Colorectal Ca Neurogenesis May Affect Prognosis

BY ROBERT FINN
San Francisco Bureau

HUNTINGTON BEACH, CALIF. — Colorectal cancer patients with evidence of new nerve growth within their tumors do far worse than those with no evidence of neurogenesis, according to a study presented at the Academic Surgical Congress.

In the study of 347 patients with colorectal cancer, Kaplan-Meier curves showed that those with stage III cancer and no evidence of neurogenesis achieved significantly greater cancer-specific overall survival at 5 years than did those with stage II cancer and a high degree of neurogenesis.

Patients with more neurogenesis had a 3.8-fold greater risk of cancer-specific death ($P = .0005$) in a multivariate analysis controlling for standard prognostic factors such as age and tumor location. The only factor that conferred a higher degree of risk was stage IV disease, with a hazard ratio of 14.7.

Suggesting that neurogenesis may be "the next angiogenesis," the lead author, Dr. Jonathan A. Wilks, raised the possibility that neurogenesis could be an attractive target for future therapeutic intervention.

Dr. Wilks, a surgery resident at Baylor College of Medicine, Houston, said that as far as he knew, nothing has been published in the literature so far regarding neurogenesis in solid tumors outside the nervous system.

Included in the study was a cohort of patients at Baylor who had their colon cancer resected within a 5-year period. All were Veterans Affairs patients; the investigators obtained all of their clinical and demographic data from their electronic medical records.

Dr. Wilks and his colleagues constructed a tissue microarray from these patients' tissue samples, and stained them with antibodies against protein gene product (PGP) 9.5, a neuron cytoplasmic marker associated with new nerve growth.

For the statistical analysis, at least 5 years of survival data were available for each patient.

The investigators looked at cancer-specific overall survival and cancer-specific disease-free survival, dividing the patients into those with no evidence of neurogenesis, those with a high level of neurogenesis (defined as more than 20 nerves per high-powered field), and those with low levels of neurogenesis (defined as 1-20 nerves per high-powered field).

A total of 20-30 patients ended up in the high-neurogenesis group, Dr. Wilks said.

He described the results as "startling."

For example, among the patients with R0 tumors (those with negative surgical margins), patients with a high degree of neurogenesis had significantly worse disease-free and cancer-specific overall survival than did those with no neurogenesis or moderate amounts of neurogenesis.

Patients who had more neurogenesis—new nerve growth—within their tumors had a 3.8-fold greater risk of cancer-specific death in a multivariate analysis.

At the 1,800-day mark, the cancer-specific overall survival was approximately 45% for patients with high degrees of neurogenesis, about 70% for patients with low degrees of neurogenesis, and about 90% for patients who had no evidence of neurogenesis in their tissue samples.

Dr. Wilks said the study's unexpected findings could be used for therapy stratification. At his institution, chemotherapy is offered to all patients with stage III disease (those with lymphatic invasion), but is not offered to those with stage II disease.

He suggested that stage II patients who have evidence of neurogenesis might be offered the option of chemotherapy, whereas stage III patients without neurogenesis might not require chemotherapy.

The presentation by Dr. Wilks was followed by a notable pause before any of the physicians in the audience asked questions.

Then one surgeon in the audience commented, "What we witnessed was a stunned silence at the end of your talk. And that's not for any lack of interest or enthusiasm. These are actually incredibly exciting results, and surprising, and I congratulate you and your team on pursuing this work."

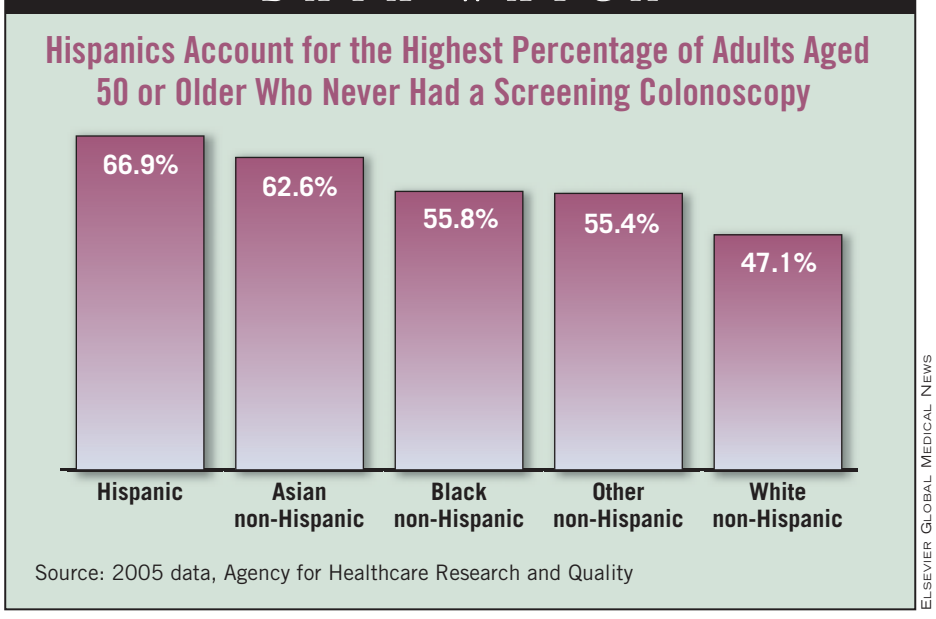
Other attendees were more guarded in their comments. In an interview, Dr. James Neifeld, chairman of the department of surgery at Virginia Commonwealth University, Richmond, said, "This represents a new and previously undescribed finding. It is much too early to get excited about this as either a prognostic factor or a potential target for therapy and will require further validation to determine its usefulness."

