Metabolic Syndrome and Post-Menopausal Breast Cancer: What's the Connection?

Excess body fat, inflammation and insulin resistance are linked to breast cancer in post-menopausal women. Here's how to lower the risk.

November 2, 2021 By Karen Collins at the American Institute for Cancer Research

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Metabolic syndrome refers to a set of conditions. It's diagnosed by the presence of at least three of five factors: large waist size, elevated fasting blood sugar (or taking diabetes medication), low HDL ("good") cholesterol, elevated blood triglycerides and hypertension (or taking blood pressure medication). Especially when occurring together, they indicate unhealthy hormonal and metabolic conditions within the body.

People who meet the criteria for metabolic syndrome also have a greater risk of heart disease compared to those who do not. And the risk of type 2 diabetes also increases.

The original focus of research on metabolic syndrome was outside the cancer sphere, but as research progressed to better understand the strong association of excess body fat with increased risk of at least 12 cancers—post-menopausal breast cancer is just one of them—the links to metabolic syndrome came to attention.

Half of U.S. women age 60 and older now meet the criteria for metabolic syndrome—a condition that increases the risk of breast cancer. It's also present in a third of women ages 40 to 59.

The Research on Risk Factor

A meta-analysis combining multiple observational studies followed women for up to 18 years and found the following:

- Metabolic syndrome is not related to pre-menopausal breast cancer risk.

- Metabolic syndrome was associated with two times the risk of breast cancer among post-

menopausal women.

- No single component of metabolic syndrome (like waist size or triglyceride levels) increased breast cancer risk nearly as much as did the presence of metabolic syndrome.

To look at how metabolic syndrome and excess body weight separately and combined affect risk of breast cancer, another team of researchers divided participants in the Women's Health Initiative (WHI) into six groups. First, women were categorized as having normal weight, overweight or obesity based on BMI. Within each group, they further divided the women whether or not they had metabolic syndrome.

Among the approximately 21,000 post-menopausal women studied:

- Obesity increased risk of breast cancer by about 50%. After statistically adjusting for the presence of metabolic syndrome, the association was reduced somewhat, but remained strong. Overweight (BMI of 25 to 29.9), especially after adjusting for metabolic syndrome, did not show an association with risk in these women.

- Metabolic syndrome increased risk of breast cancer by 28%. Again, after adjusting for BMI, the association was reduced, but remained significant.

- The greatest increase in risk was among women with both obesity and metabolic syndrome.

What's Behind the Metabolic Syndrome Link to Breast Cancer?

Excess body fat, especially deep in the abdomen, promotes chronic inflammation. Fat tissue includes cells that produce and secrete proteins that travel throughout the body promoting inflammation, which can create cell damage that leads to cancer. These inflammatory proteins also trigger steps that lead to insulin resistance.

Insulin resistance seems to play an important role in the link between metabolic syndrome and

post-menopausal breast cancer. When cells become less responsive to insulin, the body tries to secrete more and more insulin. High circulating insulin levels trigger pathways that regulate cell growth and reproduction. High insulin levels also stimulate production of the growth factor IGF-1. Breast cancer cells often have extra receptors for this growth factor, making them especially sensitive to these signals.

Increased estrogen levels are also likely part of this picture. The AICR Third Expert Report shows that risk of estrogen and progesterone receptor-positive (ER+PR+) breast cancer is the form that's particularly associated with obesity. After menopause, body fat is the primary source of estrogen production, and higher body fat often means more estrogen is available to promote estrogen-sensitive cancers. As inflammatory proteins increase, and the anti-inflammatory hormone adiponectin decreases, this further triggers greater production of estrogen.

The bottom line: excess body fat, inflammation and insulin resistance are part of a cycle that creates an internal environment that promotes development and progression of breast cancer in post-menopausal women. And all three conditions are intrinsic elements of metabolic syndrome.

AICR Recommendations as a Blueprint to Help Reduce Risk of Breast Cancer

The association of breast cancer risk with metabolic syndrome is concerning because of how common the syndrome has become. Metabolic syndrome most often occurs in people who have overweight or obesity. But it can also occur in people with normal weight. More research is needed to understand whether this signals increased risk of post-menopausal breast cancer in these women, too.

Following the AICR Recommendations blueprint—before you think you need it—is a smart strategy.

Weight: It's not all-or-nothing. AICR analysis shows that each increase or decrease in BMI is associated with differences in post-menopausal breast cancer risk. Evidence suggests the closer you are to normal BMI, the lower the risk. However, this also means that for post-menopausal women with obesity, each drop in body fat helps. And research outside of cancer supports this. For example, even if weight remains higher than recommended targets, modest weight loss reduces insulin resistance.

Physical activity helps beyond a role in weight management. Research has long shown that regular physical activity helps reduce insulin resistance. And since insulin resistance is central to the risks associated with metabolic syndrome, that adds a new perspective to your daily walk. You won't weigh less tomorrow because you walked today, but insulin sensitivity remains improved for 24 to 48 hours after physical activity.

Limiting sugar-sweetened drinks, sweets and other highly-processed foods may do double-duty. AICR analysis shows strong evidence linking these foods and drinks with weight gain and excess

body fat. In addition, frequent consumption of sugar-sweetened drinks, for example, can also promote higher circulating insulin levels and increase insulin resistance.

Plant-focused eating habits help make vegetables, fruits, whole grains and pulses (like dried beans) the largest part of your plate. These foods tend to be less concentrated in calories than other foods, so you can eat portions that satisfy hunger without promoting weight gain. And they offer so much more:

- Dietary fiber may help decrease insulin resistance. Some fiber types may help control circulating estrogen levels by blocking its reabsorption as it circulates through the gut. And some fiber types may help fight off inflammation, possibly through supporting a healthy gut microbiome.

- Antioxidant nutrients in these foods can support defenses against inflammation and the damage it produces.

- Thousands of natural compounds in these foods show potential to affect gene expression in ways that turn on tumor suppressor genes, trigger cell signaling that slows abnormal cell growth and perhaps even influences estrogen metabolism.

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