

The role of obesity in cancer development

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Being overweight has been a long-known peril to health, and scientists were able to show a relationship between body fat and cancer years ago. Of course, not every obese individual will inevitably develop cancer, but recent scientific studies show that excessive body fat has an impact on a much broader spectrum of cancers than previously thought^[1]. This applies to adults as well as children and adolescents.

In 2015, the Organisation for Economic Co-operation and Development (OECD) reported that already > 50% of adults and nearly 30% of teenagers in 34 member countries were considered overweight (body mass index, BMI ≥ 25 kg/m² body surface area), or even obese (BMI ≥ 30 kg/m² body surface area)^[2,3]. The tendency increased gradually in all countries over a period of 25 years (1990–2015). We therefore have to expect steadily rising numbers of cancers worldwide solely due to obesity in the future.

A population-based study using BMI and cancer incidence data from the GLOBOCAN project estimated that, in 2012 in the United States, about 28,000 new cases of cancer in men (3.5%) and 72,000 in women (9.5%) were due to overweight or obesity^[4]. The percentage of cases attributed to overweight or obesity varied widely for different cancer types but was as high as 54% for gallbladder cancer in women and 44% for esophageal adenocarcinoma in men.

The International Agency for Research on Cancer (IARC) as part of the World Health Organization (WHO) in 2016 reported an increased risk of cancer for at least 13 cancer types [colon cancer, esophageal cancer, renal carcinoma, uterine cancer, breast cancer (during and after menopause; also in men), liver cancer, pancreatic cancer, gall bladder cancer, ovarian cancer, gastric cancer, thyroid cancer, multiple myeloma, and meningioma]^[1]. For some of these cancers, the experts even found a dose-response relationship, implying that the risk of cancer increases with BMI^[1].

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Currently, there are many theories that could explain the increased incidence of cancer in obesity. The preponderance of the evidence suggests that a combination of different factors might be responsible. However, it should be reiterated that there is no direct link between obesity and the development of cancer.

On the one hand, obesity seems to cause a general hormonal imbalance including hyperinsulinemia and an increase in insulin-like growth factors, as well as sex hormones. In addition, hyperplastic and hypertrophic white adipose tissue (especially visceral adipose tissue) acts as an independent active endocrine organ releasing immunologically active adipokines and other hormones. These hormonal imbalances support cell growth-promoting processes^[5]. On the other hand, obesity is associated with a state of low-grade chronic inflammation. Insulin resistance and the metabolic syndrome are associated with higher circulating concentrations of inflammation-related markers, including leptin, interleukin-6, and tumor necrosis factor, many of which have been shown to enhance tumor growth. Chronic inflammation is a well-known, obesity independent critical component of tumor development and progression. Many cancers arise from sites of infection, chronic irritation, and inflammation^[6].

Obesity is only one of many important triggers of low-grade chronic inflammation, whereas per current literature there is no study published, that clearly shows that chronic inflammation is inversely related to the development of obesity.

In addition, a further mechanism that suppresses the eradication of neoplastic cells is immune paralysis, which is also due to chronic inflammation. Not least, preclinical studies showed that adipocytic progenitor cells contribute to a tumor-promoting microenvironment^[5] as well.

Controlled diet and lifestyle adjustments can lower the risk of cancer. It would be naive to believe that through a healthy diet and regular physical exercise, however, cancer development were to be prevented entirely^[7,8].

Could losing weight reduce the risk of cancer? So far, this has not been proven, although some preliminary study results suggest it^[9,10].

However, the above results should still be interpreted with caution, as the published studies were too heterogenous in their design, the populations studied and different lengths of follow-up, so that it is too early at the moment, to make definitive recommendations. Reducing the excess weight once acquired, however, is difficult for many people. For most patients, making sure to at least not gain further weight is the first step. Likewise, people with normal weight should at least try to maintain it^[1].

Bariatric or metabolic surgical interventions have shown some initial beneficial effect for primary prevention of cancer, although it is far too early to draw definitive conclusions^[11,12].

Nevertheless, weight reduction seems to provide some degree of primary prophylaxis not only concerning metabolic and cardiovascular disease, but also for developing a wide array of neoplasms^[13].

Conclusions

The increasing incidence of obesity is one of the biggest challenges facing our society's future on a global scale. In addition to other major issues, there is convincing evidence that obesity increases the risk for many types of cancer, most likely due to general hormonal imbalance and chronic low-grade inflammation processes. Nevertheless, tumor development is a multifactorial process and simple obesity does not directly cause tumor development. Controlled diet and lifestyle adjustments can lower the risk of selected cancer types as well as metabolic surgical interventions. Nevertheless, it is far too early to draw definitive conclusions, and far more research is needed to answer the many still remaining questions, particularly on the effect of weight loss programs and surgical interventions. Also, it is unclear to what extent obesity in childhood and adolescence plays in the subsequent risk of cancer in adults.

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