Study finds one-third of colorectal cancers diagnosed before 35 are hereditary

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Hereditary colorectal cancers, caused by inherited gene mutations, are relatively rare for most patients. However, researchers at The University of Texas MD Anderson Cancer Center have discovered a particularly high prevalence of hereditary cancers among those diagnosed with the disease before the age of 35. They suggest that these patients should undergo genetic counseling to determine if their families may be at an elevated risk.

Approximately five percent of all colorectal cancer (CRC) cases are caused by hereditary syndromes, such as Lynch syndrome and familial adenomatous polyposis (FAP). Among patients with early-onset CRC, generally defined as a diagnosis before age 50, the incidence of hereditary CRC tends to be higher. However, the prevalence in adolescents and younger adults has not been well characterized.

The current study, published in the *Journal of Clinical Oncology*, focused on patients diagnosed at age 35 or younger to better characterize the extent of hereditary CRC in this underrepresented age group.

The research team, led by Eduardo Vilar-Sanchez, M.D., Ph.D, assistant professor, Clinical Cancer Prevention, reviewed data from 193 patients diagnosed with CRC in this age rage that were evaluated by genetic counseling at MD Anderson between 2009 and 2013. This study represents the largest reported cohort of CRC patients diagnosed in this age range in the U.S.

"We were very surprised to find that 35 percent of that population of patients had a genetic disease," says Vilar-Sanchez, "although we hypothesized the proportion would be higher in this age group relative to the general population."

According to the American Cancer Society, colorectal cancer (CRC) is the third most common cancer among men and women in the U.S., with over 90,000 new cases expected this year. Approximately 90 percent of those cases will be diagnosed in patients older than 50.

Patients diagnosed with CRC at age 35 or younger therefore represent an extreme end of the spectrum, accounting for less than 1.5 percent of all cases. This population faces unique challenges related to disease aggressiveness, the impact of treatments on fertility and potential genetic risk to family members, explains Vilar-Sanchez.

"Based on our findings, patients under the age of 35 need to be evaluated by a genetic counselor. Period," says Vilar-Sanchez. "The translation of that information extends well beyond the patient, as there are tremendous benefits from being able to share genetic risk with their parents, siblings and many other family members."

Genetic findings important for families

In the general population, the risk of being diagnosed with CRC in one's lifetime is five percent. People with Lynch syndrome, on the other hand, have a lifetime risk of 50-80 percent. Those with FAP have a 100 percent chance of developing cancer if no preventive measures are taken.

Genetic testing in family members will identify those with high-risk mutations and allow them to take proper preventive actions, such as behavioral modification to reduce other environmental risk factors.

There's also the potential for them to participate in earlier screening, increased surveillance, prophylactic surgeries and chemoprevention studies, explains Vilar-Sanchez.

A limitation of this study was the lack of uniform genetic testing across all patients. Previously, genetic counselors tested a small number of genes sequentially based on family profile and tumor analysis until the culprit was identified. Therefore, not all patients in this cohort underwent identical testing, and some patients' underlying hereditary predisposition may have been missed.

Instead, Vilar-Sanchez says, "Our data advocates for gene panel testing in this population." Gene panel testing denotes the simultaneous analysis of dozens of genes known to influence CRC risk. This would allow all young patients to undergo comprehensive genetic testing, rather than a biased approach.

A recent study, also published in the *Journal of Clinical Oncology*, found that gene panel testing for CRC was cost-effective. Vilar-Sanchez notes that gene-panel testing is now normal clinical practice at MD Anderson.

Continuing efforts in cancer prevention

Going forward, Vilar-Sanchez would like to focus efforts on the remaining two-thirds of patients diagnosed under age 35 without an identified genetic cause. Within this group, 28.6 percent had a family history of CRC and 51.6 percent had a family history of other cancers. Strong family disease history suggests a hereditary contribution and future research will try to identify the gene mutations responsible.

In addition to genetics, early-onset CRC may be attributed to several behavioral and environmental risk factors, including diet, obesity, smoking and alcohol. These risk factors may compound minor genetic

contributions or contribute to early onset in those without a genetic component.

Cataloguing environmental and genetic factors that contribute to CRC are critical for physicians to identify those with an elevated disease risk and work to prevent cancer development.

"The best way to cure cancer is not to get it in the first place," says Vilar-Sanchez.

Provided by University of Texas M. D. Anderson Cancer Center