PillCam Shows Promise for Colorectal Screening

BY KERRI WACHTER
Senior Writer

WASHINGTON — In a multicenter study, capsule endoscopy showed promise in the detection of significant colorectal polyps, and the technique may someday offer a noninvasive alternative to conventional colonoscopy, Dr. Jacques Devière said at the annual Digestive Disease Week.

For significant lesions—those greater than 6 mm in size—or in patients with three or more polyps, the sensitivity of capsule endoscopy using the PillCam COLON was 79% and specificity was 78%, compared with conventional colonoscopy. The positive predictive value (PPV) was 75%, and the negative predictive value (NPV) was 82%, Dr. Devière reported.

A total of 275 polyps were identified with the PillCam. For polyps of any size, the PillCam had a sensitivity and specificity of 76%. PPV was 88% and NPV was 58%.

If validated, "this noninvasive technology might challenge colonoscopy for colon cancer screening and polyp detection in the future," said Dr. Devière, a gastroenterologist at the Hôpital Erasme in Brussels.

The study was sponsored by Given Imaging Ltd., maker of the PillCam COLON. Dr. Devière disclosed that he has received research support from the company.

A total of 84 patients at eight centers were included; 64% were male, and the average age was 60 years. Patients were included if they had an adenoma and were asked to come back for surveillance after 3 years, or if they were suspected of having colonic disease and were referred for conventional colonoscopy. Patients were excluded if they had Crohn's disease, small bowel tumors, radiation enteritis, or surgical anastomoses.

On the day before the procedure, patients were limited to a clear liquid diet. In the evening, they drank 4 L of polyethylene glycol preparation (Colopeg).

At 7 a.m. the next day, patients drank another liter of Colopeg, followed by 20 mg of domperidone (to aid excretion of the capsule). They swallowed the capsule an hour later. At 10 a.m., patients drank a "booster" of 45 mL sodium phosphate.

Using this regimen, 77% of patients excreted the capsule by 2 p.m. The remaining patients required a second booster of 30 mL sodium phosphate. Patients were allowed a low-fiber snack at 3 p.m. If the capsule had not been excreted by 4:30 p.m., patients received 10 mg bisacodyl.

Conventional colonoscopy was performed in all patients after the capsule was excreted that day in order to allow comparisons to be made between the two methods.

Colon preparation was rated as poor, fair, good, or excellent. Preparation was considered poor if there was a large amount of fecal residue that impaired visualization, fair if there were enough areas of evacuation to allow a reliable examination, good if there was only a small amount of residue, and excellent if no or very small amounts of residue were present.

Most patients (57%) had a good preparation, followed by 29% with a fair prep, 9% with an excellent prep, and 5% with a poor prep. "There is still some problem with the quality of the preparation," Dr. Devière said.

By the end of the battery life (10 hours), 92% of the capsules had been excreted and 4% were still in the sigmoid colon; two capsules were never eliminated from the stomach because the patients had gastroparesis. In these two patients, additional endoscopies had to be performed to push the capsules out of the stomach.

The capsule measures 11 mm by 31 mm—roughly the size of a large vitamin pill—and it has tiny cameras that capture four images per second. The capsule has a sleep mode of 2 hours to preserve the battery between the time it is swallowed and the approximate time it enters the colon. ■

Aspirin's Chemopreventive Effects Seen 10 Years After Tx Initiation

BY JONATHAN GARDNER
London Bureau

Taking 300 mg of aspirin daily for at least 5 years was shown to prevent colorectal cancer in an analysis of two large randomized trials. The effect was seen beginning 10 years after treatment was initiated.

Although this strategy might be effective in certain high-risk groups, further research is needed to elucidate the risks and benefits of aspirin chemoprevention in various clinical settings, the researchers wrote. The effectiveness of colonoscopy screening and the risk of bleeding complications with long-term aspirin use also should be considered, they noted.

Dr. Andrew Chan of the gastrointestinal unit at Massachusetts General Hospital, Boston, agreed in an accompanying commentary. "These findings are not sufficient to warrant a recommendation for the general population to use aspirin for cancer prevention," he wrote (Lancet 2007;369:1577-8).

Previous observational studies had reported a decreased incidence of colorectal cancers in regular users of aspirin, but two large trials did not demonstrate a decreased risk over 10 years of follow-up. Longer follow-up is needed, given that the delay is 10-15 years between initiation of development of an adenoma and colorectal cancer, wrote Dr. Peter Rothwell, professor of clinical neurology at the University of Oxford (England), and associates (Lancet 2007;369:1603-13).