Several other experts in the areas of colorectal and brain cancers declined to comment on the record, citing lack of expertise in neurogenesis as it relates to cancer.

In response to a question from the audience, Dr. Wilks acknowledged that the cause of the neurogenesis remains unclear. Preexisting nerve tissue could be invading the tumor, or the nerve tissue could arise from a stem cell within the tumor, he said.

Dr. Wilks stated that he had no financial relationships related to his presentation. ■

DATA WATCH



Follow-Up Care Falls Short After Colorectal Cancer Surgery

BY FRAN LOWRY
Orlando Bureau

ORLANDO — Most colorectal cancer patients who undergo potentially curative resection of their tumors after age 65 do not receive the follow-up care that is recommended in clinical practice guidelines, according to the results of a large, population-based study.

Follow-up fell short in 74% of survivors, with the greatest lapse seen in carcinoembryonic antigen (CEA) testing, which is done to detect recurrent colon cancer.

Just 30% of survivors had their CEA concentrations measured twice a year, Dr. Gregory S. Cooper reported at a meeting on gastrointestinal cancers sponsored by the American Society of Clinical Oncology.

Dr. Cooper of University Hospitals Case Medical Center, Cleveland, mined the linked Surveillance Epidemiology and End Results (SEER)–Medicare database to obtain the information used in the study.

He and his colleagues analyzed data on a total of 9,246 patients older than 65 years with local or regional colorectal cancer that was diagnosed in 2000 and 2001. All of the patients had their cancer resected with curative intent. The mean age of the patients was 77 years; 55% were female, and 87% were white.

Just 30% of patients had the requisite testing for CEA, and only 74% had a colonoscopy within 3 years.

DR. COOPER

About 76% of the tumors were located in the colon, and the remainder were located in the rectum. Likewise, 60% of cancers were local and the rest were regional. Patients who died within 3.5 years of diagnosis were excluded, as were those diagnosed with carcinoma in situ.

Medicare claims identified procedures performed between 6 and 42 months after diagnosis. These included office visits, colonoscopy, CT or PET scans, and CEA testing.

Patients were deemed to have been treated according to American Society of Clinical Oncology and National Comprehensive Cancer Network guidelines if they had at least two office visits per year, at least two CEA tests per year, at least one colonoscopy within 3 years of their resection, and a yearly CT scan for any poorly differentiated cancer.

Patients were judged to be treated in excess of the guidelines if they had CT scans for tumors that were not poorly differentiated and if they had PET scans, which are not routinely recommended.

Dr. Cooper and his colleagues found just 30% of patients had the requisite testing for CEA; 74% had a colonoscopy within 3 years, and 90% had office visits according to the recommended schedule. Forty-eight percent had CT scans, only half of which were done for poorly differentiated cancer. Seven percent had PET scans.

In all, 74% of patients failed to get the follow-up care that the guidelines recommended, 16% received care that exceeded the guidelines, and only 10% received care that met the guidelines. Patients tended to get appropriate care if they were younger, female, and had lymph node involvement at diagnosis. Older patients were less likely to receive follow-up care in accordance with the guidelines.

"This bias might have been physician driven, where the physician feels that the patient is very [elderly], and so what are they going to do with the information if they find a recurrence," Dr. Cooper suggested in an interview at the symposium.

There also was some geographic variation in adherence to the guidelines, with the West coast being less compliant than the East coast, he said.

The study was supported by the American Cancer Society. Dr. Cooper said he had no conflicts of interest to disclose. ■