Insulin resistance contributes to racial disparities in breast cancer prognosis in US women

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In a new multi-center study of U.S. women with newly diagnosed invasive breast cancer, Mount Sinai researchers have shown that insulin resistance is one factor mediating part of the association between race and poor prognosis in the disease. The findings were published in *Breast Cancer Research* on Tuesday, May 12.

Despite improvements in breast cancer diagnosis and treatment, black women with breast cancer continue to have worse prognoses on average than white women. Breast cancer prognoses also tend to be worse in patients with insulin resistance, a common condition that occurs when metabolic cells in the body don't respond adequately to insulin, causing the pancreas to make more insulin to maintain normal glucose levels. Insulin resistance is an important component of obesity, prediabetes, and type 2 diabetes. Patients with these conditions also tend to have more aggressive breast cancer subtypes and increased mortality.

"Given that obesity and diabetes epidemics disproportionately affect minority populations, it is important to understand the relationship of hyperinsulinemia, insulin resistance, and increased insulin receptor (IR) signaling on the progression of breast cancer," explained lead author Emily J. Gallagher, MD, Ph.D., Assistant Professor of Medicine (Endocrinology, Diabetes and Bone Disease) at the Icahn School of Medicine at Mount Sinai. Dr. Gallagher specializes in onco-endocrinology, the treatment of endocrine complications of oncology

treatments. "Understanding these relationships could explain the different patterns of disease seen in different racial groups and help to identify patients who would benefit from targeted therapy," she says.

This is the first cross-sectional study to examine in detail insulin resistance as a factor associated to the disparities in breast cancer prognosis between black women and white women. The study included 515 women with a newly diagnosed breast cancer; about 83 percent of the subjects were white and 17 percent black. The Mount Sinai team evaluated the women for insulin resistance, metabolic syndrome—a cluster of conditions that occur together and may include high blood pressure or high blood sugar—and obesity to investigate whether insulin is a key mechanistic link in the association between these metabolic conditions and breast cancer aggressiveness. Samples of breast cancer tissue were examined to assess the role of insulin receptor and insulin-like growth factor receptor expression in disparities in breast cancer prognoses between the racial groups.

The researchers found that insulin resistance was more prevalent in black women with invasive breast cancer than in white women and that insulin resistance mediated part of the effect of race on prognosis. Additionally, the team found that tumors from black women had a higher expression of the insulin receptor, which is what insulin binds to in the tumors. Tumors with a worse prognosis had higher expression of the insulin receptor.

"Our results raise a number of questions for future research and patient care. It will be important in future studies to explore whether lowering insulin levels or targeting IR signaling will improve breast cancer disparities," said co-senior investigator Nina Bickell, MD, Ph.D., MPH, Associate Director of Community Engaged and Equity Research of The Tisch Cancer Institute and Co-Director of the Center for Health Equity and Community Engaged Research at the Icahn School of Medicine at

Mount Sinai.

More information: Emily J. Gallagher et al, Insulin resistance contributes to racial disparities in breast cancer prognosis in US women, *Breast Cancer Research* (2020). DOI: 10.1186/s13058-020-01281-y

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