Best Surveillance of Barrett's Takes an Overview

BY MITCHEL L. ZOLER
Philadelphia Bureau

COPENHAGEN — High-resolution, white-light endoscopy was as good as more targeted endoscopy methods for diagnosing high-grade dysplasia or early cancer in patients with Barrett's esophagus, based on study results from 28 patients.

"The ability of an endoscopist to detect lesions in overview is more important than targeted imaging. For detecting lesions in Barrett's esophagus, high-quality, white-light imaging is the most important technique" available today, Dr. Jacques Bergman said at the 13th United European Gastroenterology Week.

Autofluorescence endoscopy using red light may have potential to improve overview detection of dysplasia and early cancer, but this must be proved in further studies, said Dr. Bergman, a gastroenterologist at the Academic Medical Center, Amsterdam, who also has a PhD.

The study he reported tested two other new methods for improving endoscopy sensitivity: indigo carmine chromoendoscopy (ICC), and narrow-band imaging (NBI).

ICC uses indigo carmine stain to improve visualization of dysplasia. NBI uses filters to produce red-, blue-, and green-light images that highlight different aspects of the esophageal mucosa. For example, blue light, with its shorter wavelength, provides good resolution in the superficial mucosa, while red light, with a longer wavelength, better images deeper tissue.

The study included 17 patients who had been referred to the Academic Medical Center because of suspicion of high-grade dysplasia or early cancer, 6 patients who had undergone treatment for high-grade dysplasia, and 5 patients with Barrett's esophagus who were in a routine surveillance program.

The 28 patients were randomized to an initial examination by high-resolution endoscopy with white light, plus either ICC or NBI. The examination took two biopsies from any identified abnormalities plus random biopsies at 2-cm intervals throughout the area affected by Barrett's esophagus. Patients then underwent a second examination 6 weeks later using the alternate imaging method.

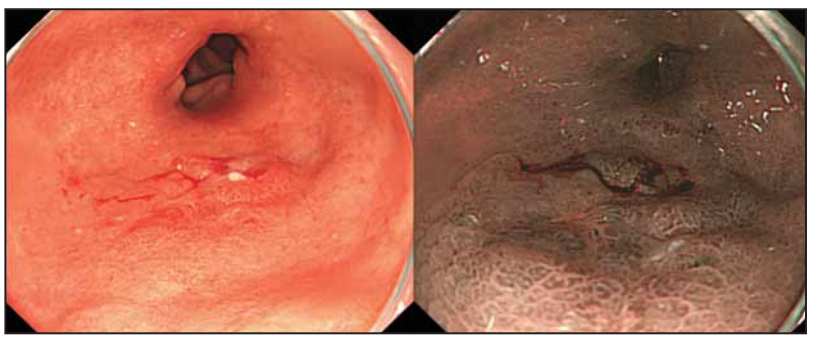
The combined imaging and biopsy data were used to make a definitive diagnosis for each patient. Overall, 14 patients were determined to have high-grade dysplasia or early cancer, 9 had low-grade dysplasia, and 5 had no dysplasia.

Of the 14 patients (93%) with high-grade dysplasia or early cancer, 13 (93%) were diagnosed by ICC, compared with 12 (86%) diagnosed with NBI, Dr. Bergman reported.

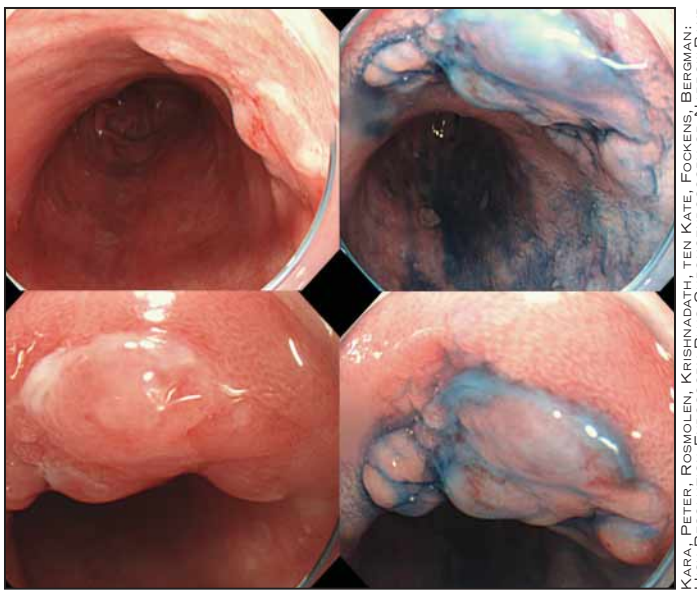
But the study's aim was to assess the ability of each method to do targeted imaging. By this standard, both methods flagged lesions for biopsy that identified high-grade dysplasia or early cancer in 11 of the 14 patients (79%).

All of these 11 patients were also diagnosed with high-grade dysplasia or early cancer by high-resolution, white-light endoscopy alone, showing that this method is as good as ICC or NBI for the overview identification of significant disease.

"The high sensitivity of white-light endoscopy reduces the potential, added value of ICC and NBI," Dr. Bergman said. ■



Shown are a high-resolution white-light image (left) and the corresponding narrow-band image (right) of a mucosal type IIa-IIc lesion.



High-resolution white-light endoscopy (left), indigo carmine chromoendoscopy (right) yield views of a malignant lesion.

