

Obesity increases the risk of breast cancer

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Translated from Le Journal de Montréal, January 11th, 2021

Obesity dramatically increases the risk of ER + hormone-dependent breast cancer after menopause. According to a new discovery, this increase is due to the pro-inflammatory effect of an estrogen, estrone, which promotes the appearance of cancer stem cells and tumor progression.

In Canada, obesity affects 3 in 10 adults and contributes to the high incidence and mortality of several chronic diseases that affect the population, including cardiovascular disease, type 2 diabetes and several types of cancer.

The COVID-19 pandemic has also revealed that being overweight is a major risk factor for complications of the disease in younger adults (50 years and under), with an approximately 50% increase in the risk of death (1).

Globally, obesity is on track to overtake smoking as the leading cause of death and is unquestionably the main public health problem we will face in the coming decades.

PRE- VS POST-MENOPAUSE

One of the consequences of this increased incidence of obesity is the increase in mortality from breast cancer (2).

About 60% of breast cancers are ER +, that is, cancer cells express the estrogen receptor, and the majority of these cancers occur after menopause.

Obesity increases the risk of developing these cancers by about 40% in postmenopausal women, but, oddly enough, not before menopause.

The mechanisms responsible for this paradox remain complex, but are likely a consequence of hormonal changes that occur following menopause.

PRO-INFLAMMATORY ESTROGEN

A recent study suggests that it is indeed the difference in two main types of estrogen present before and after menopause that may explain the contribution of excess fat to the increased risk of cancer in postmenopausal women (3).

After menopause, the level of the main estrogen present in the years of fertility, 17 β -estradiol (E2), drops considerably and it is estrone (E1) which then becomes the main estrogen in the body, especially at the level of fatty tissue.

Researchers have observed that these two types of estrogen have inflammatory actions that are completely opposite to each other.



For example, while E2 (estrogen present before menopause) decreases chronic inflammation generated by excess fat, E1 (estrogen present after menopause) on the contrary stimulates this inflammation by activating a transcription factor of DNA (NF κ B), at the heart of the molecular cascade of inflammation.

In other words, before menopause, high amounts of E2 help to counteract the pro-inflammatory effect of E1 and thus neutralize the chronic inflammation generated by excess fat.

After menopause, the exact opposite happens, and the excess of E1 over E2 creates an imbalance that promotes this inflammation.

These differences have serious implications for cancer risk, as numerous studies have clearly shown that chronic inflammation creates optimal conditions for the development and progression of cancer cells.

In addition, that is exactly what the researchers observed, with the appearance of cancer stem cells in the breast tissue, which is directly correlated with the hormonal changes caused by menopause (increase in E1 and decrease in E2).

International cancer control agencies recommend staying as lean as possible, because multiple population studies have shown that overweight is associated with an increase in at least 13 different cancers (4). In addition, overweight remains the leading cause of type 2 diabetes and the serious clinical complications that result from this disease.

- (1) Popkin BM et coll. Individuals with obesity and COVID-19: A global perspective on the epidemiology and biological relationships. *Obesity Rev.* 2020 ; 21 : e13128
- (2) Calle EE et coll. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. *N. Engl. J. Med.* 2003 ; 348:1625-38.
- (3) Qureshi R et coll. The major pre- and postmenopausal estrogens play opposing roles in obesity-driven mammary inflammation and breast cancer development. *Cell Metab.* 2020 ; 31 : 1154-1172.e9.
- (4) Steele CB et coll. Vital Signs: Trends in incidence of cancers associated with overweight and obesity - United States, 2005-2014. *MMWR Morb Mortal Wkly Rep* 2017; 66 : 1052-1058.