

## Prevalence of Nonpolypoid Colorectal Neoplasms in Adults

Researchers, led by Roy Soetikno, MD, of the Veterans Affairs Palo Alto Health Care System in Palo Alto, California, sought to evaluate the frequency of nonpolypoid colorectal neoplasms and characterize their relationship with colorectal cancer. This cross-sectional study was performed among 1,819 patients (mostly male) undergoing elective colonoscopy at a California veterans hospital during the time period July 2003 to June 2004. Patients were classified into subgroups based upon their reasons for undergoing colonoscopy (for screening, surveillance, or symptoms). The main outcome measures included endoscopic appearance, location, size, histology, and depth of invasion of the neoplasms. The results of the study were published in a March issue of the *Journal of the American Medical Association*.

The authors found the overall prevalence of nonpolypoid colorectal neoplasms to be 9.35% (95% confidence interval [CI], 8.05–10.78%; n=170). In the patient subgroups for screening, surveillance, and symptoms, the prevalence of nonpolypoid colorectal neoplasms was 5.84% (95% CI, 4.13–8.00%; n=36), 15.44% (95% CI, 12.76–18.44%; n=101), and 6.01% (95% CI, 4.17–8.34%; n=33), respectively. The overall frequency of nonpolypoid colorectal neoplasms with in situ or submucosal invasive carcinoma was 0.82% (95% CI, 0.46–1.36%; n=15), while in the screening subgroup, the prevalence was 0.32% (95% CI, 0.04–1.17%; n=2). The researchers also found that carcinoma was more likely to be contained in nonpolypoid colorectal neoplasms (odds ratio [OR], 9.78; 95% CI, 3.93–24.4) than polypoid lesions, regardless of size. The positive size-adjusted association of nonpolypoid colorectal neoplasms with in situ or submucosal invasive carcinoma was also seen in the subgroups for screening (OR, 2.01; 95% CI, 0.27–15.3) and surveillance (OR, 63.7; 95% CI, 9.41–431). The highest risk was associated with the depressed type of neoplasms (33%). Nonpolypoid colorectal neoplasms containing carcinoma were smaller in diameter compared to polypoid lesions (mean [SD] diameter, 15.9 [10.2] mm vs 19.2 [9.6] mm, respectively). The authors concluded that in their patient population, nonpolypoid colorectal neoplasms were relatively common lesions that were diagnosed during routine colonoscopy and had a greater association with carcinoma as opposed to polypoid neoplasms, independent of size.

According to Dr. Soetikno, the study demonstrated that nonpolypoid colorectal neoplasms, often considered

mainly a Japanese disease, are prevalent in the United States as well. He also noted that the study demonstrated the importance of bowel preparation, as nonpolypoid colorectal neoplasms are flat and difficult to distinguish from normal mucosa membrane, especially with inadequate bowel preparation.

## Early Data on Certolizumab Pegol in Infliximab-refractory Crohn's Disease

Initial 6-week induction data from the WELCOME trial (26-Week open-label trial Evaluating the clinical benefit and tolerability of certolizumab pegol induCtiOn and Maintenance in patients suffering from CD with prior loss of response or intolerance to infliximab) were presented at the third congress of the European Crohn's and Colitis Organization, held recently in Lyons, France. The WELCOME trial is a phase IIIb multicenter study of 539 Crohn's disease patients in whom infliximab (Remicade, Centocor) treatment was not successful. During the 6-week induction period, all patients were administered 400 mg of certolizumab pegol (Cimzia, UCB) subcutaneously at 0, 2, and 4 weeks. At Week 6, patients were randomized to continued administration of certolizumab pegol every 2 or 4 weeks. Concomitant medications included immunosuppressants (46%), corticosteroids (38%), or both (18%). By Week 6, the primary endpoint response, a decrease in Crohn's Disease Activity Index Score (CDAI) of 100 points or more from baseline was achieved in 61% of the patients. In addition, 39% of patients achieved disease remission, defined as a total CDAI score of less than 150 points.

Certolizumab pegol has shown a low incidence of injection site pain in the WELCOME trial (<2%). Common adverse events included headache, nasopharyngitis, nausea, vomiting, pyrexia, or arthralgias, while serious adverse events occurred in 7% of the patients and most commonly included gastrointestinal disorders (5%) and infections and infestations (2%).

