Prostate Cancer Radiation Boosts Rectal Ca Risk

After 5 years, these patients should start undergoing regular surveillance by sigmoidoscopy or colonoscopy.

ARTICLES BY
MITCHEL L. ZOLER
Philadelphia Bureau

HOLLYWOOD, FLA. — Radiation treatment of prostate cancer boosted men's risk of later developing rectal cancer by 70%, according to data collected in a United States cancer registry kept by the National Cancer Institute.

But the absolute risk of rectal cancer remained low in men who got radiation therapy, about 0.1%/yr, and so does not warrant curtailing radiation therapy as an option for treating prostate cancer, Nancy N. Baxter, M.D., said at a symposium on gastrointestinal cancers sponsored by the American Society of Clinical Oncology.

Instead, the finding means that men who receive radiation treatment for prostate cancer should undergo regular surveillance for rectal cancer by either sigmoidoscopy or colonoscopy starting 5 years after their radiation therapy, said Dr. Baxter, a surgeon at the University of Minnesota in Minneapolis.

Surveillance should begin even in men who are not old enough to otherwise qualify, she told this newspaper. In these men, visual surveillance once every 5-10 years would probably be adequate. Since all of the excess colorectal cancers would be in the rectum, digital rectal examinations also might be a useful surveillance method.

In the proportional hazards model, radiation treatment was associated with a statistically significant, 70% increase in the rate of rectal cancer.

During radiation therapy of the prostate, the anterior wall of the rectum is always radiated; other parts of the colon receive minimal or no radiation. The study was done to assess the impact of this exposure, she explained.

The study used data collected in the Surveillance Epidemiology, and End Results registry, which has collected follow-up information on annual samples of cancer patients since 1973. Dr. Baxter focused on patients with invasive, nonmetastatic, adenocarcinoma of the prostate who entered the registry during 1973-1994, a total of more than 85,000 men. The group included 30,552 men who had radiation treatment and 55,263 who were treated surgically.

The analysis excluded men who developed any form of colorectal cancer during the first 5 years following their prostate cancer treatment because of the low likelihood that these cancers were caused by the radiation therapy. This left 1,437 men who developed colorectal cancer during an average follow-up of 9 years; 267 of these were rectal cancers.

The unadjusted data showed an excess of rectal cancers among men who had radiation treatment. However, because colorectal cancers are much more common in older men, a multivariate analysis was done that controlled for several demographic variables including age, Dr. Baxter said at the symposium, also sponsored by the American Gastroenterological Association, the American Society for Therapeutic Radiation and Oncology, and the Society of Surgical Oncology.

In the proportional hazards model, radiation treatment was associated with a statistically significant, 70% increase in the rate of rectal cancer. Radiation therapy led to no significant rise in the rate of cancer in the rectosigmoid region, cecum, or any other part of the colorectal tract, she said.

The increased risk is roughly comparable with the added risk conferred when men age by 10 years, or among men who have one first-degree relative with colorectal cancer.

The absolute rate of rectal cancer during a 10-year period was about one case/200 men among those who had their prostate cancer managed surgically, compared with a rate of about one case/100 men among those treated with radiation. ■

Bevacizumab Improves Survival in Patients With Colorectal Cancer

HOLLYWOOD, FLA. — Adding the biologic agent bevacizumab to a standard chemotherapy regimen led to improved survival in a controlled study with nearly 600 previously treated patients with advanced colorectal cancer, according to a report at a symposium on gastrointestinal cancers sponsored by the American Society for Clinical Oncology.

This is the first time that patients with advanced colorectal cancer have received both bevacizumab, a humanized monoclonal antibody that binds to and inhibits vascular endothelial growth factor, and the chemotherapy combination known as FOLFOX4, which is oxaliplatin, 5-fluorouracil, and leucovorin. FOLFOX4 is today one of the most commonly used chemotherapy regimens for advanced colorectal cancer, and many experts consider it the first-line choice.

Bevacizumab received approval from the Food and Drug Administration last year for treatment of advanced colorectal cancer when used in combination with irinotecan plus 5-fluorouracil and leucovorin, the other commonly used chemotherapy combination for this type of cancer.

