

Increased Breast Cancer Risk: Another Implication of High Cholesterol

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In addition to being a known risk factor for heart and cardiovascular disease, recent studies have highlighted the link between high cholesterol and increased risk of [breast cancer](#). Breast cancer is the second most common malignancy in women after skin cancer. The majority of breast cancer is influenced by the stimulatory effect of estrogen on alpha-estrogen receptors on breast cells, which up-regulates their proliferation rate and the risk of estrogen receptor-positive (ER+) breast cancer (which is greatest in postmenopausal women).

Until recently, estrogen has been the only known endogenous estrogen receptor ligand (binding agent) that promotes ER+ breast tumor growth. However, new discoveries show that the cholesterol metabolite 27-hydroxycholesterol (27HC) binds to alpha-estrogen receptors, and up-regulates the rate of breast cell and breast cancer cell division.

In experimental studies 27HC has been shown to stimulate breast cancer growth in mice with transplanted estrogen-receptor-positive breast cells from humans. Human studies show that in ER+ breast cancer patients, 27HC content in normal breast tissue is increased compared to cancer-free controls, and that tumor 27HC abundance is further elevated. Increases in tumor 27HC are shown to be related to diminished expression of the 27HC metabolizing enzyme CYP7B1, which accompanies menopause.

The Perfect Breast Cancer Risk Factor Storm

It is well-documented that overweight, postmenopausal women have a threefold increase in breast cancer risk. This has been linked to higher estrogen synthesis and secretion from fat cells, which in turn overstimulate the cell division rate of breast cells, and impose other changes conducive to the development of breast cancer. In addition, it is also well-established that hypercholesterolemia is a risk factor for estrogen-receptor-positive breast cancers and is associated with a decreased response of tumors to endocrine therapies.

Evidence is mounting that the form of cholesterol that is most dangerous to the development of breast cancer is 27HC. There are three common situations whereby 27HC is typically elevated. The first is during the postmenopausal period. Serum 27HC levels increase in women after menopause, which appears to be caused by estrogen deprivation, as mice studies show that beta-estradiol up-regulates hepatic CYP7B1 expression. CYP7B1 is the enzyme that detoxifies 27HC in the liver. Thus, the rate of 27HC detoxification declines after menopause due largely to the age-related decline in estrogen that accompanies menopause.

At the same time, the synthesis of 27HC from cholesterol continues at the normal pace, which is dependent on the enzyme CYP27A1. Thus, the decline in estrogen during menopause tends to increase

circulating 27HC levels, which is exacerbated when blood cholesterol is high. As such, 27HC is shown to be higher in women with hypercholesterolemia and with obesity, which is frequently associated with hypercholesterolemia.

In mice, a high-fat, high-cholesterol Western diet elevates serum 27HC two- to threefold. In women, both dyslipidemia and obesity raise breast cancer risk and severity, with obesity particularly having an adverse impact in postmenopausal women and breast cancer promotion, especially in regard to estrogen-receptor-positive breast cancer.¹

Of note is the further [observation](#) that "the enzyme responsible for the conversion of cholesterol to 27HC (CYP27A1) is primarily expressed in macrophages. And because tumor infiltrating macrophages are associated with more aggressive tumors and worse patient outcomes, data suggests that 27HC, acting as either a circulating hormone or as a paracrine factor produced by macrophages, is a mechanistic link between hypercholesterolemia and breast cancer incidence."²

Researchers also noted that "the most aggressive human breast cancers were found to express the highest level of the enzyme that converts cholesterol to 27HC; the researchers conclude that 27HC produced within tumors - in addition to circulating 27HC - may contribute to tumorigenesis, spurring the growth and spread of the most common breast cancer in mice, and perhaps in some women."²

Statin Drugs to Reduce Breast Cancer Risk?

Some preliminary studies have found that patients taking anti-cholesterol statin drugs, which inhibit cholesterol production, demonstrate lower breast cancer incidence and decreased breast cancer recurrence.² This makes sense given that high cholesterol levels tend to raise 27HC levels, which is becoming highly incriminated in breast cancer development and progression. The flip side of the statin drug story is that the use of statin drugs is known to increase risk of liver damage, can trigger or aggravate diabetic states, increase risk of memory loss and induce joint pain. In very rare cases, it can cause life-threatening [rhabdomyolysis](#).³⁻⁴

A Better Option for Attaining Ideal Cholesterol Values

Fortunately, there are other ways to keep cholesterol in the ideal range (below 3.9 mmol/L; 150 mg/dL) for more than 90 percent of the population who are not genetically predisposed to high cholesterol problems. With respect to attaining ideal cholesterol values, health practitioners who emphasize natural approaches to health management should discuss the importance of diet, exercise and targeted natural supplements that have been shown to reduce cholesterol.

These natural approaches do not impose the side effects associated with statin drugs. Therefore, unless dealing with a patient who is at high-risk for a cardiovascular disease event (or genetically-induced high cholesterol), health practitioners should interest their patients in natural, safe approaches to the management of obesity and high cholesterol as much as possible.

The payoff appears to be not only reduced risk of cardiovascular disease, but also reduced risk of breast cancer, according to recent data. This natural approach is often overlooked in the conventional management of high cholesterol, as doctors often focus their attention almost exclusively on the role of statin drugs.

References

1. Wu Q, Ishikawa T, Siriannin R, et al. 27-hydroxycholesterol promotes cell-autonomous, ER-positive breast cancer growth. *Cell Reports*, Nov 2013;5(3):637-645.
 2. "How Cholesterol Is Fueling the Growth and Spread of Breast Cancer." *Onco'Zine* (International Oncology Network - Cancer and Hematology News), Nov. 28, 2013.
 3. Baker SL. "Statin Drugs Are Overprescribed in Healthy People Who Have No Evidence of Heart Disease." *Natural News*, Nov. 18, 2010.
 4. Young S. "Statin Drugs Will Come With New Safety Warnings. CNN Health, March 5, 2012.
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To review some of the natural strategies to lower cholesterol, access Dr. Meschino's previously published articles on this subject, including the following:

- ["Gugulipid \(Gum Guggul\): Nature's Safe, Effective Cholesterol-Lowering Supplement."](#) *DC*, May 5, 2003.
- ["Cholesterol-Lowering Diet Reduces Blood Cholesterol to Similar Degree as Prescription Statin Drug \(Lovastatin\) in Head-to-Head Clinical Trial."](#) *DC*, Feb 27, 2006.
- ["Helping Patients Achieve a Cholesterol Level Below 150 mg/dL Without Drugs - An Important Objective in the Prevention of Cardiovascular Disease."](#) *DC*, April 9, 2007.
- ["Natural Supplements Proven to Lower Cholesterol and Triglycerides."](#) *DC*, Sept. 9, 2008.

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