

# ADVANCES IN ENDOSCOPY

Current Developments in Diagnostic and Therapeutic Endoscopy

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## Risk Stratification for Esophageal Adenocarcinoma Screening and Surveillance

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**G&H** Could you describe the US epidemiology of the different types of esophageal cancer?

**SJS** Adenocarcinoma of the esophagus was once a very rare tumor in this country, but it is currently the most common form of esophageal cancer in the United States. The incidence has increased by over 600% in the past 30 years. It is the esophageal cancer that is associated with gastroesophageal reflux disease (GERD) and Barrett esophagus.

The other major type of esophageal cancer is squamous cell cancer. Squamous cell esophageal cancer is the most prevalent esophageal cancer worldwide, with particular concentration in certain parts of Asia and Africa.

In the United States, the most important risk factors for squamous cell cancer are smoking and alcohol abuse. Squamous cell cancer is also associated with certain nutritional deficiencies, whereas adenocarcinoma is associated with obesity and overeating. In addition, adenocarcinoma is primarily a disorder of white men whereas squamous cell is a cancer most often seen in Asian and black men.

**G&H** How are the obesity epidemic and the escalating prevalence of GERD and Barrett esophagus related to rising rates of esophageal adenocarcinoma?

**SJS** There are at least two theories as to why obesity might contribute to cancer in patients with Barrett esophagus. One is that obesity may predispose patients to more severe GERD, potentially in two different ways. First, obesity can increase abdominal pressure, which

might predispose to reflux. Also, overweight people tend to eat a lot of foods that can give them reflux (eg, fatty foods, chocolate).

The other theory is that obesity is associated with insulin resistance, which raises circulating levels of insulin-like growth factor-1. This growth factor can cause increased proliferation of certain cells, and increased proliferation predisposes to the development of dysplasia and, ultimately, cancer.

**G&H** Can this information, along with other risk factors, be used to stratify Barrett esophagus patients for risk of adenocarcinoma and determine a course of screening and surveillance?

**SJS** There is no easy answer as to which patients should undergo screening and surveillance. Some clinicians feel there is no point in doing it at all because there is no proof that these practices decrease morbidity and mortality from esophageal cancer in patients with GERD and Barrett esophagus. I would suggest that the bulk of the flawed evidence that we have does support some form of screening and surveillance. For example, a number of computer-generated models suggest that screening and surveillance in certain groups of patients can be beneficial.

The patients who seem to be at the greatest risk for Barrett esophagus and esophageal adenocarcinoma are white men over the age of 50, particularly if they are obese. However, that does not mean that no one else should undergo screening and surveillance. Beyond these factors, it is difficult to give any definite guidelines. We still do not know why, in people who seem to have an equal severity of reflux disease, one patient develops Barrett and cancer and the other does not. It is almost certainly a matter of genetic predisposition but we have yet to pinpoint what the genetic difference is.

Again, there is no definitive proof that by doing screening and surveillance, we are decreasing cancer mor-

bidity or mortality. There is only indirect evidence. As a result, the controversy continues.

**G&H** Are there any other theories to explain the increasing prevalence of esophageal adenocarcinoma?

**SJS** There are several. One of the most interesting recent theories as to why adenocarcinoma is occurring in the gastroesophageal junction region relates to dietary nitrate. Most dietary nitrate comes from green, leafy vegetables. Shortly after World War II, farmers in Western nations began pouring a tremendous amount of nitrate into the soil by way of nitrate-based fertilizers. Dietary nitrate is absorbed, concentrated in the salivary glands, secreted into the mouth, and then reduced to nitrite by bacteria on the tongue. When nitrite is exposed to gastric acid it can be converted into nitric oxide, which is a very reactive molecule that causes DNA damage. The reaction that converts nitrite to nitric oxide in the presence of gastric acid is almost instantaneous, so it happens where the two substances first meet, at the end of the esophagus. This could also tie in to the higher rate of this cancer in people of higher socioeconomic status. These patients are overall better nourished and eat more leafy greens. It is an interesting theory, but I don't suggest that you stop eating salads.

**G&H** What new technologies are in development to aid endoscopists in the detection of Barrett dysplasia?

**SJS** Chromoendoscopy uses dyes to stain the Barrett epithelium. The most commonly used dyes for this process are methylene blue and indigo carmine. Depending on which dye is used, certain areas that contain dysplasia can light up when viewed endoscopically. Narrow-band imaging is another new technology that picks out blue light in order to specifically view blood vessels and other features in the surface epithelium. There are also interesting data

regarding the use of endosonography, optical coherence tomography, spectroscopy, and confocal microendoscopy. High-definition endoscopy (standard endoscopy that utilizes high-definition television technology) is becoming more widely available, and I am not yet convinced that any of these other technologies will be found to be superior to high-definition endoscopy.

Presently, none of the new technologies has been shown to be clearly superior to the current clinical standard of systematic sampling of the Barrett-affected esophageal segment, where a systematic, four-quadrant biopsy technique is utilized to look for an essentially invisible lesion that may be randomly distributed. Targeted biopsy certainly should be used whenever lesions are visible.

**G&H** Are there any other new screening techniques that are less invasive and may be more feasible to administer to the entire GERD-affected population?

**SJS** Researchers in proteomics are studying protein markers that might provide diagnostic clues to a number of diseases with a simple blood test. It certainly would be nice to have a blood test that could identify high-risk patients, but there is no such test available at this time.

### Suggested Reading

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