The relationship between features of the metabolic syndrome and survival after a diagnosis of breast cancer in the Women's Health Initiative

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Background: Metabolic Syndrome (MetS) refers to a cluster of conditions typically associated with cardiovascular disease. There is increasing evidence to suggest that MetS is associated with increased risk of several different solid tumors, including breast cancer, however few studies have evaluated the relationship between MetS or its individual components and outcomes after a breast cancer diagnosis.

Methods: We evaluated the relationship between pre-diagnostic MetS and both breast cancer-specific and overall mortality among women diagnosed with invasive breast cancer in the Women's Health Initiative (WHI) Observational Study (OS). Women with a history of any other cancer prior to diagnosis, women diagnosed with DCIS or distant stage disease, and those with unknown follow-up were excluded from the analysis. MetS features included waist circumference and blood pressure measured at cohort enrollment and self-reported history of high-cholesterol and type-2 diabetes, with the latter two features modified from the Adult Treatment Panel (ATP) III clinical definition(1). MetS was defined as having any 3 of the 4 measured individual features. Eligible women were followed until date of death or last follow-up. Cox proportional hazards models were used to estimate hazard ratios and 95% confidence intervals for the association between each individual MetS feature, and the presence of MetS (3+ features), with both breast cancer-specific and overall survival, adjusted for important survival predictors.

Results: 4,347 eligible women with breast cancer were followed for an average of 9.9 years, and 956 deaths including 303 due to breast cancer were documented. We found higher all-cause mortality among breast cancer patients with MetS compared to those with no MetS features (HR=1.69, 95% CI=1.30 – 2.21), with a significant trend of higher risk with additional MetS features (p-trend <0.001). MetS was not significantly associated with breast cancer-specific mortality (HR=0.97, 95% CI=0.57 – 1.67). However, abdominal adiposity (waist circumference ≥ 88 cm) was associated with both increased overall and breast cancer-specific mortality (HR=1.31, 95% CI=1.14-1.50 and HR=1.27, 95% CI=1.00-1.61, respectively). While the overall prevalence of MetS was higher in African-American women (15%) compared to non-Hispanic white women (4%) with breast cancer, there was inadequate power to determine if racial differences exist in the association between MetS and survival.

Conclusions: MetS was associated with overall, but not breast cancer-specific survival among women participating in the WHI OS, while abdominal obesity was associated with both all cause and breast cancer-specific mortality. Further study is necessary to determine if there are racial differences in disease-specific mortality tied to features indicative of MetS in women diagnosed with breast cancer.

(1) Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation 2002;106(25):3143-421.

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