## Chromoendoscopy and Narrow-Band Imaging Versus White Light Endoscopy in Barrett Esophagus

According to the March issue of *Gastroenterology*, Jacques Bergman, MD, PhD, of the Academic Medical Center in the Netherlands, and associates conducted a study to determine the best endoscopic technique for Barrett esophagus by comparing magnified still images obtained from 22 areas with high-resolution white light endoscopy and the enhancement techniques indigo carmine

chromoendoscopy, acetic acid chromoendoscopy, and narrow-band imaging. Each area was evaluated for overall image quality, mucosal image quality, and vascular image quality by 7 endoscopists who did not have expertise in Barrett esophagus or advanced imaging techniques and by 5 endoscopists who were international experts in this field. The regularity of mucosal and vascular patterns and the presence of abnormal blood vessels were also examined and correlated with histologic evidence.

The authors found that the enhancement techniques scored higher in terms of overall image quality, mucosal imaging quality, and vascular imaging quality. Narrow-band imaging and acetic acid chromoendoscopy were the most commonly preferred techniques and were rated best for overall image quality (43% and 40% of comparisons, respectively). White light endoscopy and indigo carmine chromoendoscopy were ranked most often as the worst techniques (38% and 39% of comparisons, respectively). However, the higher image quality did not translate into a clinically relevant benefit. Interobserver agreement for the 3 features of mucosal morphology (mucosal irregularity, vascular irregularity, or the presence of abnormal blood vessels) with white light images ranged from  $\kappa=0.51$  (95% CI, 0.46–0.55) to  $\kappa=0.53$  (95% CI, 0.50–0.57) for all observers, from  $\kappa=0.43$  (95% CI, 0.33–0.54) to  $\kappa=0.53$  (95% CI, 0.41–0.64) for experts, and from  $\kappa=0.51$  (95% CI, 0.15–0.33) to  $\kappa=0.64$  (95% CI, 0.58–0.70) for nonexperts. The addition of any of the enhancement techniques to white light images did not improve interobserver agreement in these groups or the yield for detecting early neoplasia, which was 86% for all observers, 90% for experts, and 84% for nonexperts. The authors speculated that most of the essential information may already have been present in the high-quality white light endoscopy images or that the interpretation of the images may vary widely among endoscopists, possibly explaining why the expert endoscopists had a lower agreement for mucosal patterns compared to nonexperts.

### Survival in Stenting Alone or With Photodynamic Therapy in Unresectable Cholangiocarcinoma

Michel Kahaleh, MD, of the University of Virginia Health System in Charlottesville, Virginia, and colleagues evaluated survival in patients with unresectable cholangiocarcinoma undergoing endoscopic retrograde cholangiopancreatography (ERCP) with photodynamic therapy (PDT) and stent placement with patients undergoing ERCP with stent placement alone. In this study, the results of which were published in the March issue of *Clinical Gastroenterology and Hepatology*, 48 patients were palliated for unresectable cholangiocarcinoma during a 5-year period. Nineteen patients received PDT (with

porfimer sodium) and stents, while 29 patients received biliary stents alone. The researchers conducted multivariate analysis with Model for End-Stage Liver Disease score, age, treatment by chemotherapy or radiation, and number of ERCP procedures and PDT sessions to determine survival predictors. Successful therapy was defined as relief of cholangitis, jaundice, and pruritis, with a decrease of bilirubin to less than 75% of the pretreatment value within 30 days.

According to the researchers, Kaplan-Meier analysis revealed improved survival in the PDT group as opposed to the stent-only group (16.2 vs 7.4 months;  $P<.004$ ). Mortality in the PDT group at 3, 6, and 12 months was 0%, 16%, and 56%, respectively, compared to 28%, 52%, and 82%, respectively, in the stent group. The difference between the two groups was significant at 3 and 6 months but not at 12 months. Multivariate analysis demonstrated that only the number of ERCP procedures and the number of PDT sessions were significant for determining survival. Adverse events associated with PDT included skin phototoxicity requiring topical therapy ( $n=3$ ). The authors concluded that ERCP with PDT appeared to increase survival in patients with unresectable cholangiocarcinoma as opposed to ERCP alone, but were not certain whether this is the result of PDT or the number of ERCP sessions. They noted that these data should be confirmed by a prospective randomized multicenter study.

### Updated Guidelines for Barrett Esophagus

Due to the rise in the frequency of esophageal cancers in the United States and the development of scientific advances in the area of Barrett esophagus, new guidelines were recently developed by the American College of Gastroenterology (ACG) Practice Parameters Committee. These guidelines, which were published in the March issue of the *American Journal of Gastroenterology*, updated the ACG's 2002 guidelines and highlighted new recommendations for the diagnosis and surveillance of low- and high-grade dysplasia in addition to new endoscopic ablation therapies for the treatment of Barrett esophagus.

According to Richard E. Sampliner, MD, MACG, of the University of Arizona Health Sciences Center, and co-author of the updated guidelines along with Kenneth Wang, MD, of the Mayo Clinic in Rochester, Minnesota, the new guidelines recommend that low-grade dysplasia, like high-grade dysplasia, should be confirmed by an expert gastrointestinal pathologist, to avoid reading variability.

