H. pylori Eradication Cuts Gastric Cancer Incidence

BY DENISE NAPOLI
Assistant Editor

Eradication of *Helicobacter pylori* in patients with early-stage gastric cancer reduced the risk of subsequent metachronous gastric carcinoma significantly, compared with controls, in a Japanese study of more than 500 patients.

H. pylori is a known gastric carcinogen, according to the World Health Organization, and its causal effect on the development of gastric cancer has been proved in animal studies, noted the Japan Gast Study Group, which conducted the current study (Lancet 2008;372:392-7).

However, studies of the effect of eradication of the bacterium have had mixed results. Most notably, "a large-scale, double-blind randomized study in China showed that gastric cancer still occurred after successful eradication of *H. pylori* and that eradication did not lead to a significant decrease in the incidence of gastric cancer" (JAMA 2004;291:187-94).

In the current multicenter, open-label, randomized, controlled study of 544 patients with early gastric cancer who were either planning to have endoscopic treatment or who had just completed resection after endoscopic treatment, half of the patients (272) were given a drug regimen to eradicate the *H. pylori* bacterium, and half served as controls.

A modified intention-to-treat analysis included 255 patients in the treatment group and 250 patients in the control group, after 17 treatment patients and 22 controls were lost to follow-up. Three-quarters of patients in both groups were men, and all patients were aged 62-73 years.

The treatment group received a combination of lansoprazole 30 mg twice daily, amoxicillin 750 mg twice daily, and clarithromycin 200 mg twice daily for a week. All patients had follow-up clinic visits at 6 months, 1 year, 2 years, and 3 years after randomization, when they were examined endoscopically to see whether new cancer had developed. At these visits, participants also had their *H. pylori* status confirmed.

"During 3 years of follow-up after endoscopic treatment of primary gastric cancer, metachronous gastric cancer developed in 33 participants—9 in the eradication group and 24 in the control group," wrote the authors, led by Dr. Kazutoshi Fukase of the department of gastroenterology at Yamagata (Japan) Prefectural Central Hospital. There were no differences between the patients who developed cancer in each group in terms of sex, age, location of the cancer, histologic type, or depth of the invasion of the diameter of the metachronous cancers. "The risk of subsequent cancer was reduced from about 4,000/100,000 individuals a year to 1,400/100,000 individuals a year."

'Preventing gastric cancer by eradicating *H. pylori* in high-risk regions should be a priority.'

DR. TALLY

In an accompanying comment, Dr. Nicholas J. Talley of the department of internal medicine at the Mayo Clinic in Jacksonville, Fla., wrote, "The results are clear: in a high-risk population, gastric cancer rates are substantially reduced, but not abolished, by *H. pylori* eradication." The potential risks associated with *H. pylori* eradication ... are small, he added. "Preventing gastric cancer by eradicating *H. pylori* in high-risk regions should be a priority."

Both the study authors and Dr. Talley declared that they had no conflicts of interest to disclose. ■

Extensive Crohn's Disease May Elevate Risk of Colon Cancer, Dysplasia

BY MIRIAM E. TUCKER
Senior Writer

Data from a prospective colonic surveillance program involving 259 patients with chronic extensive Crohn's disease revealed a 25% cumulative risk of developing definite dysplasia or cancer by the 10th surveillance exam after an initial negative screening exam according to the findings of a longitudinal cohort study.

The cumulative risk of an initial finding of flat high-grade dysplasia or cancer after a negative screening colonoscopy was 7% after the ninth surveillance exam, with a median interval of 18 months between exams. The findings suggest that periodic surveillance colonoscopy should be part of routine management of chronic extensive Crohn's disease, said Dr. Sonia Friedman of Brigham and Women's Hospital, Boston, and her associates.

Previous studies often lumped together all patients with Crohn's disease and didn't separately examine those with extensive disease.

While the increased risk of colonic dysplasia and carcinoma in patients with chronic, extensive ulcerative colitis has been well described, less is known about those risks in patients with long-standing Crohn's disease. Previous studies often lumped together all patients with Crohn's disease and didn't separately examine those with extensive long-standing Crohn's colitis.

In 2001, Dr. Friedman and her associates reported a 22% chance of developing definite dysplasia or cancer by the fourth surveillance exam among 259 patients with chronic Crohn's disease who were followed from 1980 through 1998 (Gastroenterology 2001;120:820-6).

