Concordance of Barrett's Esophagus and Adenomatous Colon Polyps

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A. Study Purpose And Rationale

Barrett's esophagus (BE) is the condition in which columnar epithelium replaces the squamous epithelium that normally lines the distal esophagus. The condition develops when gastroesophageal reflux disease (GERD) damages the squamous esophageal mucosa and the injury heals through a metaplastic process in which columnar cells replace squamous ones. Esophageal adenocarcinoma develops in approximately 1 in 20 (0.5 percent) patients with Barrett's esophagus per year, which makes monitoring and treating BE a high priority.

The purpose of this study is to determine if patients with BE have a higher incidence of colon polyps, specifically adenomatous polyps > lcm in size which are considered to be premalignant. The development of colon cancer and adenomatous polyps are thought to arise from similar molecular mechanisms. Specifically, studies have shown an increase expression of the enzyme Cyclooxyeganse-2 (COX-2) in the pathogenesis of both Barrett's Esophagus and colon polyps

Analysis of COX-2 expression shows that it is elevated in up to 90 percent of sporadic colon carcinomas and 40 percent of colonic adenomas but is not elevated in the normal colonic epithelium. Similarly, studies have shown COX-2 protein expression to be significantly higher in patients with Barrett's metaplasia, dysplasia, and adenocarcinoma compared with normal squamous esophageal or columnar duodenal epithelia.

Given the similar molecular findings in these two pre-malignant conditions, it seems justified to perform a study comparing the concordance of these two groups. It is possible that a finding of BE could be a harbinger for increased propensity for colon adenomas.

B. Study Design and Statistical Analysis

This study will be performed via a retrospective chart review. Data from 100 patients with documented Barrett's Esophagus who also received screening colonoscopy will be collected. This data will be compared to an age and sex matched control population of 500 patients who received screening colonoscopies. The control population will consist only of asymptomatic patients who underwent colonoscopy for screening purposes.

Patients with gastrointestinal bleeding, symptoms of inflammatory bowel disease, symptoms of bowel obstruction, those with chronic GI conditions, patients with known history of GI malignancies or familial colon cancer syndromes will be excluded from the analysis (see below for full exclusion criteria).

The two groups will be analyzed using a Chi-Square analysis. Statistical significance will be determined based on an alpha of 0.05. A positive finding will include any patient with colonoscopic evidence of polyps >1cm in size or the finding of colorectal cancer of any stage.

Power analysis was used to determine the necessary group sizes required to document clinically significant differences between the BE group and the control group. A presumed 50% incidence of colon polyps in the BE group and a 33% incidence in the control group (with a 5:1 ratio of controls to BE patients) requires 417 patients in the control group and 83 patients in the BE group for a power of 80%. In our study, using 100 BE patients and 500 control patients, our findings will be statistically significant if BE patients <26% or >40% prevalence of polyps.

Subgroup analysis will be performed based on 1) Age of the patients and 2) Histopathology of Barrett's mucosa. Age related analysis will be performed because studies have shown that increasing age is directly related to the prevalence of colon polyps. Histologic analysis will be performed because of

evidence demonstrating that BE with higher grade dysplasia is associated with increased expression of molecular markers such as COX-2 (which, as previously discussed is up-regulated in both BE and colon polyps).

C. Study Procedure

This study will be performed using a systematic chart review of records from esophagogastric-duodenoscopies (EGDs) and colonoscopies that have been performed over the past 10 years.

D. Study Drugs

No drugs will be used in this study

E. Medical Device

No medical devices will be used in this study

F. Study Questionnaires

No questionnaires will be used in this study

G. Study Subjects

Data from the charts of 100 patients who have evidence of Barrett's esophagus on EGD who also have recorded screening colonoscopy data will be included in this study. All of these patients will be above 50 years of age (as screening colonoscopies are not performed on younger patients) Data from the charts of 500 patients who have had a screening colonoscopy will be included in the control group of this study.

Inclusion criteria for BE group: Patient must have documented BE via EGD with biopsy specimens documenting the grade of esophageal dysplasia. The patients will be at least 50 years of age with a screening colonoscopy performed and documented biopsy data from any relevant findings on colonoscopy.

Inclusion criteria for control group: Patients must have documented results of screening colonoscopy. Of note the screening colonoscopy must have been performed for screening purposes only. Any prior symptom or complaint that was cause for colonoscopy will be reason for exclusion.

Exclusion criteria: The following patients will be excluded form the control arm of the study:

- Patients on whom colonoscopy was performed for gastrointestinal symptoms/complaints
- Patients who showed signs of GI abnormality on prior laboratory or radiological studies
- Patients with gastrointestinal bleeding
- Patients with symptoms of inflammatory bowel disease
- Patients with symptoms of bowel obstruction
- Patients with chronic GI conditions involving the large bowel
- Patients with known history of GI malignancies
- Patients with known familial colon cancer syndromes
- Recruitment of Subjects
- Patient data will be used for chart review purposes, no additional patient recruitment will be necessary.

H. Recruitment of Subjects

Patient data will be used for chart review purposes, no additional patient recruitment will be necessary.

I. Confidentiality of Study Data

Study data will be coded without the use of names, hospital unit numbers, social security numbers, initials, phone numbers or addresses. A unique code number will be used for all study subjects.

Data will be stored in a secure location accessible only to investigators.

J. Potential Conflict of Interest

None of the investigators have any proprietary interest in any portion of this study.

K. Location of Study

All analysis will be performed at CUMC.

L. Potential Risks

No further risks or discomforts beyond the previously performed procedures will be imparted upon study subjects.

M. Potential Benefits

Patients will not have any direct benefit as a result of this study

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N. Alternative Therapies

No experimental therapies are included in this study

O. Compensation to Subjects

No payment or compensation will be given to study subjects

P. Costs to Subjects

Subjects will not incur any costs as a result of this study

Q. Minors as Resarch Subjects

No minors are included in this study.

R. Radiation or Radioactive Substances

No radiation will be used in this study.