In addition, the updated guidelines recommend that treatment for Barrett esophagus with high-grade dysplasia begin not with esophagectomy, the standard therapy, but with a more intensive biopsy protocol to exclude the presence of esophageal adenocarcinoma.

The guidelines also emphasize the role of endoscopic mucosal resection as an effective approach for the management of mucosal irregularities in high-grade dysplasia and highlight new endoscopic treatment procedures such as radiofrequency ablation and the potential use of esophageal capsule endoscopy for diagnosing and screening Barrett esophagus. The complete guidelines are available on the ACG website.

### 5-Year Data on Entecavir Treatment of Chronic Hepatitis B

At the 18th Conference of the Asia-Pacific Association for the Study of the Liver, recently held in Seoul, South Korea, researchers presented 5-year data of treatment with entecavir (Baraclude, Bristol-Myers Squibb) among patients with nucleoside-naïve chronic hepatitis B. In the study, more than 700 patients across 6 studies initiated entecavir therapy and were monitored for treatment response and resistance. This new report added data on patients receiving entecavir during their fifth year of follow-up (n=108 patients in nucleoside-naïve studies and n=33 patients in lamivudine [Epivir, GlaxoSmithKline]-refractory studies). All patients enrolled in clinical trials who had virologic breakthrough ( $\geq 1$  log increase in hepatitis B DNA from nadir, as measured by polymerase chain reaction [PCR]) or whose virus had not yet become undetectable (hepatitis B DNA levels  $< 300$  copies/mL, as measured by PCR assay) at Weeks 48, 96, 144, 192, 240, or end of dosing, were sequenced to determine whether any changes occurred in the viral genetic code to result in resistance or loss of effectiveness of entecavir.

According to the authors, no additional patients developed resistance in the fifth year (n=108). Through 5 years of treatment, the cumulative probability of developing mutations in the virus that confer genotypic resistance to entecavir was 1.2%. Among lamivudine-refractory patients who received entecavir after treatment failures with lamivudine, the cumulative probability of genotypic resistance to entecavir was 51% through the fifth year. This finding is similar to prior observations that the pre-existence of lamivudine-resistant mutations causes an increase in the rate of entecavir resistance.

### New Colorectal Cancer Screening Guidelines

New guidelines for colorectal cancer screening, which focused for the first time on prevention as the primary goal, were recently issued by the American Cancer Society Colorectal Cancer Advisory Group, the US Multi-Society Task Force, and the American College of Radiology Colon Cancer Committee. Of note, these guidelines, which were published online in *CA, A Cancer Journal for Clinicians*, added stool DNA and virtual colonography to the existing list of colorectal screening options for average-risk people

over 50 years of age and people with symptoms or risk factors for colon cancer.

In addition, the new guidelines noted that the most effective tests for detecting both polyps and cancer are:

- Flexible sigmoidoscopy (recommended every 5 years)
- Colonoscopy (every 10 years)
- Double-contrast barium enema (every 5 years)
- Virtual colonography (every 5 years)

The guidelines also specified the following types of stool tests for detection of cancer, rather than polyps:

- Guaiac-based fecal occult blood testing (recommended every year)
- Fecal immunochemical test (every year)
- Stool DNA test (frequency not specified due to lack of sufficient data)

The authors pointed out that this was the first time that such guidelines have stated preferences for one type of test over another and the first time they have discussed numerous quality issues for the different tests, in an effort to improve screening quality. The authors also pointed out that some options, such as virtual colonography and the relatively new stool DNA test, are not usually reimbursed by insurance.

#### In Brief

**According to a Japanese multicenter survey, infliximab is more efficacious in Crohn's disease with short duration,** most likely because of less frequent stenosis. (*Dis Colon Rectum*. 2008 Mar 6 [Epub ahead of print].)

**Researchers of a randomized controlled trial found that virologic response to peginterferon alfa-2a improves inflammation and fibrosis in hepatitis C virus patients with advanced fibrosis or cirrhosis** and that improving virologic response and maintaining ideal body weight are critical for achieving optimal histologic outcomes in hepatitis C virus patients. (*Aliment Pharmacol Ther*. 2008;27:542-551.)

**In a multicenter, randomized, double-blind, placebo-controlled trial of patients with predicted severe acute pancreatitis, probiotic prophylaxis with a combination of probiotic strains did not reduce the risk of infectious complications and was associated with an increased risk of mortality.** Researchers concluded that probiotic prophylaxis should therefore not be administered in this category of patients. (*Lancet*. 2008;371:651-659.)