Metabolic Health and Cancer

It's more than just weight

Obesity is a risk factor for several cancers including pancreatic, postmenopausal breast, liver, colorectal, endometrial, and renal cell, and is often accompanied by metabolic problems like high blood glucose/diabetes, high blood pressure, and abnormal lipids. However, there is a group of people who are obese but don't have all the metabolic dysfunction. Are they at the same risk as the others? Is the cancer risk only based on weight? What can we do to decrease our risk of developing these cancers?

Abstract

- **Background:** Studies of obesity with or without metabolic aberrations, commonly termed *metabolically unhealthy* or *healthy obesity*, in relation to cancer risk are scarce.
- **Methods:** We investigated body mass index (normal weight, overweight, obesity) jointly and in interaction with metabolic health status in relation to obesity-related cancer risk (n = 23 630) among 797 193 European individuals. A metabolic score comprising mid-blood pressure, plasma glucose, and triglycerides was used to define metabolically healthy and unhealthy status. Hazard ratios (HRs) and multiplicative interactions were assessed using Cox regression, and additive interactions were assessed using the relative excess risk for interaction. All statistical tests were 2-sided.
- **Results:** Metabolically unhealthy obesity, with a baseline prevalence of 7%, was, compared with metabolically healthy normal weight, associated with an increased relative risk of any obesity-related cancer and of colon, rectal, pancreas, endometrial, liver, gallbladder, and renal cell cancer ($P < .05$), with the highest risk estimates for endometrial, liver, and renal cell cancer (HR = 2.55-3.00). Metabolically healthy obesity showed a higher relative risk for any obesity-related cancer and colon (in men), endometrial, renal cell, liver, and gallbladder cancer, though the risk relationships were weaker. There were no multiplicative interactions, but there were additive, positive interactions between body mass index and metabolic health status on obesity-related and rectal cancer among men and on endometrial cancer ($P < .05$).
- **Conclusions:** This study highlights that the type of metabolic obesity phenotype is important when assessing obesity-related cancer risk. In general, metabolic aberrations further increased the obesity-induced cancer risk, suggesting that obesity and metabolic aberrations are useful targets for prevention.

This study set out to separate obesity without metabolic dysfunction (high lipids, glucose, blood pressure) and compare the risk of cancer with people who are obese and have these metabolic diseases. They found that metabolically unhealthy obesity was associated with an increased risk for any obesity-related cancer compared to metabolically healthy normal-weight people with a 2.5-3 times risk for endometrial, liver, and renal cell cancers. In men, metabolically normal obesity had a higher risk of any obesity-related cancer and colon cancer. Even metabolically normal obesity is a risk factor for cancer. Putting this together with what we learned last month regarding the relationship between cardiovascular risk and dementia, it is obvious that these metabolic risk factors are a big deal and can have major effects on our longevity.

Metabolically (un)healthy obesity and risk of obesity-related cancers: a pooled study, JNCI: Journal of the National Cancer Institute, 2023;, djad008, https://doi.org/10.1093/jnci/djad008.