**Initial EGD Dx Among Pts Eventually Dxd with Metaplasia (median, 25-75% range)**

| INITIAL DX | SUBJECTS # (%) | MONTHS TO CA | MONTHS TO CA (excluding CAs within 6mo) |
|---|---|---|---|
| **No Metaplasia** | 24 (12.2) | 71 (18, 141) | 114 (57, 157) |
| **Columnar Appearance, No Initial Bx** | 9 (4.6) | 15 (4, 62) | 61 (15, 157) |
| **Gastric Meta** | 7 (3.6) | 26 (1, 78) | 67 (26, 78) |
| **BE** | 15 (7.7) | 26 (1, 66) | 36 (26, 70) |
| **LG Dysp** | 6 (3.1) | 6 (2, 70) | 70 (9, 94)* |
| **HG Dysp** | 7 (3.6) | 2 (0.2, 17) | 86 (17, 154)* |
| **CA** | 128 (65.3) | N/A | N/A |

*<5pts, unstable estimates

W1272

**IL-6 Expression and Secretion is Increased in Patients with Barrett's Esophagus**

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Rationale & Aim:Barrett's esophagus (BE) is a pre-cancerous lesion resulting from chronic duodenogastroesophageal reflux with a significant risk of progression to esophageal adenocarcinoma. Previously it was shown that BE is associated with increased expression of Th2 cytokines. However, no studies were done to evaluate interleukin-6 (IL-6), a cytokine that has been shown to function as autocrine/paracrine growth factor in several different human cancers. We speculate that IL-6 contributes to progression to esophageal cancer by upregulating anti-apoptotic factors, which enhances development of apoptosis resistance. In this study we tested whether IL-6 is expressed in BE tissue at the mRNA and protein level. Also, we evaluated the activation of STAT3 (signal transducer and activator of transcription 3), transcription factor associated with IL-6 signaling, and the expression of two antiapoptotic proteins, Bcl-$x_L$ and Mcl-1. Methods: Endoscopic biopsies of duodenum, BE and squamous epithelium from BE patients were evaluated for IL-6 mRNA (7 patients) using RT real time PCR and expression of IL-6, phosphorylated STAT3, Bcl-$x_L$ and Mcl-1 by immunohistochemistry (10 patients). In addition, we incubated these tissues for three hours and determined IL-6 levels in conditioned media for the secretion of IL-6 by ELISA and by Human Cytokine Protein Array System. Results: Elevated levels of IL-6 were secreted from BE ($15.3 \pm 13.4$pg/mg protein) compared to duodenum ($1.2 \pm 1.7$ pg/mg), adjacent squamous epithelium ($1.1 \pm 1.2$ pg/mg) or normal squamous epithelium 5 cm away from the BE lesion ($0.8 \pm 0.9$ pg/mg). IL-6 mRNA levels were also elevated in BE compared to IL-6 mRNA in duodenum, adjacent squamous epithelium or distant squamous epithelium in 5 out of 7 patients. In addition, soluble IL-6 receptor (sIL-6R) was secreted from BE, duodenum and squamous epithelium allowing the IL-6 signal to be transduced into cells. IL-6 expression in intestinal glands in BE was also confirmed by immunohistochemistry. Strong nuclear staining for phosphorylated STAT3 was observed in BE glands. Mcl-1 and Bcl-$x_L$ were present at higher levels in the BE, while lower levels were found in duodenum or squamous epithelium. Conclusion: These data suggest that increased secretion and expression of IL-6 and upregulation of antiapoptotic proteins may contribute to the development of the apoptosis resistance in BE tissue and thus progression to cancer .

