introduction: Intercellular spaces in the mid stratified squamous epithelium of the esophagus are reported to be wider in patients with gastroesophageal reflux disease than in asymptomatic healthy individuals. This study was designed to investigate the intercellular spaces between the most superficially located esophageal epithelial cells.

Methods: Eighteen patients with erosive esophagitis, 10 patients with non-erosive reflux disease, and 18 normal asymptomatic volunteers were enrolled. Biopsy specimens were obtained from the esophageal mucosa without mucosal breaks at the frontal wall 2 cm above the squamous-columnar junction. Scanning electron microscopy was employed to investigate the tightness of the superficial cellular attachment. The intercellular spaces between the surface epithelial cells on each of three photographs taken from a biopsy sample were classified in three grades, and the score of each specimen was determined by calculating median score of three areas.
Result: Cellular attachments between surface squamous epithelial cells identified by scanning electron microscopy were remarkably diverse. The intercellular space between the most superficially located epithelial cells in patients with erosive esophagitis or non-erosive reflux disease was not different from that in asymptomatic healthy individuals.

Conclusion: Widened luminal intercellular spaces of esophageal superficial epithelium are not responsible for the induction of reflux symptoms in patients with gastroesophageal reflux disease.

O-3-6
The Relationship between Gastric Motility and Reflux Symptoms in Patients with Nonerosive Gastroesophageal Reflux Disease
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Background: More than half of patients with reflux-related symptoms have no endoscopic evidence of mucosal breaks, which is called nonerosive gastroesophageal reflux disease (NERD). The response to proton-pump-inhibitor treatment is lower for NERD patients than for those with erosive gastroesophageal reflux disease. The pathogenesis of NERD, which is thought to differ from erosive esophagitis, may be multifactorial. The role played by gastric motility in symptom generation in patients with NERD has not been examined.

Aims: To elucidate the gastric motility in patients with NERD and the efficacy of a prokinetic agent in the treatment of NERD.

Methods: Gastric motility was evaluated with electrogastrographs (EGGs) and by measurement of gastric emptying using the acetaminophen method in 26 patients with NERD and in 11 matched healthy controls. NERD patients were treated with a prokinetic agent (15mg of mosapride orally three times daily) for a period of 4 weeks, after which gastric motility was measured again. The subjective therapeutic outcome was rated as markedly improved, slightly improved, unchanged and deteriorated.

Results: Compared to the healthy controls, the NERD patients showed a significantly lower percentage of normogastria, a lower power ratio in EGGs, and delayed gastric emptying. Ten patients had normal gastric motor function (Group A), and 16 showed abnormalities of either gastric myoelectrical activity or gastric emptying (Group B). After the treatment with mosapride, gastric motility improved significantly in patients with both Group A and Group B compared to pretreatment. The subjective assessment by the patient after the treatment was markedly or slightly improved in 20.0% of Group A versus 62.5% of Group B (p<0.05).

Conclusions: More than 60% of patients with NERD showed gastric hypomotility including impaired gastric myoelectrical activity and delayed gastric emptying. Gastric hypomotility appears to be an important factor in reflux symptoms generation in some NERD patients.

O-3-7
Computer-Assisted Intestinal Contraction Detections in Small Bowel from Wireless Capsule Endoscopy Image Sequence
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Introduction: The movements of Wireless Capsule Endoscopy (WCE) manifest intestinal contraction activities along its transit time. Recognizing the contractile patterns from WCE image sequences thus suggests a non-invasive technique for studying intestinal motility. We propose a computer-assisted method to automatically detect intestinal contractions for minimal physician attentions.

Methods: The contractions are observed based on images features in consecutive frames through a coherence three-stage procedure. In Stage 1, the possible contractions are recognized by changes in the edge of the intestinal folds. Evaluating similarities in consecutive frames is implemented in Stage 2 to exclude as many non-contractions as possible. In Stage 3, a learning method utilizes the intestinal fold directional information to determine true contractions. Figure 1 illustrates the procedure for an example of 60 continuous frames.

The experimental data includes six ten-minute sequences which were extracted from different positions in the small bowel regions. For each sequence, manual detections were implemented by experts to get ground truth data. The performance of the method is evaluated by a ratio of true (and wrong) contractions detected to ground truth data.

Result: The average sensitivity is 83% true contractions detected, whereas the False Alarm Rate (FAR) is 42%. Comparisons of the results with those reported in [1] and [2] are 71.5% and 73.5% for sensitivity, and 71% and 44% for FAR, respectively. The proposed method performance is more robust and reliable.

Conclusion: We proposed a computer-assisted method utilizing spatial and temporal features of WCE image sequences to recognize the contraction patterns. The experimental results show that the method can detect a total of 83% of cases. To ensure more reliable results with different types of data, we need to reduce the FAR. In this way, the method will be feasible to develop diagnostic systems for intestinal motility dysfunction.

