MedicalXpress

Study finds correlation between number of colorectal polyps and genetic mutations

July 31 2012

Among patients with multiple colorectal polyps, the prevalence of certain gene mutations varied considerably by polyp count, according to a study in the August 1 issue of *JAMA*.

"Patients with multiple colorectal adenomas [polyps] may carry germline [those cells of an individual that have genetic material that could be passed to offspring] mutations in the APC or MUTYH genes," according to background information in the article. The authors write that guidelines for when genetic evaluation should be performed in individuals with multiple colorectal adenomas vary, and data to support such guidelines are limited.

Shilpa Grover, M.D., M.P.H., of Brigham and Women's Hospital, Boston, and colleagues conducted a study to evaluate the frequency of APC and MUTYH mutations by the number of colorectal adenomas among individuals who had undergone clinical genetic testing. The researchers also studied the relationship between the number of adenomas and age at diagnosis of adenoma and colorectal cancer and the prevalence of pathogenic APC or MUTYH mutations. The study included 8,676 individuals who had undergone full gene sequencing between 2004 and 2011. Individuals with a certain mutation of the MUTYH gene (Y179C and G396D) underwent full MUTYH gene sequencing. APC and MUTYH mutation prevalence was evaluated by the number of polyps.

Colorectal adenomas were reported in 7,225 individuals; 1,457 with

classic polyposis (100 adenomas or more) and 3,253 with attenuated (diminished) polyposis (20-99 adenomas). "The prevalence of pathogenic APC and biallelic [pertaining to both alleles (both alternative forms of a gene)] MUTYH mutations was 95 of 119 (80 percent) and 2 of 119 (2 percent), respectively, among individuals with 1,000 or more adenomas, 756 of 1,338 (56 percent) and 94 of 1,338 (7 percent) among those with 100 to 999 adenomas, 326 of 3,253 (10 percent) and 233 of 3,253 (7 percent) among those with 20 to 99 adenomas, and 50 of 970 (5 percent) and 37 of 970 (4 percent) among those with 10 to 19 adenomas. Adenoma count was strongly associated with a pathogenic mutation in multivariable analyses," the authors write.

The researchers note that their evaluation of individuals who underwent genetic testing because of a personal or family history suggestive of a familial polyposis syndrome suggests that genetic evaluation for APC and MUTYH mutations may be considered in individuals with 10 or more adenomas. "However, our results are derived from a selected cohort of high-risk individuals and need to be validated in larger populations of unselected patients."

"The mutation probabilities reported here may assist clinicians in their decision to recommend genetic evaluation and counsel patients undergoing genetic testing. However, it remains important to also consider the limitations of genetic testing at present, because one-third of patients with a classic familial adenomatous polyposis [FAP; a polyposis syndrome resulting from mutations in the APC gene characterized by multiple colorectal polyps] phenotype are found to not carry a mutation in either the APC or MUTYH gene. Such individuals should undergo periodic re-evaluation as other susceptibility genes are identified."

"At this juncture, clinicians need to carefully consider the effect of a positive or negative test result on management of patient care prior to

making decisions regarding genetic testing," write Hemant K. Roy, M.D., and Janardan D. Khandekar, M.D., of the NorthShore University HealthSystem, Evanston, Il., in an accompanying editorial.

"Appropriate patient education and informed consent prior to testing is mandatory, highlighting the integral nature of genetic counseling. Until development of more robust genomic technologies for FAP detection, complementary approaches including careful assessment of family history and biomarkers may have utility. Furthermore, these considerations for FAP may serve as a model for evaluating the wider issues associated with practicing medicine at the front lines of the genomic revolution."

More information:

JAMA. 2012;308[5]:485-492.
JAMA. 2012;308[5]:514-515.

Provided by JAMA and Archives Journals