W1273

**Length of Barrett's Oesophagus Segment: Demographic Associations and Cancer Risk**

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Introduction: Studies have suggested a higher incidence of adenocarcinoma (AC) in longer Barrett's oesophagus (BO) segments, but this has not been stratified. Although AC has been described in short BO segments =<3cm (SSB), its incidence is controversial. The influence of age, gender, smoking, alcohol and BMI on the development of BO has been studied in small series, but not their influence on segment length. Methods: Medical records of 1000 BO patients from 5 hospitals registered with UKBOR were examined. Data were extracted on age, gender, BMI, tobacco and alcohol use, and length of BO segment at BO diagnosis. Data on AC development were also abstracted. Segment lengths were categorised as SSB, >3 =<6cm and >6cm. The relationships between demographic parameters and segment length, and segment length and AC development were determined, both for overall cancer risk and true incident cancers (occurring >1 year after BO diagnosis). Results: Histology and segment length were available in 625 records. There was a small, non-significant increase in BO length with age, but no correlation between gender, BMI, tobacco and alcohol consumption and segment length. The distribution of the 28 overall and 9 incident ACs according to segment length is shown in the table. Conclusions: The risk of both overall and incident cancers is greater for SSB than for segments >3 =<6cm in length, but the greatest risk is for length >6cm (Pearson Chi squared p = 0.02). Whilst demographic factors have previously shown an influence on the risks of developing BO, there is little correlation with the length of segment which develops.

**Percentage of Adenocarcinoma by Length of Barrett's Oesophagus Segment**

| | Overall (n=625) | SSB (n=270) | >3 =<6cm (n=253) | >6cm (n=202) |
|---|---|---|---|---|
| **All AC** | 28 (4.5%) | 10 (5.8%) | 4 (1.6%) | 14 (7.1%) |
| **Incident AC** | 9 (1.5%) | 3 (1.8%) | 2 (0.8%) | 4 (2.1%) |

W1274

**Comparison of Lower pH Values in the Esophagus of Patients with Barrett's Esophagus versus Those with Erosive Esophagitis**

Roy Dekel, Isaac B. Malagon, Harinder S. Garewal, Ronnie Fass

Background: It has been demonstrated that patients with Barrett's esophagus (BE) have higher esophageal acid exposure in the distal esophagus as compared to patients with erosive esophagitis (EE). Since some bile acids may have different solubility and availability in pH ≤2, which may affect their pathogenicity, we embarked on evaluating the esophageal pH distribution in patients with BE as compared to those with EE. Aim: To determine and compare duration of lower pH (≤2) exposure in the esophagus of patients with BE vs. those with EE. Methods: Patients underwent an upper endoscopy to determine the presence of EE or BE. BE was defined by the presence of intestinal metaplasia in biopsies obtained from salmon colored mucosa extending into the esophagus. Subsequently, patients were evaluated by 24-hour esophageal pH monitoring and their tracings were thoroughly analyzed. Percentage of total and supine time of pH <4, as well as the total and supine time of pH ≤ 2 were recorded. Results: Seventy-three patients were included in this study, of those 39 had BE (36M, mean age $64.5 \pm 2.17$, age range 33-86, mean BE length $3.8 \pm 0.5$ cm, range 0.5-11 cm) and 34 had EE (25M, mean age $55.5 \pm 2.3$, age range 28-78, LA grading: A-12, B-12, C-7, D-3). Esophageal mean percent total time pH <4 was significantly higher in BE patients as compared to those with EE ($14.9 \pm 1.66$ versus $8 \pm 1.0$, $p = 0.001$). Mean percent total time pH ≤2 was also significantly higher in BE patients ($2.8 \pm 0.53$ versus $1.16 \pm 0.3$, $p = 0.01$). When percent total time pH<4 in the supine position was evaluated, results were similar. The mean percent supine time pH <4 was significantly higher in Barrett's esophagus as compared to erosive esophagitis patients (Mean $15.6 \pm 2.3$ vs. $5.9 \pm 1.8$, $p = 0.002$). Mean percent supine time pH ≤2 was also significantly higher in the Barrett's esophagus group ($3.3 \pm 0.7$ vs. $1.1 \pm 0.7$, $p = 0.04$). Conclusions: BE patients demonstrate a significantly higher exposure to low (pH ≤2) esophageal pH values, most notably in the supine position, as compared to patients with EE. Further studies are needed to determine if this higher intensity of acid exposure is pathogenic on its own or in combination with bile acids.