References:
Oral Session 4: Clinical

Chairpersons: Kazuma Fujimoto, Jose D. Sollano

O-4-1

PPI Maintenance Therapy Can Control Patients with Severe Reflux Esophagitis in Japan

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Introduction: Patients with severe reflux esophagitis (RE) experience persistent daytime or nighttime heartburn, and some sustain severe damage including ulceration, stricture and Barrett’s esophagus, which can lead to development of adenocarcinoma. Since December 2000, patients with severe RE have been treated with proton pump inhibitor (PPI) maintenance therapy in Japan. However, there have been no reports regarding whether PPI maintenance therapy affects clinical course of patients with severe RE. The aim of this study was to clarify whether patients with severe RE could be controlled by PPI maintenance therapy.

Methods: Study subjects were 124 patients (57 men, 67 women; mean age, 70.9 years) with severe RE who were followed up for a mean period of 6.7 years (range, 4.0 – 17.8 years) after diagnosis. Severe RE was defined RE of grade C or D according to the Los Angeles classification system. Esophageal complications related to severe RE (esophageal ulcer bleeding, esophageal stenosis, Barrett’s esophagus and Barrett’s esophageal cancer) were investigated before and after December 2000. Then clinical course and features were also examined in patients with severe RE who had any esophageal complications after December 2000.

Result: Sixty-four patients (51.6%) suffered from any esophageal complications such as esophageal ulcer bleeding (n=47, 37.9%), esophageal stenosis (n=11, 8.9%), Barrett’s esophagus (n=12, 9.7%) and Barrett’s esophageal cancer (n=1, 0.8%). However, incidence of esophageal complications decreased significantly after December 2000 [36/82 (43.9%) before vs. 25/124 (20.2%) after, p<0.05]. There were 25 patients with esophageal complications after December 2000, but 17 of 25 patients (68%) had no PPI or stopped PPI maintenance therapy. There occurred no serious side effects related to PPI maintenance therapy such as pneumonia, bone fracture related to osteoporosis and/or enlarged gastric corpus polyps during observation periods.

Conclusion: PPI maintenance therapy is safe and prevents any esophageal complications. Patients with severe RE could be controlled by PPI maintenance therapy in Japan.
Oral Sessions

O-4-2
Quality of Life in Non-Erosive Reflux Disease (NERD) Before and After Treatment with Low Dose and Standard Dose Esomeprazole in Thai Patient

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Background: Gastroesophageal reflux disease (GERD) is a chronic disease significantly impairs quality of life. SF-36 questionnaire can be used as a valid questionnaire in most studies to evaluate all aspects in the GERD-related quality of life, it contains 8 domains (physical functioning, role physical, bodily pain, general health, vitality, role emotional, social functioning and mental health).

Objective: To evaluate the Quality of life in Non-Erosive Reflux Disease (NERD) before and after treatment with low and standard dose esomeprazole in Thai patient by Thai version SF-36 questionnaire. Furthermore, we aimed to use GERD specific disease related quality of life questionnaire and frequency of the symptoms per week as a visual analog scale to compared the before and after treatment scores of both treatment regimens.

Methods: The study included 90 NERD patients who were seen in the Department of Gastroenterology at the Bhumiphol hospital between December of 2006 and January 2008. The diagnosis of NERD was base on typical and classic heart burn and/or acid regurgitation symptoms. In all patients, esophagogastroduodenoscopy (EGD) was performed by the same physician to exclude structural disease (e.g. peptic ulcer, esophageal cancer) and erosive esophagitis. The patients were randomly assigned using block of four into two groups a standard dose 40 mg/day esomeprazole group (N = 45) and a low dose 20 mg/day group (N = 45). After the first visiting, patients had received any dose of esomeprazole, with subsequently visiting at week 4 and 8. The questionnaire was done in every visit.

Results: In before treatment, a group of 40 mg esomeprazole had mean total SF-36 score lower than group 20 mg esomeprazole statistically significant (41.76 vs. 51.73). Baseline general quality of life in 40 mg esomeprazole is worse than 20 mg. Meanwhile, in after treatment group, both groups of 20 or 40 mg had score higher than before treatment group at week 4 and 8 significantly. Mean total SF-36 score (after treatment at week 4 and 8) in 20 mg esomeprazole improved 72.69% ((89.33-51.73) / 51.73 * 100 %)) and 40 mg esomeprazole improved 120.65%(( 92.07-41.76) / 41.76 *100 %)). Furthermore, the improvement was not statistically significant comparing 20 mg and 40 mg esomeprazole group.

Conclusion: This is our preliminary report because the number of the patients that should be included in this study are not completely yet. This study showed that both low dose and standard dose of esomeprazole can improved the general quality of life by assessing with SF-36 Thai version although the improvement among two groups has no statistically significant. It may be reasonable to initiate the treatment in a non-erosive reflux disease patient with low dose of esomeprazole.

O-4-3
Intragastric pH Effect of Novel Proton Pump Inhibitor Ilaprazole in H. pylori Negative Healthy Volunteers: A Pharmacodynamics and Safety Study

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Introduction: Since PPIs are core drugs in the treatment and maintenance of GERD, newly developed PPI is expected to have a stronger acid suppressive effect. This open, randomized crossover study was designed to compare the effect of ilaprazole and omeprazole on intragastric pH in healthy Chinese.