Now they report an update in those same patients, all of whom had at least 7 years of Crohn's colitis affecting at least one-third of the colon. Those in whom the results of screening colonoscopy were negative were contacted for a repeat examination at 2 years. Patients with results classified as indefinite (IND) for dysplasia were contacted for extensive repeat biopsies within 1 year, while those with one area of flat low-grade dysplasia (LGD) were contacted for repeat endoscopy within 1-6 months. Patients with recurrent or multifocal flat low-grade dysplasia (LGD), high-grade dysplasia (HGD), or cancer were referred for surgery. Those with "adenoma-like" polypoid dysplastic lesions that had been removed were contacted for repeat endoscopy within 1-6 months [Epub doi:10.1016/j.cgh.2008.03.019]).

A total of 1,424 examinations (screening and surveillance) was performed, with a median of 5 per patient. In all, 90% of the patients had extensive colitis, and 31% had undergone segmental colon resection. At the initial screen, definite dysplasia was found in 18 patients (7%). Of those 18 patients, 13 had LGD (7 polyps, 6 flat), 2 had HGD (both flat), and 3 had carcinoma (all masses). There were no colonoscopic complications, the investigators said.

The prevalence of definite dysplasia or cancer was significantly higher among patients who were older than 45 years than in those younger, but the prevalence for those older than 45 did not vary with disease duration.

In surveillance exams, a first positive finding of definite dysplasia or cancer was found in 30 patients, including LGD in 22 (14 polyps, 8 flat), HGD in 4 patients (2 polyps, 2 flat), and carcinoma in 4 patients (2 polyps, 2 masses). Analysis of several factors, such as age greater than 45 years or disease duration longer than 20 years at exam, family history of cancer or inflammatory bowel disease, female gender, pancolitis, and prior resection, did not identify any as consistent predictors of risk for dysplasia or cancer over time.

Compared with age- and gender-based cancer registry data from the general population, the 11 cancers detected in this study were significantly more than the 1.13 expected, suggesting that patients with extensive Crohn's disease are indeed at increased risk for developing colon cancer, Dr. Friedman and her associates said.

The calculated cumulative risks—25% for LGD, HGD, or cancer, and 7% for flat HGD or cancer by the 10th surveillance exam—are high, considering that 31% of the screening exams and 4.8% of the surveillance exams were preceded by a partial colon resection. However, these data parallel those of studies of cancer in ulcerative colitis patients with similar extent and duration of disease, they commented. ■

History May Portend Better Cancer Outcome

BY MARY ANN MOON
Contributing Writer

A family history of colon cancer raises the risk of developing the disease, but it also appears to be associated with a better prognosis, researchers reported.

Patients with stage III colon cancer who had a family history of the disease had significantly fewer recurrences and significantly better mortality 5 years after their diagnosis than did those with no family history of colon cancer in a study of over 1,000 patients.

This apparent benefit became stronger as the number of affected family members increased, said Dr. Jennifer A. Chan of the Dana-Farber Cancer Institute, Boston, and her associates. They assessed the influence of family history on survival using data on 1,087 patients with colon cancer who participated in a National Cancer Institute–sponsored clinical trial of adjuvant chemotherapy. All patients had undergone complete surgical resection of the primary tumor in 1999-2001, and all had regional lymph node metastases but no distant metastases at that time.

A total of 195 of the patients reported a family history of colon cancer in first-degree relatives. However, none had the hereditary colorectal cancer syndromes of familial adenomatous polyposis or hereditary nonpolyposis colorectal cancer. After a mean of 5 years of follow-up, cancer recurrence or death occurred in 57 of these patients with a family history of the disease (29%), compared with 343 of the patients who did not have a family history (38%).

Cancer recurrence or death occurred in 30% of patients with one affected relative and in 23% of patients with two or more affected relatives, compared with 38% of those who had no affected relatives, the authors said (JAMA 2008;299:2515-23).

This protective effect persisted when the data were adjusted to account for numerous predictors of cancer recurrence and survival, including the possibility that patients with a family history may have had earlier tumor detection precisely because of this history. These patients all were subjects in a rigorously controlled, randomized clinical trial, so they all had the same disease stage, the same treatment and follow-up care, and the same extensive background data on possible confounding factors. The investigators noted that their findings "support the hypothesis that a relatively common … genetic predisposition may not only influence colorectal cancer risk but also patient survival." ■

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