Barrett's Screening Based on Inadequate Evidence

BY DOUG BRUNK
San Diego Bureau

SAN DIEGO — Current screening and surveillance guidelines for Barrett's esophagus and associated neoplasia are not supported by strong evidence, Dr. Marcia Irene Canto said at a meeting jointly sponsored by the AGA Institute and the Japanese Society of Gastroenterology.

"There is currently insufficient evidence for sedated esophagogastroduodenoscopy [EGD] screening, but it may be more cost effective than surveillance if only Barrett's patients with dysplasia diagnosed by screening are then followed," said Dr. Canto, director of clinical research in the division of gastroenterology and hepatology at Johns Hopkins University, Baltimore.

As for current surveillance practices, "the biopsy protocol detects cancer, but current guidelines regarding increased surveillance intervals in Barrett's patients without dysplasia would lead to missed high-grade dysplasia and cancer," she said. "We need better endoscopic techniques and better risk stratification."

Dr. Canto explained that current practices for screening and surveillance of Barrett's esophagus are not based on randomized, controlled trials (level I evidence) or even well-designed cohort or case-control trials (level II evidence). Rather, current practice is based on decision analyses, case series, case reports, or flawed clinical trials (level III evidence), opinions of expert authorities based on clinical evidence, descriptive studies, or reports of expert committees (level IV evidence), and insufficient evidence to form an opinion (level V evidence).

"The rationale for screening and surveillance is to improve survival, but more and more we are trying to prevent cancer in Barrett's patients," she said. "It's a different approach, by detecting high-grade dysplasia and intervening with ablation endoscopic mucosal resection or esophagectomy in this precancerous phase."

Data on 783 patients from five prospective studies and one patient registry suggest that the risk of cancer in Barrett's esophagus is related to the grade of dysplasia. The risk for patients with no dysplasia stands at 2%, while the risk for those with low-grade and high-grade dysplasia is 7% and 22%, respectively.

Dr. Canto noted that there are no randomized, controlled trials on the evidence for surveillance in Barrett's esophagus, only three retrospective case series and one ongoing prospective study. But data from those studies indicate that the 2-year survival rate seems to be improved for patients who undergo surveillance, compared with those who don't (86% vs. 46%). "And an economic analysis of surveillance in general suggests that if you target patients with dysplastic Barrett's, it probably is cost effective," she said.

The evidence against surveillance is largely based on the fact that most Barrett's patients die from other causes. "When you look prospectively, the risk of cancer in Barrett's is really low: about 0.5%-1.2% per year," she added. "Therefore, EGD, which is the standard way of doing surveillance, is very costly."

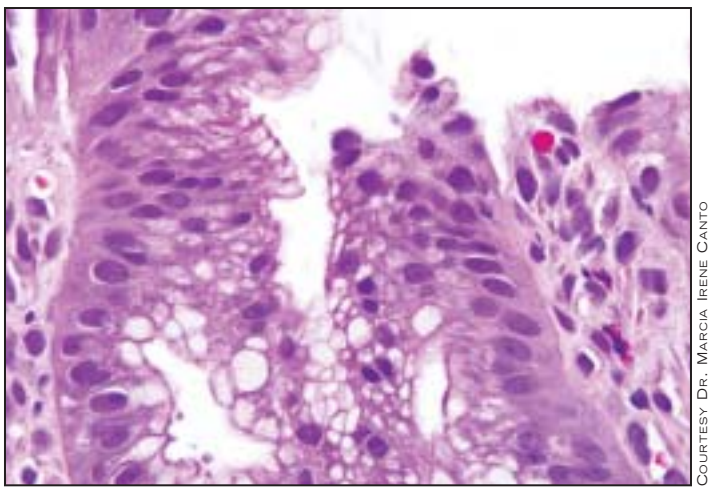
Moreover, the optimal surveillance technique remains unknown. "Across the United States there is such inconsistency in techniques for surveillance," she said. "Many practicing gastroenterologists do not follow any particular biopsy or surveillance technique."

Since clinicians at Johns Hopkins began endoscopic surveillance in 1994, the prevalence of occult cancer in 39 Barrett's patients with high-grade dysplasia has decreased from 43% to 21%. None of the 15 patients who had some type of biopsy protocol or imaging technique implemented in their surveillance had occult cancer, while 8 of the 24 who did not follow a biopsy protocol clearly had occult cancer. "This is even with modern endoscopy techniques, so there is some benefit to trying to do that," Dr. Canto said.

For a Barrett's patient with no dysplasia, the American Gastroenterological Association (AGA) recommends a second EGD 1 year later, and then surveillance every 5 years (Gastroenterology 2005;128:1468-70).

The American College of Gastroenterology (ACG) guidelines are similar, but recommend surveillance every 3 years (Am. J. Gastroenterol. 2002;97:1888-95).

