GERD Unresponsive to Proton Pump Inhibitors: Stop and Look for a Motility Disorder!

Chethana Kanaparthi, MD, Sreedevi Atluri, MD, Nigar Sofia, MD, Sury Anand, MD. The Brooklyn Hospital Center, Brooklyn, NY.

Purpose: Gastroesophageal reflex disease (GERD) is a common gastrointestinal disorder with a high prevalence in the western world. The presentation can vary from no symptoms to esophageal and extra-esophageal symptoms. Due to the absence of a clear-cut definition and minimal side effects from therapy, many patients with non-specific symptoms are treated with long-term proton pump inhibitors (PPI). A substantial group of patients report no relief of symptoms despite maximal acid suppression in addition to dietary and lifestyle modification. A recent consensus statement has recommended motility workup in patients who have GERD refractory to PPI with normal endoscopic findings. However, there is a lack of data on the prevalence of motility disorders in this patient population.

Methods: A retrospective chart review was conducted of all pts > 19 years of age who underwent esophageal manometry from Jan 2009 to April 2011 for any indication. All patients with a diagnosis of GERD who failed to respond to PPI metabolism criteria to be subjects in this study. Patients with an alternate diagnosis which explained their symptoms were excluded.

Results: Sixty one patients underwent esophageal manometry from Jan 2009 to April 2011. 26 subjects (age 63 +/- 10.5 yrs; 15% male) underwent manometry for PPI unresponsive GERD. All subjects underwent upper endoscopy prior to manometry. Endoscopy findings were normal in 23.77% had recorded mild gastritis or esophagitis. 87.5% had recorded hiatal hernias. All subjects were negative for H. pylori. 15/57 of the 26 subjects had peristaltic abnormalities on manometry. 13/50 subjects with peristaltic abnormalities had non-specific motor disorders with normal lower esophageal sphincter pressure, low amplitude peristalsis, simultaneous/reterograde contractions and poor bolus transit. 13/50 subject had findings compatible with achalasia of the esophagus. 1/38 subject had findings consistent with esophageal spasm.

Conclusion: This limited study suggests that patients labeled as GERD who are unresponsive or partially responsive to PPI should be routinely evaluated for a motility disorder of the esophagus. Once identified, the motility abnormality will lead to a different workup and therapeutic plan.

Downstream Effects from the Establishment of a New Radiofrequency Ablation (RFA) Program for Barrett’s Esophagus in a Tertiary Medical Center

Ji Young Bang, MBBS,1 Shyam Varadarajulu, MD,1 Thomas Lynch, Director of Administration and Finance,2 Jeannitta Blakey, RN,2 C. Mel Wilcox, MD,2 Shujian Peter, MD.1 1. Department of Internal Medicine, University of Alabama at Birmingham, Birmingham, AL; 2. Division of Gastroenterology-Hepatology, University of Alabama at Birmingham, Birmingham, AL.

Purpose: RFA is well accepted as a minimally invasive option for the eradication of dysplasia in Barrett’s esophagus. However, the establishment of a new RFA program incurs significant costs to a health care facility. Our aim was to evaluate the downstream effects of a newly established RFA program at a tertiary referral center.

Methods: All patients referred for Barrett’s esophagus-associated dysplasia were enrolled prospectively in a database. Details on patient demographics, referring services, technical details of the RFA, other adjunctive investigations or procedures performed in conjunction with RFA and patient follow-up were documented.

Results: Fifty-one new patients (mean age 64 years, SD = 11.1; male [n = 45]) underwent 116 RFA procedures (median 3 per patient [range, 1-4]) over an 18-month period. While 26% of the referrals were from within the University Health System, the other 74% of the referrals were from outside facilities or physicians (p = 0.02). Procedural indications were low-grade dysplasia in 32 (63%), high-grade dysplasia in 17 (33%), and high-grade dysplasia with concurrent carcinoma in situ in 2 (4%) patients. Thirty of the fifty-one (59%) patients required other procedures either in conjunction with or following the RFA and included EMR of focal neoplasia (n = 5), transesophageal EUS (n = 16), confocal endomicroscopy (n = 10) and chemoradiation (n = 2). Two of the 51 patients (4%) required inpatient observation (24 hrs) following RFA for the management of pain/bleeding. No major complications were encountered. The payer mix was private insurance in 46% and Medicare/Medicaid in 54%. Since program initiation, average total revenue per patient (without an estimation of the downstream revenue) is $5,900, of which $4,600 is the hospital-generated revenue and the remaining $1,300 is the professional fee revenue. Also the ratio of collection to hospital charges for RFA was 22%, which is comparable to EUS (25%) and better than ERCP (15%).

