The Effects of Diabetes and Glycemic Control on Cancer Outcomes in Individuals with Metastatic Breast Cancer

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Background: While a well-established relationship between diabetes and breast cancer exists, it remains unclear how diabetes impacts breast cancer outcomes. This study aims to determine the impact/association of diabetes and hyperglycemia on cancer progression and mortality in individuals with metastatic breast cancer.

Methods: Patients with metastatic breast cancer between 2010-2021 were identified using the metastatic breast cancer database at a single academic center. The Research Patient Data Registry, a data warehouse of all patients receiving care in the hospital network was then used to determine the diabetes status of each participant. A participant was categorized as having diabetes if they fulfilled pre-specified criteria (international classification of diseases (ICD) 9 or 10 code for diabetes, or a hemaglobin A1c ≥6.5%, or a random blood glucose (RBG) ≥200 mg/dL and documented use of glucose-lowering agents), while controls were defined as individuals who did not fulfill the previous criteria. We evaluated the effects of diabetes on 1) overall survival (OS) and 2) the interval from initiation of first-line metastatic therapy to initiation of a second-line regimen due to documented progression of disease (a surrogate measure of progression-free survival). The impact of glycemic control on OS and duration of first-line therapy was also assessed.

Results: We compared 244 patients with diabetes (median age 57.6 years) to 244 patients without diabetes, who were matched for age, gender, ethnicity and hormone-receptor (HR) status. OS at 5 years (diabetes: 54%, CI; 47-62% vs. controls: 56%, CI; 49-63%, p=0.65) and freedom from initiating a second-line regimen at 2 years (diabetes: 43%, CI; 36-50% vs. controls: 44%, CI; 36-51%, p=0.33) were not statistically different between groups. However, in an 8-year landmark subgroup analysis, OS was better amongst controls than those with diabetes (diabetes [n=27]: 67%, CI; 48-86% vs. Controls [n=28]: 87%, CI; 73-100%, p=0.047at 10 years). Poor glycemic control (median RBG >180 mg/dL or median HbA1c >7%) was not associated with increased mortality at 5 years but was associated with a trend towards worse freedom from initiating a second-line regimen at 2 years when compared to good glycemic control. In a sub-group analysis based on HR status, there were no differences in OS at 5 years, or freedom from initiating a second-line regimen at 2 years between the two glycemic groups (≤180 mg/dL vs >180 mg/dL on two or more occasions in a month) for any of the HR subgroups.

Conclusions: These data provide some reassurance that hyperglycemia may not be a major contributor to overall mortality in the first 5 years, in most individuals with metastatic breast cancer. However, amongst longer-term survivors, diabetes was associated with worse survival, suggesting that individualized diabetes and glycemic goals should, therefore, be considered in patients with metastatic breast cancer.

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