Methods: A post-hoc analysis was conducted on data from a multicenter, open-label study (D9612L00083) in which patients aged 18–70 y who had a history of HB (≥2 d/wk for the past week and on average for the past 3 months) underwent endoscopy and symptom assessment at baseline followed by treatment with esomeprazole 40 mg once daily for 4 weeks. For the post-hoc analysis, the following potential predictors of EE at baseline were considered: age; sex; race; body mass index (BMI); Helicobacter pylori status; duration of GERD; history of EE; baseline frequency and severity of HB, acid regurgitation, dysphagia, and epigastric pain; and patient-reported time to HB relief with antacids and H2-receptor antagonists. Each variable was tested separately in a univariate logistic regression model (α-level, 0.05) with the presence of EE as the dependent variable. From the 4 candidate models generated by stepwise logistic regression and backward elimination, a multivariate model was selected using Akaike’s information criterion. The final model was internally validated using “leave one out” cross-validation.

Results: Of 399 patients who had baseline endoscopy, 205 (51.4%) had EE. Full data for modelling were available for 180 patients with and 178 without EE. In the univariate models, older age, male sex, higher BMI, greater HB frequency and severity, greater acid regurgitation severity, white race, longer history of GERD, previous history of EE, and faster time to HB relief with antacid use were significantly predictive of EE (P < 0.05). The multivariate model selected included the variables of age, sex, HB frequency, race, EE history, and time to relief of HB with antacid use. The c-index of the model using cross-validation was moderate at 0.76. At a sensitivity of 80%, the model provides specificity of 53%, a positive predictive value of 63%, and a negative predictive value of 72%. The model included a novel predictor in time to HB relief with antacid use. Patients whose HB symptoms were relieved within 0–15 minutes of antacid use had 5 times the odds of having EE versus those who had no relief with antacid use.

Conclusion: Modelling of this type can help predict which types of patients presenting with GERD symptoms have EE and may aid physicians in diagnostic decisions and the selection of appropriate pharmacological therapy.
Purpose: Achalasia is the most thoroughly studied of the esophageal motility disorders. Manometric criteria include an aperistalsis esophageal body (always required), elevated lower sphincter pressure, high residual pressure and elevated esophageal pressures relative to gastric. The latter three are not required to make the diagnosis. Using these criteria alone some patients are difficult to classify. Multichannel Intraluminal impedance (MII) is combined with traditional manometry (MII-EM) to characterize diseases in terms of pressure and/or transit abnormalities and anecdotally appears to have a characteristic pattern in achalasia. The aims of our study were to describe the MII characteristics of achalasia and compare to patients with normal esophageal manometry.

Methods: A retrospective review of all patients with MII-EM testing done at our esophageal lab from 7/03–12/06 identified patients with achalasia and those with a normal manometry. Baseline and post swallow impedance for 10 liquid and 10 viscous swallows in both groups were measured. Descriptive statistics were used for describing frequencies and T test for the differences between the means. Exclusion criteria included incomplete records and previous treatment for those in the achalasia group.

Results: 74 eligible patients with achalasia and 172 normal were identified. Achalasia patients had no normal bolus transit. The baseline impedance (expressed in Ohms (Ω) as means ± SE) in the achalasia and normal group was 1114 ± 99 v/s 2130 ± 73 respectively (P = 0.01). This changed to 483 ± 40 v/s 1853 ± 63 after 10 liquid swallows and 450 ± 99 v/s 2012 ± 55 after 10 viscous swallows respectively (pre post swallow, P < 0.01 for achalasia, P = ns for normals).

Conclusion: Patients with achalasia have no normal bolus movement with MII, low baseline impedance that progressively decreases after multiple swallows in contrast to normal who have stable impedance even after multiple swallows. This MII triad is diagnostic of achalasia. These MII findings are likely due to a dilated fluid filled esophagus at baseline and the inability to effectively clear a bolus in achalasia. MII allows confirmation of manometric diagnosis in difficult cases. Further study is required to determine if MII can make the diagnosis of achalasia independent of manometry.

The Evaluation of Definitive Radiation Therapy for Patients with Stage II-III Squamous Cell Carcinoma of the Esophagus

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Purpose: The aim of this study is to evaluate the outcome of the patients with stage II-III esophageal cancer treated with radiation therapy.

