

# ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

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## Screening for Barrett Esophagus With a Nonendoscopic Sponge Capsule



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### **G&H** What is the current standard method used to screen patients for Barrett esophagus?

**RF** The current diagnostic method is endoscopy or biopsy. Different countries have different thresholds for referring patients who have a history of gastroesophageal reflux symptoms and indigestion for an endoscopy. Generally, no population-based screening program exists across countries or health care systems for Barrett esophagus the way there is for colon cancer. A decision to perform endoscopy is generally based on symptom-generated referral.

### **G&H** Are there any screening guidelines for Barrett esophagus?

**RF** Yes, there are guidelines produced by national societies, such as the British Society of Gastroenterology in the United Kingdom and the American Gastroenterological Association and the American Society for Gastrointestinal Endoscopy in the United States. These guidelines are in broad agreement and state that population-based screening is not recommended. However, they do suggest that patients who have chronic gastroesophageal reflux disease and multiple risk factors, such as abdominal obesity, male sex, white race, and age over 50 years, should be considered for a screening endoscopy. A family history of Barrett esophagus or esophageal adenocarcinoma should lower the threshold for referral.

### **G&H** How effective and practical are these guidelines?

**RF** Like any guideline, these are not enforced. It is up to the practitioner to read the guidelines and follow them. The purpose of looking for Barrett esophagus is to try to prevent deaths from esophageal cancer and to intervene early. One of the challenges with esophageal cancer is that the vast majority of cases present at quite an advanced stage. In the United Kingdom—and likely elsewhere—there is a large amount of variation in referral practices.

### **G&H** Should screening be reserved for patients with symptoms of Barrett esophagus?

**RF** Not all patients with Barrett esophagus have gastroesophageal reflux symptoms. They probably nearly all have reflux of acid or bile, but they do not necessarily present with symptoms.

The decision regarding who to investigate also depends on which tests are available. Endoscopy is a routine procedure but can be viewed as invasive, uncomfortable, and costly for the health care system. Population-based screening with a simple and effective method such as a blood test would be ideal.

There have been experts who have advocated for patients to receive an upper gastrointestinal endoscopy at the same time as their colonoscopy. However, this would be

quite an undertaking, logistically. Therefore, an important consideration for screening is the availability of the method, as well as the effectiveness and cost of that method.

### **G&H** What is the role of the sponge capsule in nonendoscopic screening?

**RF** The sponge capsule (Cytosponge, University of Cambridge) was designed to provide screening that is more patient-friendly and less costly to the health care system than an endoscopy, while using a more sophisticated molecular technology to assess patient samples than endoscopy or biopsy.

### **G&H** How does the procedure work?

**RF** The sponge capsule is a pill approximately the size of a multivitamin that is attached to a string. Compressed inside the capsule is a spherical sponge. Once the capsule is swallowed, it dissolves in approximately 5 minutes, and the sponge emerges. After 5 minutes, a nurse pulls the sponge out by the string and stores the sponge in a standard specimen container with preservative at room temperature. The specimen can then be sent to a laboratory using standard transport. The sample is stable in a refrigerator and can be kept for several weeks before processing, if necessary.

### **G&H** Is any special preparation required for the patient?

**RF** Aside from abstaining from food for several hours before the procedure, the patient does not need to do anything to prepare. The sponge capsule is intended to be a test for primary care physicians. Patients do not have to go to a specialist center, and they do not need any sedation. They just swallow the capsule with water, and the capsule travels with a string down to the top of the stomach.

### **G&H** What is the advantage of this technique over endoscopy or biopsy?

**RF** When patients undergo endoscopy and biopsy to evaluate Barrett esophagus, endoscopists take random biopsies in a practice known as the Seattle protocol. The endoscopist obtains 4 biopsies every 2 cm and processes the samples to a slide. A pathologist then examines the samples with a microscope. One of the problems with biopsies is sampling bias. A diagnosis of Barrett esophagus should be straightforward because it can be seen with an endoscope, but it is identifying the areas of dysplasia that is important in order to identify patients who need endoscopic therapy to prevent progression to cancer. In contrast to endoscopy,

when the sponge capsule is withdrawn, cells are collected from along the entire length of the esophagus, which should lead to much less sampling bias.

### **G&H** Are there any disadvantages or risks associated with this procedure?

**RF** With this procedure, patients may experience slight discomfort when the string is at the back of their throat and when the sponge is pulled out. From my own experience of undergoing the procedure, the removal of the sponge caused watery eyes, but the procedure was very brief. In studies conducted by my colleagues and I at the University of Cambridge, patients found this technique acceptable and often preferable to endoscopy.

Some patients are concerned that the string may break; however, in our 2 large studies of more than 1600 patients, this has not been an issue. If string breakage were to occur, the sponge could be retrieved via endoscopy.

Bleeding is the other potential hazard, just as it is a risk when obtaining a biopsy. This also has not been a problem in our studies.

### **G&H** How does this technique detect Barrett esophagus?

**RF** The collected cells, which have been gathered from the entire length of the esophagus, are spun down to create a homogeneous cell pellet. This pellet is embedded in paraffin, similar to a biopsy, and sections of it are tested for trefoil factor 3 (TFF3). TFF3 is a very specific protein that is expressed in Barrett esophagus cells and does not present in normal esophagus or stomach cells. An antibody stain determines whether TFF3 (and therefore the Barrett esophagus cells) is present, with a positive or negative score. Even if the specimen expresses a stain in only 1 cell, the test is positive.

### **G&H** How should patients be managed if the test is positive?

**RF** If a patient's test is positive, more tests would be performed using cells from the same sponge capsule specimen to determine the likelihood for progression to cancer by searching for molecular evidence of dysplasia. Endoscopists would test for mutations in *P53*, a well-recognized cancer gene. Patients with gene mutations would undergo an endoscopy with the plan that they will receive treatment to remove dysplastic areas with a procedure such as endoscopic resection or ablation therapy if there is no visible lesion. The rapid advances in endoscopic treatment available mean that it is now reasonable to consider screening more seriously than in the past, when the only option for patients was esophagectomy.

**G&H** Are there any patients in whom this procedure should be avoided?

**RF** Patients with swallowing difficulties or any alarm symptoms suggestive of cancer should undergo an urgent endoscopy, not a sponge capsule. Patients on anticoagulants or with varices are at a greater risk for bleeding and should also be excluded.

**G&H** What are the priorities for research and development in this field?

**RF** Early diagnosis is essential for improving outcomes in esophageal cancer. By the time a cancer is detected, it is usually too late to treat. This field needs better diagnostic tests that are less invasive than endoscopy and that also use molecular technologies to provide more objective diagnostic readouts than pathology. Molecular testing for diagnosis is very important, as are tests that are inexpensive, effective, simple, and safe so that they can be used on a population-wide basis.

*Dr Fitzgerald is named on patents relating to the Cytosponge and diagnostic assays. This technology has been licensed to*

*Covidien (now Medtronic) by the Medical Research Council in the United Kingdom.*

**Suggested Reading**

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