The new results "show that bevacizumab is effective when it's given with a drug that is not irinotecan," commented Robert J. Mayer, M.D., director of the Center for Gastrointestinal Oncology at the Dana-Farber Cancer Institute in Boston.

But because the new study was done in previously treated patients (they had all failed treatment with irinotecan and 5-fluorouracil), it's inappropriate to view the results as a basis for using bevacizumab plus FOLFOX4 on previously untreated patients, cautioned Bruce J. Giantonio, M.D., lead investigator of the study and an oncologist at the University of Pennsylvania in Philadelphia. The results raise the possibility of using bevacizumab plus FOLFOX4 as first-line therapy, "but that approach needs further study," he said.

This is the first time that patients with advanced colorectal cancer have received both bevacizumab and the chemotherapy combination FOLFOX4.

Bevacizumab is marketed by Genentech as Avastin. The current study was sponsored by the National Cancer Institute and run by the Eastern Cooperative Oncology Group. Genentech provided the bevacizumab used in the study.

Patients with advanced colorectal cancer who had previously been treated with irinotecan and 5-fluorouracil were randomized to one of three study arms: FOLFOX4 alone, 10 mg/kg of bevacizumab given intravenously once every 2 weeks, or both regimens. The study's primary outcome was overall survival. Full results on the 249 patients who were treated with bevacizumab alone have not yet been reported, but this arm of the study was closed prematurely because of a trend toward worse outcomes, Dr. Giantonio said.

After a median follow-up of 18.4 months, the 290 patients treated with both bevacizumab and FOLFOX4 had a median survival rate of 12.5 months, compared with a 10.7-month median survival rate among the 289 patients who were treated with FOLFOX4 alone, a statistically significant difference.

A hazard ratio analysis showed that adding bevacizumab cut mortality by 26% compared with using FOLFOX4 alone, he reported at the symposium, also sponsored by the American Gastroenterological Association, the American Society for Therapeutic Radiation and Oncology, and the Society of Surgical Oncology.

The combination regimen was also generally well tolerated compared with FOLFOX4 alone, Dr. Giantonio said. The combination produced a larger number of certain grade 3 toxicities: neuropathy, hypertension, bleeding, nausea, and vomiting. ■

Fecal Blood Fails to Flag High Colon Cancer Risk

NEW ORLEANS — Fecal occult blood testing was ineffective at selecting people with an increased risk of colorectal adenomas or cancer, based on a review of 147 people who had follow-up colonoscopy.

"Fecal occult blood testing did not appear to select for people with colonic neoplasia and should be replaced by alternative screening methods," Christopher M. Mathews, M.D., said at the southern regional meeting of the American Federation for Medical Research.

His study used data collected by Clinical Outcomes Research Initiative, an endoscopy database created by the American Society for Gastrointestinal Endoscopy. Using this database, Dr. Mathews and his associates identified 663 people who underwent colonoscopy during 1999-2004 following a positive result on a fecal occult blood test.

They then cross-referenced this list with the computerized patient record system of the Veterans Affairs medical system. They found that 147 of the 663 people screened had VA records and were further identified through their medical records as being asymptomatic at the time of colonoscopy with no prior history of colorectal cancer or polyps.

All 147 people were men, and 69% were white; 67% were at least 60 years old. Among the 48 men younger than 60, 44% were found to have colorectal adenomas by colonoscopy, and none had colorectal cancer. Among the 99 men aged 60 or older, 45% had colorectal adenomas, and 4% had colorectal cancer. Overall, there was a 45% prevalence of adenomas and a 2.7% prevalence of colorectal cancer, said Dr. Mathews, a gastroenterologist at the VA Medical Center in Memphis.

These prevalence rate were compared with the rates in an unselected, general population, as documented in two independent autopsy studies. In an autopsy study done in the United States in 1978, the prevalence of colorectal adenomas was 47%, and the prevalence of colorectal cancer was 3.7%. In an autopsy study done in the United Kingdom in 1982, the prevalence of adenomas was 33%, and the prevalence of colorectal cancer was 2.2%.

The comparison showed that the prevalence of colorectal neoplasia in asymptomatic, average risk men who had positive results on fecal occult blood tests was not appreciably different from the prevalence seen during autopsy in an unselected population, Dr. Mathews said. ■