Methods: Between 1999 and 2006, 87 patients with squamous cell esophageal carcinoma were treated with radiation therapy (RT) or concurrent chemoradiotherapy (CRT) at Gunma University Hospital. Seventy-four patients were men and 14 patients were women, and the median age was 71 years (range: 48–93 years). According to TNM staging system (UICC, 2002), 29 patients were stage II (IIA: 23, IIB: 6), and 58 patients were stage III. Radiation therapy consisted of 40–46 Gy with anteroposterior opposing field including the primary tumor and positive regional lymphnodes with optimal margins with conventional fraction followed by external beam boost up to 50–70 Gy (median: 64 Gy). Chemotherapy was administered concurrently with radiation therapy to 50 patients, and the 30 patients received the regimen contained cisplatin or nedaplatin (CRT-PT) and the 20 patients received the regimen consisting of docetaxel (CRT-DOC).

Results: At the end of this study, there were 27 survivors with a median follow-up period of 20 months (range: 6–85 months). The 2- and 3-year disease specific survival rates (DSS) were 44% and 29% for all 87 patients, 71% and 44% for stage II, and 31% and 22% for stage III. The difference of DSS between the patients with stage II and stage III was statistically significant (P = 0.0016). The CR rate and the 2- and 3-year DSS for the CRT group were 34%, 44%, 29%, respectively, and these results were better than those for the RT group of 24%, 43%, 19%, respectively, however, these differences observed were not statistically significant. The outcomes of the patients with CRT-DOC regimen resulted in almost the same as those of CRT-PT regimen group.

Conclusion: Our results revealed that definitive radiation therapy for squamous cell carcinoma of the esophagus is effective. Further investigations of the protocol of radiation therapy technique or chemotherapy are needed to clarify the impact of CRT on prognosis of the patients with this disease.

EGFR, p-Erk and p-AKT Expression in Barrett's Esophagus (BE): A Prospective Pilot Study

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Purpose: BE is a recognised precursor of esophageal adenocarcinoma (EA). However, the rate of progression of BE to adenocarcinoma is very low (0.5% per year). Identification of biomarkers that predict progression to dysplasia and adenocarcinoma is important. Epidermal growth factor receptor (EGFR) is activated in EA, which in turn cross activates the proliferative Erk and the antiapoptotic Akt pathways. Prospective data regarding the expression of these biomarkers in BE are scanty. We explored the expression of EGFR, p-Akt, and p-Erk in a prospective pilot study in patients with BE and BE with dysplasia.

Methods: 21 patients with BE, and 9 patients with BE with dysplasia were prospectively enrolled. Esophageal mucosal samples were obtained endoscopically in all cases. Uniform tissue processing and fixation techniques were applied. Immuno-histochemical staining for EGFR, p-Akt, and p-Erk was performed using validated techniques. Informed consent was obtained from all participating patients.

Results: EGFR expression was seen in all but one BE cases; 13 (61%) had strong positive expression. 18 BE cases (90%) showed positive expression of either p-Akt or p-Erk. There were total 9 cases of BE with either low grade (7) or high grade (2) dysplasia .8 out of these 9 cases showed positive expression of p-Akt while p-Erk was expressed in all. Strong positive expression of p-Akt and p-Erk was noted in 4 and 3 cases of BE with dysplasia, respectively. Significant correlation was observed between p-Akt and p-Erk expression in the whole study cohort [Kendall’s tau = 0.3591, (P = 0.0403)]. Due to the small sample size, no statistical correlation could be inferred between expression of EGFR, p-Akt, p-Erk and the presence of low or high grade dysplasia.

Conclusion: Association between p-Akt and p-Erk can lead to a survival and growth advantage for the affected premalignant cells. Whether this association leads to an aggressive course in BE or if this represents a pre-dysplastic change is unknown at this time. A larger study in BE patients with the above biomarkers is warranted.

Histology     EGFR + (++++) p-Akt + (++++) p-Erk + (++++)
BE (21)             20 (13)                18 (8)                 20 (3)
Dysplasia (9)      9 (7)                   8 (4)                 9 (3)

Objective Documentation of the Link between Gastroesophageal Reflux Disease and Obesity

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