Excess body fat increases risk of digestive system cancers

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Obesity increases the risk of developing cancers of the digestive system and it is the person's fat mass, rather than size, that is the main obesity-related risk factor for these cancer types, according to a new study

published in the journal *PLOS Medicine* by researchers at the University of Cambridge and Karolinska Institutet.

Previous observational studies have shown that a high BMI (body mass index) is linked to several cancer types.

In the current study, researchers used data from the UK Biobank and large international consortia and a method called Mendelian randomisation to investigate which cancers are causally linked to body size and how components such as fat mass, BMI and height affect this risk.

They studied whether genetic variants that predispose an individual to having increased fat mass, BMI or being taller also predisposed them to having higher risk of 22 different cancer types.

"Body weight is often affected by the presence of cancer or the cancer treatment. Looking at genes rather than an individual's height or weight reduces the risk of finding non-causal associations in observational data," says Susanna Larsson, associate professor at the Institute of Environmental Medicine at Karolinska Institutet and joint last author of the study.

BMI and cancers of the digestive system

Genetic predisposition to being tall was consistently associated with slightly increased risk across the different cancer types investigated. Genetic predisposition to high BMI was associated with increased risk of cancers of the digestive system, particularly liver, stomach, esophageal and pancreatic cancer, but not with increased risk of overall cancer.

The increased risk of digestive system cancers was primarily attributable to genes that influence fat mass.

"This means that fat mass is a more important risk factor than body size and that high BMI is not necessarily a risk factor for many different cancer types, but mainly for cancers of the digestive system," says Susanna Larsson.

Moreover, genetic predisposition to increased BMI was associated with an increased risk of endometrial, ovarian, and lung cancer, but with a decreased risk of breast and prostate cancer.

Higher risk with more cells

The study did not provide evidence about the mechanisms behind the associations, but it is generally thought that tall people have higher cancer risk because they have more cells in their body.

According to the researchers, the link between fat mass and digestive cancers may be driven by increased consumption of cancer-causing substances in fatty food, or increased levels of fatty tissue increasing inflammation in the digestive tract.

Links between obesity and gender-specific cancers are likely driven by the production of reproductive hormones in fatty tissue.

More information: Mathew Vithayathil et al, Body size and composition and risk of site-specific cancers in the UK Biobank and large international consortia: A mendelian randomisation study, *PLOS Medicine* (2021). DOI: 10.1371/journal.pmed.1003706

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