Meat Intake, Genetics Raise Colorectal Cancer Risk

A small study finds the NAT2 *genotype appears to activate the carcinogenic amines produced when red meat is cooked.*

BY KATHLEEN LOUDEN
Contributing Writer

CHICAGO — High intake of red meat has been linked to increased risk of colorectal cancer in many studies, and a new study has found a possible reason.

NAT2 genotype appears to activate carcinogenic heterocyclic amines produced in cooked red meat and in cigarette smoke, the investigators reported at the annual Digestive Disease Week.

Using data from nearly 33,000 women enrolled in the prospective Nurses' Health Study, Andrew Chan, M.D., and his coauthors examined the risk of incident colorectal cancer according to *NAT2* genotypes, meat intake, and smoking. They matched 183 women with colorectal cancer to 443 controls (Int. J. Cancer 2005;115:648-52).

They found that the acetylator genotype alone did not significantly increase cancer risk. However, women with rapid acetylator genotypes had a markedly increased risk of colorectal cancer if they consumed more than half a serving a day of beef, pork, or lamb, he reported. Their risk was three times that of women who ate less red meat; if they also were longtime smokers, they had a nearly 18-fold increased risk. Among slow acetylators, meat intake did not raise the risk of colorectal cancer.

"We definitely found in a large population that women who consumed less red meat decreased their colorectal cancer risk," Dr. Chan said.

He cautioned, however, that their sample size of 183 patients was too small.

The research does suggest that some women may be more genetically predisposed to the higher risk of colorectal cancer associated with meat and smoking, Dr. Chan said.

They plan future studies to analyze data they collected on cooking methods, to determine whether the method and temperature for cooking meat influence the risk of cancer.

The Nurses' Health Study is a set of investigations studying the risk factors of major chronic diseases in women. ■

VIVIAN E. LEE

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Study: Early Analgesia Not Associated With Delayed Appendicitis Diagnosis

NEW YORK — Early use of analgesia in patients with abdominal pain is not associated with a delay in the diagnosis of acute appendicitis, according to findings from a case-control study.

"In the past surgical literature, there have been statements that we should not give early analgesia to patients with undifferentiated abdominal pain until we have a surgical consultation or a final disposition is determined," said Steven P. Frei, M.D., an emergency physician at Lehigh Valley Hospital and Health Network, Allentown, Pa.

Previous studies that have questioned this reasoning have primarily used surrogate markers such as examination findings before and after analgesia rather than actual outcomes such as true delayed diagnosis of acute appendicitis, Dr. Frei said at the annual meeting of the Society for Academic Emergency Medicine.

In a study of 961 adults with acute appendicitis who were treated by emergency physicians in a three-hospital health network during 1998-2002, 132 patients who had a delayed diagnosis were no more likely to have taken either a nonsteroidal anti-inflammatory drug (NSAID) or opiate within 2 hours of their initial exam than were 132 control patients who did not have a delayed diagnosis of acute appendicitis, Dr. Frei reported.

Similar percentages of patients with a delayed diagnosis and patients without a delayed diagnosis had early use of the NSAID ketorolac (20% vs. 17%, respectively), an opiate (26% vs. 21%), or any of those two types of drugs (41% vs. 35%); some patients received both kinds of medication.

The investigators matched the control patients with cases on age, gender, Alvarado score (a numeric value based on eight signs and symptoms of acute appendicitis), and year of diagnosis. They defined patients with a delayed diagnosis as those who were discharged after their first emergency department visit or had longer than a 20-hour delay from the initial examination to surgery.

The findings did not change when patients with a delayed diagnosis were compared with all patients in the database who had a nondelayed diagnosis, not just nondelayed patients who were matched with delayed-diagnosis patients.

Most patients receiving analgesic medication early had 30 mg of ketorolac intravenously and/or parenteral dosing of 4-6 mg of morphine, 50-75 mg of meperidine, or 50-100 mcg of fentanyl.

—Jeff Evans

CLINICAL CAPSULES

Extra CT Colonography Findings

Extracolonic findings during CT colonography are common, but identify a substantial number of clinically important abnormalities in men, regardless of their risk for colorectal cancer, reported Judy Yee, M.D., of the University of California at San Francisco, and her colleagues.