"Is this evidence-based?" Dr. Canto asked. "Guidelines written by the GI societies are based on current data and decision analyses in terms of what the best surveillance interval is. There will never be the equivalent of the National Polyp Study for colon cancer surveillance."



COURTESY DR. MARCIA IRENE CANTO

Histology slide shows low-grade dysplasia in a biopsy sample obtained from a patient with Barrett's esophagus.

For a Barrett's patient with low-grade dysplasia, the AGA recommends an EGD every 6 months for 1 year, then increasing the surveillance interval to every 1-2 years. The ACG guidelines are similar, but they recommend surveillance every year.

For a Barrett's patient with high-grade dysplasia, the American Society for Gastrointestinal Endoscopy recommends confirming the diagnosis with two experienced pathologists and then offering the patient surgery or endoscopic therapy (Gastrointest. Endosc. 2006;63:570-80). The patient should then undergo surveillance every 3 months for at least 2 years.

The ACG guidelines are similar but recommend endoscopic mucosal resection for more severe disease.

Preliminary results from a prospective multicenter study of 618 patients show that the prevalent cancer risk within 1 year of diagnosing the index lesion was 6.7% (Clin. Gastroenterol. Hepatol. 2006;4:566-72). Furthermore, when the researchers followed the patients, the risk of cancer in patients with no dysplasia was 0.5% per year while the risk of cancer in patients with low-grade dysplasia was similar at 0.6% per year.

So far, regression of low-grade dysplasia has occurred in 66% of patients. Dr. Canto pointed out that 53% of the incident high-grade dysplasias or cancers developed after two EGDs with no dysplasia. "So what if you have the patient back at year 5 according to the AGA guidelines, but the patient developed a Barrett's cancer or high-grade dysplasia in year 2?" she asked. "We don't have the evidence for increasing the surveillance intervals. In fact, preliminary evidence from this paper suggests that Barrett's high-grade dysplasia or cancer might be missed if you followed the AGA guidelines."

Screening for Barrett's esophagus and associated neoplasia presents another quagmire. The ACG guidelines state that patients with chronic GERD symptoms are most likely to have Barrett's esophagus and should undergo upper endoscopy, but an AGA technical review concluded that there is no direct evidence that has validated the use of screening for esophageal cancer in the United States.

Dr. Canto said that this is in part because 40% of Barrett's patients with cancer have no GERD symptoms and fewer than 4% have Barrett's diagnosed before the cancer is diagnosed.

One study concluded that screening 50-year-old men with symptoms of GERD to detect adenocarcinoma associated with Barrett's esophagus is probably cost effective, but continuing surveillance of patients who have Barrett's esophagus but no dysplasia is costly, even if screening occurs at 5-year intervals (Ann. Intern. Med. 2003;138:176-86).

Candidates for screening include patients with erosive esophagitis, those with chronic severe GERD, white males over age 50 regardless of symptoms, those with a family history of Barrett's and adenocarcinoma, those who are obese, and postcholecystectomy patients (Am. J. Gastroenterol. 2004;99:2107-14).

Current endoscopic tools for screening include a standard videoendoscope (sedated or unsedated), an unsedated thin videoendoscope, an office-based thin battery-powered endoscope, and wireless capsule endoscopy. ■

FDA Advises Halt in Use of Two Flexible Endoscope Washers

BY ELIZABETH MECHCATIE
Senior Writer

The Food and Drug Administration is advising health care providers to stop using two models of a machine used to wash and disinfect flexible endoscopes, if the providers have an alternative method of disinfection.

The machines are the System 83 Plus Washer/Disinfector and the System Plus 83 Mini-flex Washer/Disinfector, which are manufactured by Custom Ultrasonics Inc. A statement issued by the FDA on Feb. 7 says that the agency and company signed a consent decree of permanent injunction, in which the company agreed to stop manufacturing and distributing the machines until it brings its methods and controls used to manufacture the machines into compliance with FDA's good manufacturing requirements. The company also agreed to develop and implement adequate written medical device reporting procedures, according to the statement.

The FDA is not aware of any adverse events resulting from this problem, the statement says, but adds that a potential health hazard exists because improperly cleaned and disinfected endoscopes "can be a source of transmission of pathogens between patients, causing life-threatening infections."

The agency advised health care providers who use the machines to stop using them if they have other options, including using another device or "following appropriate protocols to manually wash and disinfect the device." If they have no alternative, they "should carefully weigh the risks and benefits of using these products," the FDA said.

In a letter to customers dated Feb. 8 and posted on the company's Web site, Custom Ultrasonics said that it was cooperating with the FDA and expected to be in compliance with the FDA's regulations and have the matter resolved "very shortly."

The letter stressed that the company was not aware of any reports of an infection or disease transmission associated with the proper use of the System 83 Plus, and that it was safe and effective for cleaning and high-level disinfection of flexible endoscopes "when used in accordance with its labeling." The System 83 Plus machines have been used to reprocess several million flexible endoscopes over the past 20 years, according to the letter. ■