Methods: Totally 12 healthy volunteers (6 men and 6 women, mean age 25 years) were enrolled. Subjects were randomized into four groups, treated with different dose of ilaprazole (5mg, 10mg or 20mg) and omeprazole 20mg orally once daily for 5 days. Each subject was underwent three dosing period and one control period, with an interval of two-week washout phase. Intragastric pH was continuously monitored for 24 h on days 1 and 5 of each dosing period. CYP2C19 genotypes were analyzed to exclude the metabolizers effect on the PPIs.

Result: The percentage of time with intragastric pH >4 was statistically higher (P < 0.05) in subjects receiving 20 mg ilaprazole than in those receiving omeprazole in the first day after administration (91.02% vs 76.61%), while there was no difference at the day 5. The percentage of subjects with maintained pH >4 for at least 12 h on day 1 (83.3% vs 33.3%) and on day 5 (100% vs 58.3%) was higher after administration of 20mg ilaprazole than after omeprazole (both P < 0.05). The percentage of time in the night with pH<4 was lower in ilaprazole 10mg and 20mg group than in the control group. No difference between extensive metabolizers (EM) and poor metabolizers (PM) on ilaprazole’s acid suppressive effect could be observed. There was no record of adverse effect in all doses of ilaprazole groups.

Conclusion: Ilaprazole 20 mg once daily presents more effective in elevating intragastric pH than omeprazole, and thus offers a potential for improved efficacy in GERD symptoms release.

O-4-4
Patient-Directed Treatment Approach to Control Symptom Recurrence in Patients with Erosive Esophagitis

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Background: Effective acid suppression is the current standard of care for the healing of erosive esophagitis (EE) and the relief of symptoms of gastroesophageal reflux disease (GERD). However, given the chronic relapsing course of reflux symptoms, patients...
require re-treatments which may vary in interval and duration. For a variety of reasons, patients may or may not consult their physicians during these relapses.

**Objective:** To determine the treatment practices that patients with erosive esophagitis adopt when their symptoms recur after complete healing of erosive esophagitis.

**Methods:** Patients with endoscopy-documented healing of EE after completing 4-8 weeks of proton pump inhibitor (PPI) therapy, and have reported satisfactory resolution of symptoms during their last clinic visit but did not report for follow-up in the out-patient clinic for a 3-6 monthly interval, were included in this study. They were contacted by telephone and interviewed rigorously regarding strategies they have adopted when heartburn, acid reflux and abdominal pain recurred. Patients were also asked regarding their subjective assessment of the overall outcome, i.e., satisfactory relief of GERD symptoms, from their chosen treatment strategy.

**Results:** From 110 patients in our database this year, 70 patients responded to our telephone request for follow-up interview. Recurrence of GERD symptoms was experienced by 33 (47%) patients after discontinuation of PPI treatment. The most common symptoms during recurrence were epigastric pain (58%), bloatedness (27%) and heartburn (15%). Seventy-three percent (73%) of the patients took their medications immediately upon symptom recurrence and 23% took medications only when symptoms had become disturbing. Most patients (91%) opted to take medications on an on-demand schedule, taking them only days that they had symptoms, i.e., 3% took medications 5 times a week, 10% two times a week, 25% once a week and 42% took medications only once every 2 weeks. Only 17% took drugs daily. The medications included in their strategy were PPIs (55%), H2RAs (24%), antacids (12%), antispasmodics (6%), and prokinetics (3%). Forty-six percent (46%) chose to continue their prior PPI medications, 39% decided to shift to another drug, and 3% asked advise from relatives or friends for a change in their medications. Majority of patients (91%) reported relief of symptoms, i.e., excellent (30%), good (61%). Only 9% reported unsatisfactory relief of symptoms with their self-chosen treatment strategy.

**Conclusions:** When GERD symptoms recur, patients who chose not to consult their physicians adopt an on-demand intake of acid-suppressing medications. Using this self-directed treatment approach, most patients report a satisfactory overall relief of their GERD symptoms.

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**O-4-5**

**Halitosis – Could It Be Another Extra-Esophageal Symptom of GERD?**

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**Introduction:** Patients are reluctant to consult halitosis to doctors because of regarding halitosis as just the result of unsanitary oral health in spite of troublesome. Moreover, quite many cases with halitosis do not experience improvement with oral gargling or scaling. Some studies already have shown the close relationships between gastrointestinal health and halitosis including ours (Gut and Liver, in press, 2008). In previous study, we measured volatile sulfur compounds (VSCs) among the people who have the injured gastric mucosa, checking VSC levels by halimeter using oral air or gas chromatography by gas chromatography of gastric juice and reached to the conclusion that halitosis might have significant correlation with mucosal damage after *H. pylori* infection. The clue we found from previous study was that the injured gastric mucosa have potential of generating VSCs based on the fact that there was statistical difference in VSC levels between eroded esophageal mucosa and non-eroded. In this study, we measured VSCs in GERD patients in order to define the relationship between eroded esophageal mucosa and halitosis, shedding the possibility that halitosis could be one of extra-esophageal symptoms of GERD.

