

Protein levels indicate risk of death in some colorectal cancer patients

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A pair of proteins may help explain why people with surgically removed colorectal cancer and who are overweight, physically inactive, and follow a Western-pattern diet may have an increased risk of dying of the disease or other causes, Dana-Farber Cancer Institute scientists report in a new study.

The researchers found that in people who have undergone surgery for colorectal cancer, the levels of two insulin-related proteins in their blood before diagnosis predicted their chances of dying from the cancer or other conditions. Patients with high prediagnosis levels of insulin-like growth factor binding protein-1 (IGFBP-1) were more than half as likely to succumb to the disease; while those with high levels of C-peptide were nearly twice as likely to die. The results are being published online by the *Journal of Clinical Oncology* on Dec. 8

The study was the first to consider whether proteins whose blood levels are influenced by lifestyle factors can be a gauge of a patient's chances of surviving stage I-III colorectal cancer. It was designed to explore why people with certain characteristics -- namely, obesity, physical inactivity, and an unhealthy diet -- have an increased risk of colon cancer, cancer recurrence, and death. Such lifestyle factors can lead to high levels of circulating insulin, a hormone that may bind directly to colon cancer cells and spur their growth. High insulin levels also lead to numerous alterations in other blood proteins, which may influence cancer cell growth.

"We don't know yet whether the two proteins identified in this study are part of the actual mechanism that promotes colon cancer recurrence or whether they are simply 'markers' for risk of colon cancer recurrence and death," says the study's lead author, Brian Wolpin, MD, MPH, of Dana-Farber and Brigham and Women's Hospital (BWH). "But the results underscore the growing evidence that lifestyle choices can have an impact on the risk of recurrence in patients with surgically removed colorectal cancer."

Using data from the Nurses' Health Study and the Health Professionals Follow-up Study -- two long-term studies tracking participants' health -- investigators examined prediagnosis levels of four insulin-related proteins in 373 people who later developed stage I-III colorectal cancer. All four proteins are known to increase or decrease in response to lifestyle factors such as overweight, physical inactivity, and poor nutrition.

Levels of two of the proteins were unrelated to colon cancer recurrence or death. The connection between IGFBP-1, C-peptide, and mortality, however, was strong. Patients with the highest levels of IGFBP-1 had a 56 percent lower risk of death during the study period, and a 57 percent lower risk of dying from colorectal cancer. Researchers speculate that the protein may exert a protective effect by blocking other growth factors that contribute to colon cancer cell proliferation.

High levels of C-peptide, by contrast, doubled the risk of overall death in people with cancer but were not significantly associated with death from colorectal cancer itself. This may be because of an even stronger link between high insulin levels of other potentially fatal diseases such as heart disease and stroke, or because C-peptide is not as accurate a measure of insulin-related hormonal changes as other proteins, the study authors speculate.

Source: Dana-Farber Cancer Institute

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