W1275

**Multilayered Epithelium in a Rat Model of Barrett Esophagus**

Yinghao Su, Michael Klein, Ming Fang, Raj K. Goyal, Xiaoxin Chen, Chung S. Yang

Abstract Background: The multilayered epithelium (ME) consisting of squamous and metaplastic goblet cells has been described at the neo-squamocolumnar junction and within intestinal metaplastic mucosa in human Barrett esophagus (BE). We have described a rat model of CLE that shows phenotypic similarity to human BE. We performed studies to see if multilayered epithelium can be recognized in an animal model of BE and to study its phenotype. Materials and Methods: 8 week old rats received esophagogastroduodenal anastomosis (EGDA) and were sacrificed when 35 week old. Esophagi were removed, swiss-rolled and sectioned serially to examine the entire esophagus. Alcin blue/periodic acid Schiff(AB/PAS ) and high iron diamine/Alcin blue (HID/AB) were used for mucin staining. The differentiation markers (including CK7,CK20, CK14, Das-1, villin and pS2) and tumor-related gene products (including p53, c-myc and COX-2) were examined immunohistochemically. Results: 6 of 30 EGDA rats (20%) showed foci of multilayered epithelium that occurred at the neo-squamocolumnar junction and also away from the junction in the middle and the proximal esophagus. ME consisted of both squamous and columnar components with the columnar and goblet cells either on the top or middle or bottom of squamous cells. Foci of ME were easily missed in the conventional H&E stained tissues but were clearly revealed with AB/PAS staining. Multiple foci were found in one case. The mucinous cells like in human ME contained sulfomucin and sialomucin, but unlike in human ME the neutral mucin was absent. By immunohistochemistry, the mucinous cells in ME showed strong immunoactivity of CK7 and negative signal of CK20. For differentiation markers, the mucinous cells in ME foci showed moderate to strong cytoplasmic staining of villin and weak immunoactivity of Das-1 and pS2. The squamous component and the mucinous cells showed moderate cytoplasmic staining of CK14, a basal squamous epithelium marker. The tumor-related gene products such as p53, c-myc and COX-2 are negative in ME, but were expressed in the BE in the lower esophagus. No adenocarcinoma or adenosquamous carcinoma was seen in relation of ME. Conclusion: ME in rats shows morphologic, histochemical and differentiation features similar to the ME in human patients with BE. ME may represent early stage lesion in the development of BE. Since there are no esophageal submucosal glands in rats, these studies suggest that BE in the rats may arise from basal multipotential cells of the squamous mucosa.

W1276

**Surveillance Endoscopy Does Not Impact Survival of Patients With Barrett's Esophagus**

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Background: Survival benefit of surveillance endoscopy in Barrett's esophagus (BE) is unproven. We performed a cohort study to assess a potential survival benefit of surveillance endoscopy in BE. Methods: We did a retrospective cohort analysis of all biopsy proven BE patients that had an index endoscopy at our institution between 1990 and 2001. Survival was compared between patients that underwent regular surveillance endoscopy and those did not (opted out or not offered surveillance endoscopy). Baseline differences in co-morbidity of the 2 groups were adjusted by using a validated, weighted index, Charlson's comorbidity index (CCI). Adjustment for candidate predictors of survival, including health-seeking behavior was done by using Cox's Proportional Hazard Regression. Survival in strata of the co-morbidity index was determined. Mortality data were obtained from hospital records, state and national death indices. Results: 213 patients with Barrett's esophagus had an index endoscopy in the study interval. 106 were in a regular surveillance program whilst 107 did not undergo surveillance. Median age at diagnosis was 55 years, 98% were white and 66.7% were males (no differences between the surveillance and non-surveillance group). 180 patients had metaplasia only, 32 developed low-grade dysplasia, 6 high-grade dysplasia and