**Method:** Group 1 consists of control group, who have no GERD-related symptoms and no evidence of reflux related erosion or ulcer on endoscopy and Group 2 were consists of GERD A – B – C – D, classified based on LA classification. All the patients were checked VSCs with both halimeter using oral air and gas chromatography by gastric juice.

**Results:** There was a statistical difference in the levels of VSCs of exhaled breaths or aspirated gastric juices between Group 1 and Group 2 (p <0.0001), suggesting VSCs could reflect the eroded epithelial damages of acidic reflux. However, there was no significant difference in VSCs according to the severity of GERD defined by LA classification. Taken together, halitosis could be reflected esophagogastrroduodenal mucosal injury and the association of *H. pylori* infection, but couldn’t be the biomarker for GERD.

**Conclusion:** Erosive changes in esophageal mucosa were highly associated with the levels of VSC, suggesting that halitosis might be the result of esophageal erosive lesions, as biomarker for GERD, discriminating NERD.
**Poster Session 1**
*Chairpersons: Yuji Naito, Udom Kachintorn*

**P-1-1**

**Histopathologic Characteristics of Salmon Pink Mucosal Patches in the Distal Esophagus of Gastroesophageal Reflux Disease (GERD) Patients**

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**Background:** The recent Montreal Consensus on GERD included the term endoscopically-suspected esophageal metaplasia (ESEM) to represent salmon pink mucosa which projects cephalad from the gastroesophageal junction noted during upper endoscopy. It may be labeled only as Barrett’s epithelium after columnar epithelium with intestinal metaplasia is observed in the histopathological examination of the corresponding biopsies. However, in those patients without mucosal breaks or the typical tongue-like mucosal projections characteristic for Barrett’s esophagus, there are also discrete islands/patches of salmon pink mucosa sometimes noted in their distal esophagus, often separated from the Z line of the cardioesophageal junction by a thin band of normal appearing esophageal mucosa.

**Objective:** To describe the histology and presence of columnar epithelium with intestinal metaplasia (CIM) in the biopsy of salmon pink patches of mucosa in the distal esophagus noted during upper endoscopy of patients complaining of GERD symptoms.

**Methods:** Patients who complained of heartburn, acid regurgitation and/or epigastric pain which is more attributable to GERD were included in this study. All patients underwent upper endoscopy to examine for erosions and mucosal breaks, ulcers or Barrett’s epithelium, as well as, other lesions in the stomach and proximal duodenum. In particular, salmon pink patches of mucosa in the distal esophagus but have no continuity with the Z-line of the gastroesophageal junction were biopsied for histopathologic examination. All specimens were subjected to H&E and alcian blue staining process. Histologic changes compatible with GERD, i.e., basal cell hyperplasia, elongation of the rete pegs to >15% of the lamina propria, intraepithelial infiltration of inflammatory cells, as well as, presence of columnar epithelium with intestinal metaplasia were examined in all the patients.

**Results:** Sixty-seven (67) patients who underwent upper GI endoscopy due to GERD symptoms [heartburn and/or acid regurgitation (46%), epigastric pain (35%), bloatedness (19%)] had patches of salmon-pink mucosa in the distal esophagus. Histopathological examination of these biopsies revealed columnar epithelium with intestinal metaplasia (CIM) in 54 (81%) patients, basal cell hyperplasia and elongation of rete pegs in 10 (15%) patients and chronic inflammation only in 3 (4%) patients.

**Conclusion:** Endoscopic findings of discrete islands or patches of salmon pink mucosa in the distal esophagus of GERD patients represent changes compatible with reflux esophagitis, including Barrett’s epithelium.

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**P-1-2**

**48-Hour Wireless Esophageal pH Monitoring Increases Sensitivity in Detecting Abnormal Esophageal Acid Exposure**

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**Introduction:** Reflux monitoring has been traditionally based on the detection of 24-hour acid reflux by a transnasal catheter. Recently, the Bravo 48-hour wireless pH monitoring device has been touted as a significant advance in the diagnosis of gastroesophageal reflux disease. The aim was to compare the diagnostic sensitivity of the two modalities.

**Methods:** Thirty-four patients with non-erosive reflux disease (NERD) were prospectively evaluated. Patients enrolled in the study received both wireless pH monitoring and conventional catheter monitoring simultaneously on the 1st day. The catheter monitoring terminated after the first 24 hours and the wireless pH monitoring continued till the end of the 2nd day. Increased acid exposure was defined by a Johnson-DeMeester score greater than 14.7.

**Result:** Of the 34 patients under evaluation, 32 patients were eligible for the study. According to the wireless pH monitoring, increased acid exposure was documented in 17 (53.1%) patients, with 12 (37.5%) patients being abnormal on both days. Wireless pH monitoring suggested isolated 1st or 2nd day acid exposure in 1 (3.1%) and 4 (12.5%) patients, respectively. By comparison, the traditional catheter monitoring only revealed increased acid exposure in 12 (37.5%) patients on the 1st day. The wireless pH monitoring method revealed 41.7% more patients with increased acid exposure than the conventional catheter method.