Conclusion: A significant number of new referrals and additional procedures are generated by a newly established RFA program by means of downstream effects with substantial financial benefit.

DNA Abnormalities in Benign Barrett’s Esophagus (BE) Are Associated with Subsequent Progression to Esophageal Adenocarcinoma (EAC)

2011 ACG Presidential Poster

William Buliewicz, MD, MSc,1 Grant Carlson, BS,2 Tiffany Chouinard, BS, CG(ASCP),3 MB(ASCP),4 Robert Gasparini, BS,5 Melissa Luc, MS, CCG(ASCP),6 Scott Gasparini, BS,7 Theresa Emory, MD,8 Jackie Makapugay, MD,9 Nicholas Shaheen, MD, MPH: 1. Department of Medicine, Division of Digestive Diseases, University of North Carolina Hospitals, Chapel Hill, NC; 2. NeoGenomics Laboratories, Fort Myers, FL; 3. GI Pathology, Memphis, TN; 4. Highlands Pathology Consultants, Kingston, TN.

Purpose: To assess for DNA abnormalities in benign BE (no dysplasia or low-grade dysplasia [LGD]) that precede and are associated with high-grade dysplasia (HGD) or EAC.

Methods: Patients with benign BE and a second biopsy taken 6-36 months later were identified from the GI laboratory database. Progressors had HGD or EAC on their follow up biopsy while non-progressors had stable histology. Four probe fluorescence in situ hybridization (FISH) assay (MYC[8q24], p16[9p21], HER2[17q12], and ZNF217[20q13.2]) was performed on the baseline benign pathology specimen to evaluate for DNA abnormalities. Assay results were quantified by the percentage of cells with single probe gains, multiple probe gains, homozygous 9p21 loss, and any probe gain with any 9p21 loss. Results were considered positive if they exceeded thresholds previously associated with the presence of EAC. The prevalence of DNA abnormalities was compared among progressors and non-progressors using non-parametric tests.

Results: 21 progressors and 15 non-progressors were identified and analyzed. Progressors were older (median age 62 vs 44) and had more LGD at baseline (29% vs 0%). Gender (92% male) and time between biopsies (median 25 months) were not significantly different. Multiple gains abnormalities were significantly more prevalent in progressors (8/21, 38%) compared to non-progressors (0/15) (see table) (p = 0.01). Abnormalities in single gains, 9p21 loss, and combined gain and loss were more frequent among progressors (5-19% vs 0% in non-progressors) but did not reach statistical significance. At least one DNA abnormality was detected by FISH in 43% of progressors (9/21) and 0% of non-progressors (p<0.01).
Conclusion: DNA abnormalities in subjects with benign Barrett's histology were associated with subsequent progression to cancer. Future study is necessary to determine if analysis of genetic abnormalities in benign BE can reliably predict patients at risk for progression.

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<th>Prevalence of DNA abnormalities</th>
<th>Multiple Gains &gt;4%</th>
<th>Single Gains &gt;16%</th>
<th>Homozygous 9p21 loss &gt;5%</th>
<th>Gains and 9p21 loss &gt;4%</th>
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<td>No progression (n = 15)</td>
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<td>4 (19%)</td>
<td>1 (5%)</td>
<td>2 (10%)</td>
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Do Positive PET/CT Scans for Esophageal Disease Preclude Endoscopic Treatment of Early Esophageal Adenocarcinoma?

Gang Sun, MD,1 Jianmin Tian, MD, MSPH,1 Ganapathy Prasad, MD,1 Lori Lutzké, RN,2 Louis Wong Kee Song, MD,1 Navtej S Buttar, MD,1 Kenneth Wang, MD,1 1. Gastroenterology and Hepatology, Barrett’s Esophagus Unit, Rochester, MN; 2. Department of Gastroenterology and Hepatology of Chinese PLA General Hospital, Bei Jing, China.

Purpose: CT-fusion positron emission tomography (PET/CT) with fluorine 18 fluorodeoxyglucose (FDG) has been increasingly applied for staging of patients with esophageal adenocarcinoma (EAC) for its detection of regional and distant metastases (LNM); however, the role of PET/CT scan in identifying candidates who are suitable for endoscopic therapy (≤ T1a stage) is still unknown. Our initial hypothesis was that the volume of tumor necessary to be positive in the esophagus could preclude endoscopic therapy due to the size and depth of invasion. The aim of this study was to evaluate the association of positive esophageal PET/CT scans and depth of tumor invasion based on histopathology.