Their analysis focused on the British Doctors Aspirin Trial and the UK Transient Ischaemic Attack Aspirin Trial; there was a median follow-up of 23 years in both trials.

During that follow-up period, subjects who took at least 300 mg of aspirin a day for at least 5 years were significantly less likely to develop colorectal cancer than were controls (hazard ratio [HR] 0.63), according to a pooled analysis of the two trials. The researchers found no significant effect on any other type of cancer.

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Taking 300 mg of aspirin a day for 5 years reduces the risk of colorectal cancer.

The preventive effect was strongest in years 10-19, when the HR for aspirin users was 0.60, but a significantly reduced HR of 0.74 was seen in years 20 and later for the subjects who took aspirin. No significant preventive effect was seen at 0-9 years (HR 0.92).

The British Doctors Aspirin Trial randomized doctors in 1978 and 1979 into a group of 3,429 taking a daily dose of 500 mg of aspirin and a control group of 1,710 who took nothing. Treatment continued for 5-6 years.

The UK Transient Ischaemic Attack Aspirin Trial randomized 2,449 patients over age 40 who had already had a transient ischemic attack or mild ischemic stroke to receive daily doses of either 1,200 mg or 300 mg of aspirin, or placebo. Recruitment took place between 1979 and 1985, with the trial ending in 1986. The researchers performed a subgroup analysis of only those patients who took aspirin for at least 5 years.

The researchers identified trial participants who had developed cancer through cancer registries and death certificates. ■

Aspirin May Reduce Risk of Certain Colorectal Cancers

BY LEANNE SULLIVAN
Associate Editor

Regular aspirin use for at least 10 years appears to reduce the risk of colorectal cancers that overexpress cyclooxygenase-2, Dr. Andrew T. Chan and his associates reported.

The researchers mailed questionnaires every 2 years to 121,701 women in the Nurses' Health Study and 51,529 men in the Health Professionals Follow-Up Study to determine aspirin use and incidence of colorectal cancer. The women (age range at entry, 30-55 years) received the survey starting in 1976, and the men (age range at entry, 40-75 years) received it starting in 1986.

More detailed questions on aspirin use, including frequency and amount, were added in 1980 for the women and in 1992 for the men. For women, regular aspirin use was defined as taking two or more 325-mg aspirin tablets per week; for men, it was defined as using aspirin at least twice a week (N. Engl. J. Med. 2007;356:2131-42).

Medical and pathology reports were obtained for participants who reported colorectal cancers, said Dr. Chan of Massachusetts General Hospital and Harvard Medical School, Boston, and his associates.

During follow-up, 636 specimens sufficient for immunohistochemical analysis were obtained from patients with confirmed colorectal cancer. Of the 636 tumors, 423 (67%) were COX-2 positive, or had moderate or strong expression of the enzyme.

The researchers analyzed the association between the expression of COX-2 in the tumors and the patients' use of aspirin, and calculated multivariate relative risk after adjustment for factors including age, gender, smoking, BMI, exercise, family history of colorectal cancer, history of polyps, and meat and alcohol consumption.

The multivariate relative risk of colorectal cancer for aspirin users vs. nonregular users was a significant 0.64 for COX-2–positive cancers and a nonsignificant 0.96 for COX-2–negative tumors. Thus, aspirin use was of benefit only in tumors in which COX-2 was overexpressed. However, this benefit was not seen until aspirin had been used for more than 10 years.

A greater amount of aspirin use also was associated with lower incidence of COX-2–positive disease, with more than five tablets per week associated with significantly fewer such cancers; the association was not significant for COX-2–negative disease. This "is consistent with the results of studies in which higher doses of aspirin were required to inhibit COX-2 than to inhibit COX-1," the investigators noted.

The results of this observational study "suggest that the anticancer benefit of aspirin is mediated, at least in part, by inhibition of COX-2," Dr. Chan and his associates concluded.

In an accompanying editorial, Dr. Sanford D. Markowitz of Case Western Reserve University, Cleveland, pointed out that aspirin use has its own risk of adverse effects (N. Engl. J. Med. 2007; 356:2195-8).

Researchers "need to ask whether there are alternative strategies for targeting the COX pathway that have better efficacy or lower rates of adverse effects," Dr. Markowitz said. Inhibitors of the COX-2–generated prostaglandin PGE_2 receptors or synthases "might provide better specificity for the prevention of colon cancer and, hence, reduced adverse effects," he suggested. ■