**Conclusion:** Both conventional 24-hour pH monitoring and the 48-hour wireless pH monitoring are valid and reliable recording devices for measurement of esophageal acid exposure. However, the Bravo system may improve the sensitivity in detecting abnormal esophageal acid exposure.

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Reflux Patterns according to the Degree of Acid Hypersensitivity in Patients with Acid Hypersensitive Esophagus Using Multichannel Intraluminal Impedance pH Monitoring

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Introduction: Acid hypersensitive esophagus may be related to increased acid clearance and decreased acid exposure in esophagus. To compare the reflux patterns according to the degree of esophageal acid hypersensitivity using multichannel intraluminal impedance pH monitoring (MII-pH).

Methods: Acid perfusion test (APT) with VAS for severity of pain was performed in 92 patients with NERD. Fourteen subjects with positive response could be divided into 2 groups according to the symptom-provoking times after acid perfusion; 7 acid ultra-hyper-sensitive (<1 min) group (AHH) and 7 acid hypersensitive (>2 min) group (AH). We compared the severities of pain by APT, and reflux parameters by MII-pH in two groups.

Results: Symptom-provoking times by APT were median 52s (10-60 s) in AHH and 180 s (120-360 s) in AH. Symptom severities using VAS were not different between two groups. Abnormal total % of time pH<4 was shown in 2 patients in AH and not in AHH. Positive SI was shown in 1 patient in AHH and 3 patients in AH. There were no significant differences between 2 groups in mean acid clearance time (72.1±50.0 s vs. 85.4±65.8 s in AHH vs. AH), mean bolus clearance time (10.7±4.0 s vs. 13.9±7.4 s), and number of proximal extent (mean 15 vs. 28). Pure gas reflux events were tended to high in AH than AHH (median 14 vs. 18, P=0.097).

Conclusions: AH may related to more abnormal acid exposure to esophagus and have more reflux related symptoms than AHH, without any differences in acid clearance profiles and reflux patterns according to acidity, composition of refluxate.

Reflux Profile of Chinese GERD Patients: A study Using Combined Multichannel Intraluminal Impedance-pH Technique

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Background: To investigate the reflux profile of Chinese GERD patients with the aid of combined multichannel intraluminal impedance-pH (MII-pH) monitoring technique.

Methods: Consecutive patients presented with GERD symptoms were enrolled. Patients were divided to erosive esophagitis (EE) group, non-erosive reflux disease (NERD) group and functional heartburn (FH) group after upper endoscopy, combined MII-pH monitoring and rabeprazole test. Another 20 healthy controls (HC) were recruited.

Results: Sixty-four GERD patients including 20 cases of EE, 22 cases of NERD and 22 cases of FH, together with 20 cases of HC were enrolled. There were more episodes of liquid reflux and proximal reflux in EE and NERD than that in FH and HC (P<0.05). Patients in FH and HC groups had higher proportion of mixed reflux (P=0.000). The percentage of acid reflux in EE and NERD was much higher, while there was a higher percentage of weakly acidic reflux in FH and HC (P=0.000). No significant difference was found in MII-pH parameters between groups with and without response to rabeprazole test except recumbent percentage time of esophageal pH value below 4 and episodes of proximal reflux.

Conclusion: EE and NERD patients had more liquid and proximal reflux episodes than FH patients and healthy controls. Acid and liquid reflux was predominant in the former two groups, while weekly and mixed reflux was predominant in the later two groups.
reflux episodes compared to the 30 min fasting periods. In patients with positive 24 hr esophageal pH test results, spicy meals increased acid reflux number at the 2nd hr (16.6±4 vs 7.6±4, p<0.05) of the study compared to standard meals but not at the 1st hr (10.8±12 vs 10.4±9). Although the % esophageal acid exposure time was increased during the 2nd hr after spicy meal, there was no significant difference compared with standard meal (56±14% vs 45±34%, p>0.05). In contrast, in patients with negative 24 hr esophageal pH results, spicy meal produced no significant effect compared to standard meal. Retention of food in the stomach at 30, 60, 90, and 120 min after meal were 81±5%, 68±11%, 45±9%, and 30±8 %, respectively, for spicy meals and 79±11%, 59±13%, 43±16%, and 29±15%, respectively for standard meal. The gastric retention at 60 min was significantly greater after spicy meals compared to standard meals (p<0.05). Intragastric pH (1.4±0.6 vs 1.4±0.5) and GERD symptom scores were similar after ingestion of spicy meals and standard meals (p>0.05).

Conclusions: GER are increased after ingestion of both spicy and standard meals compared to fasting periods. However, increases of the acid reflexes were sustained longer after spicy meals compared to standard meals as the numbers of esophageal acid reflexes after spicy meal were similar at the 1st hr but greater at the 2nd hr. spicy meal also induces more gastric retention at the 1st hr postprandial period. This study suggests that chili may play roles on the modulation the numbers of acid refluxes and gastric motor function in GERD patients.