CT colonography identified 596 extracolonic abnormalities in 315 of 500 male patients screened for colorectal cancer. Of 45 patients with abnormalities deemed clinically important, 35 had not been previously identified; they included renal and adrenal masses, pulmonary nodules, and abdominal aortic and iliac artery aneurysms (Radiology 2005;236:519-26).

The percentage of patients with clinically important extracolonic findings did not differ significantly between the 194 patients who were at average risk for colorectal cancer and the 306 who were at high risk (6.2% vs. 10.8%, respectively). Follow-up imaging studies were performed in 25 of the 35 patients with previously undiagnosed lesions; 13 of the patients required surgery or further monitoring. The cost of additional imaging performed because of extracolonic findings averaged $28 per patient.

Hemochromatosis Screening

Nearly all individuals who are identified as having hemochromatosis through genetic screening of cheek-brush samples for *HFE* mutations are willing to undergo management and treatment, according to a prospective study.

Martin B. Delatycki, M.B., of the University of Melbourne, and his associates detected homozygous Cys282Tyr mutations in *HFE* in 51 of 11,307 individuals who attended workplace screening sessions; 4 patients were already aware of their condition. Almost all of the newly identified homozygous individuals (46 of 47) agreed to enter into an appropriate program of medical management. In homozygous patients, elevated fasting transferrin saturation levels were found in 19 of 23 men and 11 of 23 women. All patients with high levels of serum transferrin underwent regular phlebotomy to reduce ferritin levels to within the normal range. Liver biopsies performed in four of the six men who met criteria for a biopsy showed either advanced precirrhotic liver fibrosis or moderate hemosiderosis with mild portal fibrosis (Lancet 2005;366:314-6).

New-Onset Diabetes as Marker

New onset of diabetes in patients older than 50 years has the potential to be a marker for early pancreatic cancer, reported Suresh T. Chari, M.D., and colleagues at the Mayo Clinic, Rochester, Minn.

In a review of 2,122 Rochester residents who were 50 years or older and developed diabetes at some point during 1950 through 1994, 18 (0.85%) went on to have pancreatic cancer. The cancer was identified an average of about 6 months after diabetes criteria were met. In 10 of those patients, the cancer was diagnosed less than 6 months after first meeting criteria for diabetes. The crude 3-year incidence of pancreatic cancer in patients with diabetes 50 years of age or older was 310 per 100,000 patient-years. Diabetic patients with pancreatic cancer were about 4.5 times more likely to have first met criteria for diabetes on or after age 70 years than were diabetic patients without pancreatic cancer (Gastroenterology 2005;129:504-11).

"For hyperglycemia to be a clinically useful marker of early cancer one will have to screen asymptomatic individuals for hyperglycemia," and the success of the strategy "will depend largely on our ability to differentiate pancreatic cancer–induced diabetes from type 2 diabetes using a serologic marker," the investigators wrote. "Because our population was neither screened for diabetes nor [screened] for pancreatic cancer, the benefit of screening for pancreatic cancer using diabetes or hyperglycemia as a marker cannot be answered by the present study and deserves a prospective analysis."

Hereditary Colorectal Ca

The median age of onset of colorectal cancer in individuals of families with mismatch repair gene mutations for hereditary nonpolyposis colorectal cancer may be much older than previously reported, according to Heather Hampel, M.D., of Ohio State University, Columbus, and her colleagues.

The median age at diagnosis was 54 years in men and 70 years in women in a group of 70 Finnish families at risk for hereditary nonpolyposis colorectal cancer (HNPCC) that comprised 88 probands and 373 individuals who tested positive for a germline mutation in *MLH1* or *MSH2* (Gastroenterology 2005;129:415-21).

Those ages are 10-15 years higher than the previous estimates of age at onset for colorectal cancer among HNPCC patients in the literature, which are typically 44-45 years. "Our data strongly suggest that in the diagnosis of HNPCC, limiting molecular studies to patients with an early age at diagnosis will miss many cases," the researchers wrote. Microsatellite instability and immunohistochemical staining "would best be applied to all new colorectal cancer cases and not just to a limited high-risk subset."

—Jeff Evans