New Imaging Methods May Aid Dx of Barrett's

BY JEFF EVANS

White light endoscopic methods for Barrett's esophagus screening and surveillance could soon be overtaken by more accurate endoscopic techniques, the most promising of which appears to be narrow band imaging, based on new research.

Narrow band imaging (NBI) may offer the best accuracy in detecting metaplasia, dysplasia, and cancer while reducing the number of biopsies needed to detect changes in esophageal tissue.

White light endoscopy typically relies on random biopsy sampling using the four-quadrant protocol to detect tissue changes, which endoscopists adhere to poorly, said Dr. Prateek Sharma, professor of medicine at the University of Kansas and the Veterans Affair Medical Center, Kansas City.

COURTESY DR. PRATEEK SHARMA

NBI could "dramatically change how we do biopsies in patients with Barrett's esophagus," Dr. Prateek Sharma said.

Other techniques, such as autofluorescence imaging and confocal endomicroscopy, potentially could serve complementary roles to white light endoscopy or NBI during screening and surveillance, said Dr. Sharma, who has evaluated NBI with his colleagues over the past 5 years.

These technologies "have the ability in the future to dramatically change how we do biopsies in patients with Barrett's esophagus and potentially help us increase the yield of dysplasia and cancer [and] probably even decrease our biopsy burden," Dr. Sharma said in an interview.

The current standard of care for biopsying patients with Barrett's esophagus—the four-quadrant protocol—takes a random tissue biopsy every 90 degrees in every 2-cm length of esophagus that contains Barrett's metaplasia.

Dr. Sharma cited several reasons why the four-quadrant protocol is flawed. The random biopsying may miss dysplastic and cancerous segments in the Barrett's tissue because "if you take a biopsy in the 12 o'clock position, you are hoping that the dysplasia or early cancer is also in that position. It could be in the 1 o'clock or 2 o'clock position and you would just miss it."

In addition, only about half of patients actually undergo the full biopsy protocol. A recent study of nearly 11,000 patients with Barrett's esophagus who were undergoing surveillance biopsying in the Caris Diagnostics pathology database found that only 51% of patients underwent the full biopsy protocol as recommended by the American College of Gastroenterology guidelines for Barrett's surveillance.

Increasing length of affected tissue was associated with less compliance with the full protocol. Not surprisingly, lower adherence to the protocol was associated with a lower rate of detecting dysplasia, after stratifying the patients based on their length of tissue affected by Barrett's (Clin. Gastroenterol. Hepatol. 2009;7:736-42).

During esophageal endoscopy with NBI, white light is filtered to pass blue light (and some green light) to shine on esophageal tissue. Because hemoglobin in blood selectively absorbs blue light, clinicians can look for irregularities in the patterns of blood vessels or surface mucosa, which have been correlated with histologic findings of dysplasia or cancer in previous studies.

To determine if targeted biopsies with NBI could detect Barrett's metaplasia and dysplasia or cancer better than does high-definition white light endoscopy (HD-WLE) alone, Dr. Sharma and his colleagues at the VA Medical Center and two other centers (Amsterdam Medical Center and the Medical University of South Carolina, Charleston) conducted a study of 123 patients who were referred for Barrett's screening or surveillance.

They were randomized to an exam with HD-WLE, followed later by NBI, or first NBI and then HD-WLE. In each case, a separate investigator performed the second procedure 6-8 weeks after the first procedure without knowing the results of the first.

This study design was "rigorous" and "one of the most robust for an imaging study," he said.

During HD-WLE, the investigators took biopsies with the four-quadrant technique in every 2-cm length of affected tissue. The patients had an average age of nearly 60 years and were mostly men and white.

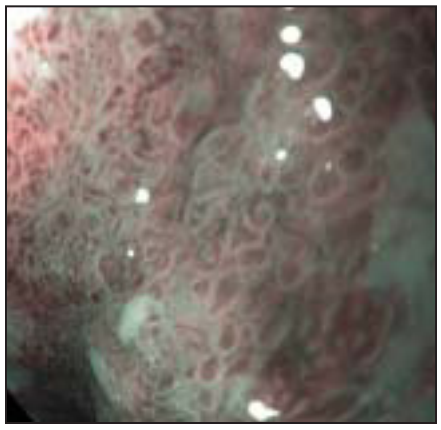
At the annual Digestive Diseases Week, Dr. Sharma reported that the rate of detection of intestinal metaplasia in the patients' biopsies—the study's primary end point—was 85% for each modality. The detection of patients with neoplasia (low- and high-grade dysplasia and/or cancer) also was not significantly different between NBI (71%) and HD-WLE (55%).