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**Poster Session 2**

**Chairpersons: Kazuhide Higuchi, Poong-Lyul Rhee**

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**P-2-1**

**Risk Factor of Erosive Esophagitis for Adults with Normal Z-line in Korea**

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**Introduction:** About one-third to one-half of GERD patients have erosive esophagitis. Prevalence of erosive esophagitis is gradually rising in Korea. There have been many cross-sectional studies on risk factors of erosive esophagitis. However, the risk factor of erosive esophagitis occurred in adults with normal Z-line is not well known.

**Aims:** In this study, we investigated the incidence and risk factor of erosive esophagitis in adults with normal Z-line.

**Methods:** We did a study on a consecutive series of subjects who underwent gastrofiberscopy for stomach cancer screening at the Center for Health Promotion, Korea university Ansan hospital in Korea, from January 2002 through December 2004. A total of 11,288 patients were screened. Of these, 1,221 subjects who had normal Z-line with follow up period of more than two years were eligible for this study. Subjects were asked to answer a questionnaire on their education level, alcohol intake, smoking habit, amount of exercise, stress score and comorbidity. Waist circumference and body mass index was checked along with serum laboratory tests. Abdominal ultrasonography was performed to assess the presence of fatty liver. Gastrofiberscopy was performed during the follow up. Erosive esophagitis was subgrouped according to endoscopic findings of grade M (minimal change) and Los Angeles Classification. Grade M included blurred Z-line and whitish discoloration or hyperemia of distal esophagus.

**Results:** Mean follow up time was 34.4 months (24~58). Erosive esophagitis occurred in 133 patients (10.9%). From those who had erosive esophagitis, 86 cases were grade M (7.0%), 41 were LA-A (3.4%) and 6 were LA-B (0.5%). However, none was found to have more than LA-C. In univariate analysis, gender, education level, amount of alcohol intake and smoking, waist circumference, serum triglyceride and uric acid level proved to be a risk factor of erosive esophagitis. In Multivariate analysis, only waist circumference proved to be a significant risk factor.

**Conclusions:** Incidence of erosive esophagitis in adults with normal Z-line was 10.9%. Waist circumference can be a predicting factor for erosive esophagitis.

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**P-2-2**

**Characteristics of Barrett’s Esophagus in Korea**

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**Introduction:** Barrett’s esophagus (BE) is diagnosed when specialized intestinal metaplasia (SIM) is detected histologically in endoscopically suspected columnar-lined esophagus (CLE). It is a premalignant condition and plays a pivotal role in the development of esophageal adenocarcinoma. It has traditionally been believed to affect Asians less frequently. The aim of this study was to determine the prevalence of BE and possible associated risk factors in Korea.

**Methods:** A retrospective analysis of 70 103 patients who had undergone their first upper endoscopies was performed using computerized medical records. Of these, 696 (1%) patients had suspected CLE. After screening by telephone, 480 were enrolled. The clinical and endoscopic characteristics of histologically identifiable BE and endoscopically suspected CLE not confirmed by biopsy (suspected CLE without SIM) were investigated.

**Results:** Barrett’s esophagus was present in 151 patients (0.22%) with a mean age of 53.8 ± 10.9 years. BE was more commonly found in men. BE was associated with a set of features distinct from suspected CLE without SIM; older age, greater predominance of male sex, more frequent smoking history, and more frequent acid regurgitation symptom.

**Conclusions:** Barrett’s esophagus remains less common in Korea than in Western countries. Old age, male sex, smoking, and acid regurgitation symptom were significant risk factors.
P-2-3

Adenocarcinoma of the Esophagus in Korea – A 10-years Trend from a Single Tertiary Center-

Introduction: The incidence of esophageal adenocarcinoma has increased during recent decades in the Western Europe and United States. The aim of this study was to determine the trend of esophageal adenocarcinoma in Korean single tertiary center.

Methods: We reviewed the records of 1502 patients with esophageal cancer in Samsung Medical Center from January 1998 to December 2007.

Result: There were 1391 patients with squamous cell carcinoma and 25 patients with adenocarcinoma of esophagus. Annual rate of esophageal adenocarcinoma per 1,000 upper gastrointestinal endoscopy was 0.076 in 1998, 0.056 in 1999, 0.096 in 2000, 0.140 in 2001, 0.067 in 2002, 0.064 in 2003, 0.043 in 2004, 0.038 in 2005, 0.037 in 2006, and 0.037 in 2007. The ratio of adenocarcinoma to squamous cell carcinoma was 0.012 in 1998, 0.01 in 1999, 0.031 in 2000, 0.04 in 2001, 0.021 in 2002, 0.02 in 2003, 0.013 in 2004, 0.012 in 2005, 0.012 in 2006, and 0.011 in 2007.

Conclusion: Unlike the Western Europe and United States, squamous cell carcinoma was most common esophageal cancer in our center. The incidence of esophageal adenocarcinoma has not increased.