Methods: PET/CT scan and pathology reports of consecutive EAC patients who underwent endoscopic mucosa resection (EMR) were reviewed. Patients with abnormal uptake in cervical and abdominal lymph node or the presence of distant lesions on PET scans were excluded. A negative PET was defined as no abnormal uptake, while positive PET scans have visible esophageal thickness or mass in PET/CT fusion imaging with a SUV > 3. Indefinite PET scan cases included those who lack of typical uptake pattern such that it is impossible to differentiate inflammation from malignancy. The depth of EAC invasion was categorized as either T1a (intramucosa), T1b (submucosa), T2 (muscularis propria), or T3 (adventitia) based on either EMR or esophagectomy histopathology reports.

Results: Totally 130 eligible EAC patients from 2000 to 2010 were identified. All had PET/CT scans performed within 6 months of the index EMR that found EAC. 60 cases had negative PET 30 were positive; and 40 were indeterminate, of which 45% (18/40) had lesions ≤ T1a stage. After excluding these 40 indeterminate cases, the final analyses were based on 90 cases. The mean age was 64.9 ± 12.0 years; 86.7% were male; 23 had esophagectomy; 27 (28.9%) were T1a; 49 were T1b; 12 were T2 and 2 were T3. And 30 (33.3%) had positive PET scan. 60 (66.7%) had negative PET scan. Among 30 cases with positive PET/CT results, 30.0% (9/30) had T1a lesions. 33.3% of patients had positive PET scans in both T1a and ≥T1b groups. Overall PET scan results were not associated with T staging based on pathology findings. There was no difference in age (> 70 y/o), gender, and rate of esophagectomy between the positive and negative PET scan cases.

Conclusion: Positive esophageal CF-fusion PET scans do not indicate a tumor bulk that precludes endoscopic mucosal resection for the treatment of early esophageal cancer.

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Evaluation of Fully Covered Removal Wallflex Stent for Benign Esophageal or Gastric Disorders

Niraj Jani, MD,1 Nyan Latt, MD,1 Venkataraman Palabindala, MD,1 Bharath Alanudemumangurum, MD,2 1. Greater Baltimore Medical Center, Baltimore, MD; 2. Sinai Hospital, Baltimore, MD.

Purpose: To evaluate the efficacy and complications of fully covered removal esophageal wallflex stents for benign esophageal or gastric disorders.

Methods: Retrospectively evaluated all patients from 2010-2011 in two institutions that had a fully covered esophageal wallflex stent placed for a benign esophageal or gastric condition. All patients with esophageal strictures had been previously treated with dilation and had no long-term response. Data collected included indication for insertion, efficacy, stent related complications, and follow-up after removal.

Results: Twenty-two stents were placed in 11 pts (mean age 52 yo, 8 M, 3 F). The indications for stent insertion were dysphagia in eight patients and post-operative leak in three patients. Dysphagia was secondary to peptic stricture in 3 patients, radiation-induced stricture in 2 patients, anastomotic stricture in 1 patient, hyperesophaginous mass in 1 patient, and mediastinal collection causing pseudoachalasia in 1 patient. Stent insertion was successful in all patients and sizes included, 10 mm x 60 mm in 3 patients, 18 mm x 100 mm in 5 patients, 23 mm x 120 mm in 3 patients. The mean time until stent removal was 48 days. Post-procedure, 64% of patients complained of pain and 100% of patients complained of severe reflux in areas where the stent crossed the esophageal-gastric junction. Dysphagia was improved in 87% of patients after stent placement and most tolerated at least a soft diet. Post-operative leak was closed in all 3 patients after a mean of 71 days. Stent removal was easily achieved in all patients. Ulceration was noted at the proximal and distal margin of the stent in all patients, as well as, esophagitis is those patients whose stent crossed the esophageal-gastric junction. Resolution of dysphagia after stent removal was achieved in 62% of patients. Stent migration was noted in 2 patients.

Conclusion: Fully covered removal wallflex stents are an effective and safe modality for treating refractory dysphagia and post-operative leaks. Pain and esophagitis were the most frequent adverse effects observed.

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Histologic and Endoscopic Correlation in Eosinophilic Esophagitis

2011 ACG Presidential Poster

Eric Johnson, MD,1 Samuel Barasch, MD,1 Bashmi Agni, MD,1 Eric Gaumnitz, MD,2 1. University of Wisconsin Hospital and Clinics, Department of Medicine, Madison, WI; 2. University of Wisconsin Hospital and Clinics, Department of Pathology, Madison, WI.

Purpose: Eosinophilic esophagitis (EoE) is an increasingly recognized cause of dysphagia and food impaction in adults. EoE is a clinicopathologic diagnosis characterized by esophageal dysfunction, a variety of endoscopic findings, and esophageal biopsies showing a predominance of eosinophilic inflammation.