NBI detected more lesions overall with high-grade dysplasia or cancer than did HD-WLE (19 vs. 13). Lesions with any type of dysplasia (low- and high-grade dysplasia and cancer) also were found with NBI significantly more often than with HD-WLE (81 vs. 67).

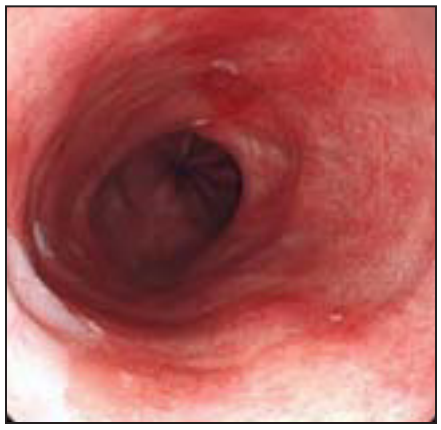
NBI required significantly fewer biopsies per procedure than did HD-WLE (3.6 vs. 7.6).

Dr. Sharma reported that he receives grant and research support from Olympus America, which manufactures the NBI device used in the study, and also from Mauna Kea Technologies.

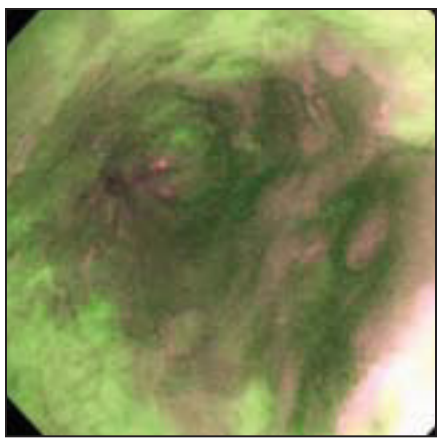
The American Society for Gastrointestinal Endoscopy funded the study. ■



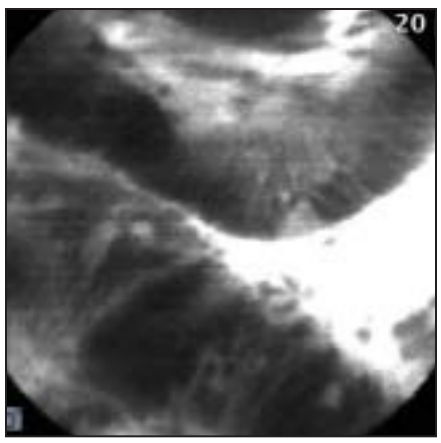
NBI accurately detects the dysplastic tissue seen in Barrett's esophagus.



White light endoscopy relies on random tissue biopsy to detect Barrett's.



Autofluorescent imaging has a high false-positive rate for Barrett's tissue.



Confocal endomicroscopy may be useful as an adjunct to NBI.

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Autofluorescence and Confocal Imaging

Autofluorescence imaging is a "broad-based imaging tool" that can monitor changes in the pattern of distribution of autofluorescent proteins in the esophagus when normal mucosal tissue becomes dysplastic or cancerous, Dr. Prateek Sharma explained.

Tissue patches that are found to be dysplastic or cancerous could then be targeted for biopsy. However, research suggests that autofluorescence imaging may have a false-positive rate that is too high to be useful as a standalone screening and surveillance procedure for Barrett's esophagus because tissue patches that have been flagged as dysplastic or cancerous may be normal or inflamed tissue.

In another study presented at Digestive Diseases Week by Dr. Sharma's research group, autofluorescence imaging conducted with a prototype multimodality endoscope from Olympus America Inc. had poorer sensitivity for detecting high-grade dysplasia or cancer than did narrow band imaging (NBI) in 25 patients who were undergoing surveillance of Barrett's or endoscopic treatment of high-grade dysplasia or cancer. Autofluorescence imaging detected a total of 23 abnormal areas in 11 patients, whereas NBI located 19 abnormal areas in 12 patients.

"The jury is still out on autofluorescence, and we still need further studies to define its exact role," he said.

The broad-based technique of NBI or autofluorescence imaging also might be combined with a third, much more focused technique called confocal endomicroscopy, which is a "way of doing in vivo histology," Dr. Sharma said.

In areas of tissue that already have been highlighted as abnormal with NBI or autofluorescence imaging, this method could take a micrometer-level view of irregularities in glands, increases in cell sizes, and changes in the entire arrangement of cells. However, no study has yet been published that combines confocal endomicroscopy with another technique.