Healthy lifestyle may help mitigate high genetic risk of cancer

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Healthy lifestyle factors such as abstinence from smoking and drinking, low body mass index, and exercise correlated with decreased cancer incidence, even in individuals with a high genetic risk, according to results of a study published in *Cancer Research*, a journal of the American Association for Cancer Research.

"Our findings indicate that everyone should have a healthy lifestyle to decrease overall cancer risk," said co-senior author of the study Guangfu Jin, Ph.D., a professor at Nanjing Medical University. "This is particularly important for individuals with a high genetic risk of cancer."

As genetic research continues to uncover loci, or areas in DNA, with specific changes that influence cancer risk, researchers can define polygenic risk scores (PRS)—personalized estimates of an individual's cancer risk—based on a patient's unique combination of these changes. However, most PRS are generated for a specific cancer type, rather than for overall cancer risk.

"A PRS indicating risk of a certain cancer is important but not enough," Jin said. "We tried to create an indicator—the cancer polygenic risk score (CPRS)—to measure the genetic risk of cancer as a whole."

Jin and colleagues calculated individual PRS for 16 cancers in men and 18 cancers in women, using available data from genome-wide association studies. They then used statistical methods to combine these scores into a single measure of cancer risk, based on the relative proportion of each cancer type in the general population. Separate CPRS were generated for men and women.

To validate their CPRS, the researchers utilized genotype information from 202,842 men and 239,659 women from the UK Biobank, a cohort of general-population participants recruited from England, Scotland, and Wales between 2006 and 2009, and calculated a CPRS for each

individual. Patients with the highest quintile CPRS were nearly twice as likely (for men) and 1.6 times as likely (for women) to have a cancer diagnosis by their most recent follow-up, in 2015 or 2016.

Notably, 97 percent of patients in the study had a high genetic risk (top quintile) of at least one cancer type. "This suggests that almost everyone is susceptible to at least one type of cancer," Jin said. "It further indicates the importance of adherence to a healthy lifestyle for everyone."

UK Biobank participants were surveyed upon enrollment for various lifestyle factors, including smoking and alcohol consumption, body mass index, exercise habits, and typical diet. Based on these factors, Jin and colleagues classified each patient as having an unfavorable (zero to one healthy factors), intermediate (two to three healthy factors), or favorable (four to five healthy factors) overall lifestyle. Patients with an unfavorable lifestyle and the highest quintile genetic risk were 2.99 times (in men) and 2.38 times (in women) more likely to develop cancer than those with a favorable lifestyle and the lowest quintile of genetic risk.

Among patients with high genetic risk, the five-year cancer incidence was 7.23 percent in men and 5.77 percent in women with an unfavorable lifestyle, compared with 5.51 percent in men and 3.69 percent in women with a favorable lifestyle. The decreased percentages are comparable to the cancer risk in individuals with intermediate genetic risk, Jin said. Similar trends were observed in all genetic risk categories, suggesting that patients could benefit from a healthy lifestyle regardless of genetic risk.

"We hope our CPRS could be useful to improve a person's awareness of their inherited susceptibility of cancer as a whole and facilitate them to participate in healthy activities," Jin said.

Limitations of this study include the fact that only the strongest genetic risk loci were included in the individual PRS, which disregards the influence of loci with weaker effects. Researchers also noted an imbalance in the number of loci included between different cancer types, which can potentially skew their individual impact.

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