MINDFUL PRACTICE

CT for Colon Cancer Screening

BY JON O. EBBERT, M.D., AND ERIC G. TANGALOS, M.D.

The Problem

A long-time patient returns for a regularly scheduled examination. He is 50 years old and has a history of hypertension and depression. His blood pressure is at goal, and his depression is in remission with an SSRI. You told him last year that he needs to have colon cancer screening at the age of 50, and he has been thinking about it, talking with friends, and researching it on the Internet. He has decided he wants to have a CT scan instead of colonoscopy and asks you if this is appropriate.

The Question

How sensitive and specific is CT colonography for detecting adenomas and cancers of the colon?

The Search

You log on to PubMed (www.pubmed.gov) and enter "computed tomography AND colon cancer." You find a relevant study. (See box at right.)

Our Critique

Colorectal cancer is the third most common cancer and the second leading cause of cancer death in the United States. The lifetime risk for colorectal cancer is 1 in 20. According to the recently updated U.S. Preventive Services Task Force (USPSTF) recommendations: "The evidence is convincing that screening for colorectal cancer with fecal occult blood testing, sigmoidoscopy, or colonoscopy detects early-stage cancers and adenomatous polyps." Available evidence is convincing that the screening can reduce colorectal cancer mortality among individuals aged 50-75 years. Notably, the USPSTF suggests that CT colonography could reduce colorectal cancer mortality among individuals who would otherwise refuse screening, but CT colonography is not included as a recommended screening tool. The conclusions regarding CT colonography in these guidelines were influenced by the inadequately quantitated risk associated with the 7%-15% of CT exams with extracolonic findings. Another important part of this equation is the natural history of colon polyps. Previous studies suggested that an average of 5.5 years is required for the transformation of 10 mm or larger adenomatous polyps into cancer. However, smaller polyps can and do increase in size and transform. CT colonography will miss only 10% of lesions larger than 10 mm but will identify only 65% of all lesions 5 mm or larger. Although colonoscopy is not perfect and misses roughly 13% of polyps 5 mm or larger, CT colonography may miss twice as many of the same size.

Clinical Decision

The patient finds out that his insurance carrier will not cover CT colonography under any circumstances. He is now calling your office and wants to talk with you over the phone regarding a new DNA stool test for detecting colon cancers.

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C.D. Johnson, et al.

Accuracy of CT colonography for detection of large adenomas and cancers. N. Engl. J. Med. 2008;359:1207-17.

► **Setting:** 15 clinical sites in North America.

► **Participants:** Participants were age 50 years or older and were scheduled to undergo routine colonoscopy. They were excluded if they had melena or hematochezia on more than one occasion in the last 6 months; lower abdominal pain, inflammatory bowel disease, or familial polyposis syndrome, or a serious medical condition associated with an increased risk of complications from colonoscopy; undergone colonoscopy in the preceding 5 years; anemia or a positive result on fecal occult blood testing.

► **Diagnostic Procedure:** CT colonography included stool tagging, laxative purgation, and fluid tagging. Mechanical insufflation was used, and 1 mg of glucagon was administered 7-15 minutes before the examination. Study data were randomly assigned to be read independently. For each of the observed abnormalities, location and size were noted. Radiologists were instructed to record only lesions measuring 5 mm or larger.

► **Reference Standard:** After the CT colonography, colonoscopy was performed according to the protocol at each of the clinical sites. Endoscopists performed colonoscopies without knowledge of the CT colonography results, and lesions were photographed during the withdrawal phase. Colonoscopy and CT colonography were performed on the same day in 99% of 2,531 participants. For patients in whom a 10-mm or larger lesion was detected on CT colonography but not on colonoscopy, repeat colonoscopy was recommended within 90 days. Tissue samples of all lesions 5 mm or larger were reviewed centrally using standard definitions. Lesion size was determined from the pathology report when possible, and lesions were matched using an algorithm using size and location. Colonoscopy results and pathologic examination of tissue specimens were the reference standard for determining size, location, and histologic type.

► **Results:** Complete CT colonography and colonoscopy results were available for 2,531 subjects. The per-patient mean (plus or minus standard deviation) sensitivity, specificity, positive predictive value, and negative predictive value for lesions 10 mm or larger were 0.90 plus or minus 0.03, 0.86 plus or minus 0.02, 0.23 plus or minus 0.02, and 0.99 plus or minus less than 0.01, respectively. Three adverse events occurred: severe nausea and vomiting after CT colonography; hematochezia after snare polypectomy requiring 2 days of hospitalization; and *Escherichia coli* bacteremia after both procedures. Extracolonic findings were observed in 66% of patients, but only 16% required additional evaluation.