P-2-4

Esophageal Adenocarcinoma in Shanghai China: A Retrospective Study

Introduction: To investigate the characteristics and trend of esophageal adenocarcinoma in Shanghai China.

Methods: Pathologically diagnosed esophageal carcinoma was collected from January 2005 to March 2008 in Shanghai Ruijin Hospital. Patients’ previous history, endoscopy, surgery and histopathology were reviewed. Telephone follow-up was made on patients with esophageal adenocarcinoma focusing on previous history of GERD and related endoscopic evidences. The UICC criterion was applied to differentiate the histological origin of GEJ adenocarcinoma.

Result: A total of 341 esophageal cancer were identified with an average age of 61±15 years and a male:female preponderance of 4.41. Dysphagia (82.0%) and retroxophoid pain (20.9%) were the most common symptoms. The upper-, mid- and lower- esophageal cancer accounted for 21, 257 and 63 cases, respectively. Three hundred twenty-two (94.4%), eight (2.3%) and eleven (3.2%) patients were pathologically diagnosed as squamous carcinoma, adenocarcinoma and other types, respectively. Compared with 22/701 (2.9%) patients of esophageal adenocarcinoma during 1999 and 2004, no statistical significance (P=0.473) was shown regarding the rate of esophageal adenocarcinoma during 2005 and 2008. Among the 8 patients (male:female=7:1) with adenocarcinoma, upper- and mid- esophageal adenocarcinoma was identified in one and two patients, respectively. Adenocarcinoma involving both lower esophagus and cardia were documented in the rest 5/8 patients: although all five lesions were present simultaneously with Barrett’s esophagus, only one of them was consistent with the Siewert criteria for ‘true esophageal adenocarcinoma’. In the above-mentioned 8 adenocarcinoma patients, one patient pre-surgically received multiple EGDS for acid-reflux symptoms without evidence of endoscopic positive GERD while another six patients did not have a previous history of GERD. Short-segment Barrett’s esophagus was detected in a patient 1 year prior to surgery.

Conclusion: Esophageal adenocarcinoma accounts for a small proportion in the total esophageal cancer in Shanghai, China. The pattern for development of esophageal adenocarcinoma may differ from that in Western countries.

P-2-5

The Comparison of the Demographic and Clinical Profiles between Patients with Erosive Esophagitis and Esophageal Cancer

Background and Aims: There is a paucity of epidemiologic data on the association between gastroesophageal reflux and the risk of adenocarcinoma of the esophagus. Persons with recurring symptoms of reflux have an eightfold increase in the risk of esophageal adenocarcinoma. In daily practice we must evaluate the clinical data of our reflux patients for the possibility of esophageal cancer. The purpose of this study was to evaluate of the demographic and clinical profile of erosive esophagitis and esophageal cancer.

Methods: Consecutive patients presenting to the endoscopy unit of Private Hospital in Jakarta with the indication of the upper gastrointestinal symptoms were examined for the presence of erosive esophagitis and esophageal cancer were prospectively evaluated. Demographic information (gender and age), data on tobacco use and family history of esophageal disease were recorded for all patients. The diagnosis of erosive esophagitis and esophageal cancer was assessed by senior endoscopists. Some alarm symptoms were noted.

Result: Of the 1718 endoscopies performed, 13.33 % was diagnosed as an Erosive esophagitis and 0, 41 % with esophageal cancer. Patients with esophageal cancer were older than patients with erosive esophagitis. Most of patients of reflux esophagitis came to the hospital due to dyspeptic symptoms (75, 11%) and only 9,17 % with reflux symptoms (heart burn and regurgitation). The mean age was 44.58 +/- 15.24 years old for Erosive Esophagitis and 53.14 +/- 15.96 % year old for esophageal cancer (P< 0.05). The upper GI bleeding was found in 29 cases (12.66 %) in Erosive esophagitis and 28.57 % cases
Prevalence of Irritable Bowel Syndrome in Patients with Gastroesophageal Reflux Disease in Japan

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Background and Aim: Gastroesophageal reflux disease (GERD) and irritable bowel syndrome (IBS) are most common diseases of GI tract. Several studies showed a strong overlap between GERD and IBS. IBS was found in 31-70% of GERD patients in Western countries. The aim of this study was designed to examine prevalence of IBS in Japanese GERD patients and their clinical characteristics.

Methods: 78 GERD patients (42 men and 36 women, mean age 64.3 yr) and 78 control subjects (37 men and 41 women, mean age 60.7 yr) were enrolled. Diagnosis of GERD was based on the presence of typical GERD symptoms such as heartburn and acid regurgitation and the examination of upper GI endoscopy. Diagnosis of IBS was based on the Rome III criteria and subdivided into IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), mixed IBS (IBS-M) and unsubtyped IBS (IBS-U) by predominant stool pattern. Efficacy of treatment with proton pump inhibitor (PPI) was divided into PPI responder defined as the complete relief of GERD symptoms, PPI partial responder as the partial improvement of symptoms, and non-responder as no change or worsening of symptoms.