KARA, PETER, ROSMOLEN, KRISHNADATH, TEN KATE, FOCKENS, BERGMAN: HIGH-RESOLUTION ENDOSCOPY PLUS CHROMOENDOSCOPY OR NARROW-BAND IMAGING IN BARRET'S ESOPHAGUS. ENDOSCOPY 2005;37:929-36. ©GEORG THIEME VERLAG KG

Novel PPI-NSAID Pill May Prevent GI Mucosal Injury

HONOLULU — A novel fixed-combination tablet comprising an immediate-release proton pump inhibitor plus an enteric-coated NSAID showed considerable promise for the prevention of upper GI mucosal injury in a pilot study, Dr. W. James Alexander reported at the American College of Gastroenterology's annual meeting.

Large clinical trials are being planned to evaluate the efficacy of the fixed-combination drug, which is designed to ensure adherence to gastroprotective therapy when recommended for NSAID users, explained Dr. Alexander, senior vice president of product development and chief medical officer at Pozen Inc., Chapel Hill, N.C.

Pozen has been issued a patent for the fixed-combination tablet, known for now as PN 100. Each tablet contains 15 mg of immediate-release lansoprazole surrounding a core of 500 mg of naproxen, which has a pH-sensitive enteric coating.

Dr. Alexander reported on 60 healthy volunteers randomized to 14 days of one of three treatment regimens: PN 100, twice daily; 500 mg of enteric-coated naproxen, twice daily; or 15 mg of delayed-release lansoprazole in the morning plus naproxen 500 mg, twice daily, which is the type of gastroprotective regimen most often used.

Endoscopy performed on day 14 by a gastroenterologist blinded to treatment status revealed 5 subjects in the PN 100 group had Lanza grade 3 or 4 mucosal lesions, compared with 15 subjects on twice-daily enteric naproxen and 14 on delayed-release lansoprazole plus naproxen twice daily. Two patients on enteric naproxen developed gastric ulcers, as did one on delayed-release lansoprazole plus naproxen. None of the PN 100-treated subjects developed gastric ulcers.

The mean cumulative number of erosions found at endoscopy on days 8 and 14 was 10 in the PN 100 group, 26 with enteric naproxen alone, and 19 with delayed-release lansoprazole plus naproxen. Twenty-four hour gastric pH monitoring indicated nocturnal acid suppression was better with PN 100 than with delayed-release lansoprazole plus naproxen.

—Bruce Jancin

Genetic Polymorphism Test Could Identify Barrett's Patients at Risk for Progression

BY KATE JOHNSON
Montreal Bureau

MONTREAL — Genetic testing of patients with Barrett's esophagus to determine their risk for progression to esophageal adenocarcinoma might be a reasonable consideration in the near future, according to Alan G. Casson, M.B., professor of surgery at Dalhousie University in Halifax, N.S.

In a recently published paper presented at the annual meeting of the Canadian Association of Thoracic Surgeons, Dr. Casson showed that the *CCND1* G870A polymorphism is found with increasing frequency through the chronic inflammation spectrum from gastroesophageal reflux disease (GERD) through Barrett's esophagus (BE) and on to esophageal adenocarcinoma (EACA).

"The contribution of this polymorphism to susceptibility of defined stages of progression to esophageal adenocarcinoma suggests [that] the incorporation of *CCND1* genotype analysis in endoscopic Barrett surveillance programs may allow better stratification of individuals at increased risk for malignant progression," he wrote (Cancer 2005;104:730-9).

"This now needs to be tested in larger prospective studies, but it looks promising," he said.

The analysis included 307 patients enrolled in a prospective case-control study designed to evaluate risk factors and molecular alterations in GERD (126 patients), BE (125), and EACA (56).

Compared with healthy, asymptomatic controls (95), all patients had elevated levels of the *CCND1* A/A genotype, after adjustment for age and gender, Dr. Casson said. And the prevalence of this abnormality increased from GERD (odds ratio 2.8) through BE (OR 3.7) and EACA (OR 5.9).

In the second part of the study, which was presented as an award-winning poster at the 13th World Congress of Gastroenterology, Dr. Casson's team identified obesity, smoking, and increased alcohol consumption as significant predictors of risk for progression of GERD and BE to EACA.

Obesity was identified as the main lifestyle risk factor for EACA (OR 4.67), followed by smoking (OR 3.86), whereas increased alcohol consumption was a risk factor for GERD (OR 2.69) and BE (OR 3.86).

The study found that a diet high in vitamin C can decrease the risk of GERD (OR 0.4), BE (OR 0.44), and EACA (OR 0.2), and that multivitamin supplementation further reduced the risk of EACA (OR 0.17).

Other work presented by Dr. Casson's team—at both the Canadian Association of Thoracic Surgeons meeting and the World Congress of Gastroenterology—supports the hypothesis that a chronic inflammatory process is behind the progression from GERD to EACA.

The study found a progressive increase in levels of nitrotyrosine, a marker for nitric oxide–induced cellular damage, in esophageal tissue samples from patients with GERD (4%), BE (20%), and EACA (35%).

It also found nitrotyrosine expression present in 43% of EACA patients, compared with 22% and 24% of BE and GERD patients, respectively.

Nitric oxide damage has been implicated as a potential causative factor in *p53* mutations, and the studies also found higher levels of these mutations in EACA patients, compared with BE and GERD patients. ■