Infliximab Earning Place As Crohn's First-Line Rx

BY DAMIAN McNAMARA
Miami Bureau

ORLANDO — Infliximab, alone or in combination with azathioprine, was superior to azathioprine monotherapy for inducing steroid-free remission and mucosal healing in a study of 508 patients with moderate to severe Crohn's disease.

Many physicians who treat Crohn's disease patients with the anti–tumor necrosis factor–α agent infliximab (Remicade) do not use it first line, Dr. William J. Sandborn said. However, based on the study findings, doctors might want to consider prescribing the agent sooner, forgoing the classic step-up therapy, he said.

'Anti–tumor necrosis factor therapy should be considered in patients [earlier].'

DR. SANDBORN

"We have compelling evidence that anti–tumor necrosis factor therapy should be considered in patients [earlier]," Dr. Sandborn said at the annual meeting of the American College of Gastroenterology.

The multicenter, phase IIIb Study of Biologic and Immunomodulator-Naive Patients with Crohn's Disease (SONIC) included people who had previously failed 5-aminosalicylate therapy and/or who were steroid dependent. A total of 41% of participants were taking steroids at baseline; 52% were men, and the mean age was 34 years. The median baseline Crohn's Disease Activity Index was 275.

As the study name suggests, participants had no prior exposure to biologic or immunomodulator agents, including azathioprine (Imuran), 6-mercaptopurine, and methotrexate. A meeting attendee commented that many previous trials showed no significant benefit when azathioprine was added to infliximab. "All other trials were retrospective and looked at patients who failed azathioprine previously, whereas if you are naive to the drugs, you have a better chance of getting synergy," Dr. Sandborn replied. Use of azathioprine in the United States is off label for Crohn's disease.

"As early as week 6, infliximab (either as monotherapy or in combination with azathioprine) was superior to azathioprine for corticosteroid remission, and in addition the combination was also superior to infliximab monotherapy after 10 weeks," said Dr. Sandborn, professor of medicine and vice chair of the division of gastroenterology and hepatology, Mayo Clinic, Rochester, Minn.

Participants were randomized into three groups. In all, 170 received azathioprine 2.5 mg/kg per day plus a placebo infusion; another 169 received a placebo capsule and infliximab 5 mg/kg infusions; and the 169 others in the combination group received azathioprine 2.5 mg/kg and infliximab 5 mg/kg infusions. The infusions were given at weeks 0, 2, and 6, and every 8 weeks thereafter through 30 weeks.

At 26 weeks, corticosteroid-free clinical remission was achieved by 31% of the azathioprine monotherapy group, 44% of the infliximab monotherapy patients, and 57% of the combination group.

Also at 26 weeks, a secondary end point of mucosal healing was achieved by 17% of the azathioprine monotherapy group, 30% of the infliximab monotherapy patients, and 44% of the combination group.

"Infliximab and azathioprine, when started together, are superior to azathioprine alone. Infliximab monotherapy was superior to azathioprine monotherapy," said Dr. Sandborn, the principal investigator for the SONIC trial. Centocor Inc., manufacturer of infliximab, funded this research. Mayo Clinic receives consulting fees for work provided by Dr. Sandborn from Centocor, Abbott Laboratories, and UCB Pharma. Dr. Sandborn had no disclosures related to azathioprine.

A subgroup of 204 patients had both elevated C-reactive protein levels and lesions on baseline examination. In this subgroup, corticosteroid-free clinical remission was attained by 28% of the azathioprine monotherapy group, 57% of the infliximab monotherapy group, and 69% of the combination group. Dr. Sandborn said this was "a very significant finding."

At week 30, a higher proportion of patients in the azathioprine monotherapy group, 24%, experienced at least one serious adverse event, compared with 16% of the infliximab monotherapy group and 14% of the combination therapy group.

The rate of serious infections was relatively low and was similar across treatment groups, Dr. Sandborn said. Specifically, eight serious infections were reported in the azathioprine monotherapy group, four occurred in the infliximab monotherapy group, and there were six in the combination therapy group. ■