Results: Prevalence of IBS in GERD (14 of 78, 17.9%) was significantly higher compared with control (4 of 78, 5.1%). Subtype of IBS in GERD was 8 (57.1%) of IBS-D, 3 (21.4%) of IBS-C, 2 (14.3%) of IBS-M, and 1 (7.1%) of IBS-U. There was no difference of IBS overlap between erosive esophagitis and non-erosive reflux disease. Among GERD patients, there were no differences of gender, smoking habits, drinking habits, and body mass index between GERD with IBS and GERD without IBS, but ages of GERD with IBS was younger than GERD without IBS. 60 (77%) GERD patients were PPI responders, 10 (13%) partial responders, and 8 (10%) non-responders. Rate of response to PPI treatment in GERD patients with IBS was significantly lower compared with GERD without IBS (p<0.01). Conclusion: The prevalence of IBS in Japanese GERD patients was high and overlap of IBS in GERD affected efficacy of treatment with PPI.

Erosive esophagitis was more prevalent in patient with persistent epigastric pain. The severity of epigastric pain correlates with finding of erosive esophagitis.
P-3-3

Is Abdominal Obesity a Risk Factor for Erosive Esophagitis?
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Background: An association between obesity according to body mass index (BMI) and gastroesophageal reflux disease (GERD) has been reported, although study results have been inconsistent. Recently, abdominal obesity has been concerned as an important risk factor of various diseases. However, it is not known whether abdominal obesity is associated with GERD. Therefore, we carried out a cross sectional study to determine the association between abdominal obesity and erosive esophagitis.

Methods: We consecutively enrolled 3,801 subjects (mean age 45 yr, 42% women) who underwent upper endoscopy for routine health evaluation. After examination of upper endoscopy, the severity of erosive esophagitis was graded from A to D according the LA classification. BMI, waist circumference (WC) and waist-hip ratio (WHR) were measured to classify overweight, obesity and abdominal obesity. According to BMI and WC, subjects were divided to 4 groups (overweight without abdominal obesity (Group 1), overweight with abdominal obesity (Group 2), obesity without abdominal obesity (Group 3), and obesity with abdominal obesity (Group 4).

Results: Among total subjects, 376 (9.9%) had esophageal erosions (338, mild erosive esophagitis (LA-A, B) and 38, severe erosive esophagitis (LA-C, D)). BMI was significantly higher in those with esophageal erosions (EE) than those without EE (24.6±3.2 vs 23.7±3.0 kg/m², p<0.01). WC was also significantly higher in those with EE than those without EE (84.1±9.5 vs 81.1±9.3 cm, p<0.01), but WHR had no significant difference between those with EE and those without EE (0.89±0.06 vs 0.87±0.16, p=0.059). When subjects were divided to 4 groups according to BMI and WC, the groups with abdominal obesity had more frequent prevalence of EE than the groups without abdominal obesity(9.0% in Group 1, 10.4% in Group 2, 12.8% in Group 3 and 13.4% in Group 4, p<0.01).

Conclusion: The results in this study suggest that abdominal obesity, measured by waist circumference is a risk factor of erosive esophagitis. Further study will be necessary to prove the influence of abdominal obesity in causing the erosive esophagitis.

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Endoscopic Treatments of PPI-Refractory Gastroesophageal Reflux Disease
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Introduction: The concept of using endoscopic therapy for the treatment of symptomatic gastroesophageal reflux disease (GERD) is a relatively recent development. EndoCinch suturing system (C.R. Bard, Inc. Billerica, MA, USA) are approved for use in the US and the Europe and was introduced in Japan in 2002. Recent multicenter studies in the US and the Europe have demonstrated that endoluminal gastroplication (ELGP) using EndoCinch improved heartburn and regurgitation. We evaluated the effectiveness of ELGP on PPI-refractory GERD in a Japanese population.

Methods: The principal indication criteria for ELGP were patients have a symptom of GERD and endoscopic Los Angeles grade M, A, B, or C esophagitis. Exclusion criteria were age under 18 years, pregnancy, dysphagia, endoscopic Los Angeles grade D esophagitis, obesity (BMI>40), previous esophageal surgery, and hialtal hernia more than 2 cm long. We recruited 14 patients (12 men, 2 women, range: 19 - 82 years). Grade M esophagitis was diagnosed in 8 patients, grade A in 2 patients, and grade B in 4 patients. A set of investigations (endoscopy, pH-measurement, and symptom assessment) was performed before ELGP to assess clinical outcome. The follow up period was 2 – 13 months.

Result: ELGP was performed in 13 patients, and failed in 1 patients. The average duration of the procedure was 44 minutes (range: 23 – 67 minutes). 8 patients (57%) can be reduced medications. Approximately half of all previously placed sutures were present and tight at the time of repeat endoscopy. Adverse events consisted of a mucosal tear in 1 patients (7%) and failed the procedure. There were no major adverse events and deaths.

Conclusion: ELGP is an effective and safe procedure for treating PPI-refractory GERD in a Japanese population, although long-term follow-up studies to investigate durability are required.
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