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Racial Differences in Breast Cancer Therapeutic Toxicity: Implications for Practice

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Abstract

Disparities in treatment intensity can contribute to racial disparities in overall breast cancer survival. A natural extension of measuring racial disparities in treatment intensity is consideration of the distribution of treatment toxicities, symptoms, and distress that lead to chemotherapy dose reductions, holds or early termination. There is growing evidence that therapeutic toxicity during early-stage breast cancer treatment may be greater among Black women than White. Important components of symptom management involve the communication of symptoms, the self-care abilities of the patient, the patient's perception of the clinical encounter, and the patient centeredness of the clinical encounter. Racial differences in the symptom reporting, the clinical "reception" and response to symptoms, the prescribed management, and the patient adherence to symptom management requires further investigation. Further research must also consider the structural inequities, as well as institutional and interpersonal racism that contribute to racial differences in cancer symptom burden leading to potential decreases in dose intensity of potentially life-saving early cancer treatment.

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Even after controlling for stage, comorbidity, age, and insurance status, Black women with breast cancer in the United States have the lowest 5-year survival as compared with all other races for stage-matched disease (1). A possible explanatory piece of the breast cancer disparity puzzle is disparity in treatment intensity, or the relative dose intensity (RDI) of early-stage breast cancer (ESBC) chemotherapy. RDI is defined as the ratio of actual to expected dose intensity per standard regimen and considers dose administered, number of cycles delivered, and the interval between cycles (2).

When applied to adjuvant chemotherapy for breast cancer, an RDI of < 85% is associated with lower disease-free survival and overall survival (2–3). Racial disparity in the RDI of the prescribed first breast cancer chemotherapy is evident in many population clinical trials (4–5). Weycker and colleagues analyzed RDI for 2,228 women ESBC (stages I–IIIA) from 65 community oncology/hematology clinics in 35 states between 2004 and 2010. Overall

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incidence of dose delays was 31%, dose reductions 24%, and low RDI was evident in 26% of the chemotherapy regimens (6).Racial delineation was not included in the publication.

In our team's study of Black women receiving ESBC chemotherapy (American Cancer Society, RSGT-09–150-CPHPS; The Attitude, Communication and Treatment Intervention to Reduce Breast Cancer Treatment Disparity), we found alterations in RDI at even greater levels. The trial was the test of an educational intervention for Black women (stages I–III) recommended to receive ESBC chemotherapy (7). The intervention utilized a Black breast cancer survivor to explain the chemotherapy rationale in relation to the patient's pathology report, while addressing the patient's concerns and fears. Of the 121 Black women recommended to receive ESBC chemotherapy, 99% began recommended chemotherapy, but 39.7% ($n = 48$) had some reduction in dose intensity (less than prescribed dose), early treatment cessation or delay. Among this study cohort, 33.3% ($n = 41$) did not receive 85% of the prescribed chemotherapy by the recommended midpoint and 39.7% ($n = 48$) by the prescribed endpoint (7).

Not all analysis of racial differences in breast cancer found differences in overall dosing. A systematic search of 12 published articles (1987 through June 2017) within four databases of U.S.-based treatment, examined the influence of race on chemotherapy delays, cessation, or dose reductions among women with ESBC (8). Black patients were significantly more likely than Whites to have delays to initiation of adjuvant therapy of 90 days or more, and were significantly more likely to discontinue ESBC chemotherapy. However, this analysis did not find a significant association between race and chemotherapy dosing when larger numbers of patients with more advanced (stage III) breast cancer were included. Limitations that precluded possibly finding the relationship between race and chemotherapy dosing for all patients were the inconsistent definitions of dose reductions among the 12 articles (8).

A possible explanation for racial dosing disparity is disparity in treatment toxicity, prompting the clinical need to adjust chemotherapy doses through dose reductions, holds or early termination. There is growing evidence that toxicity during ESBC treatment is greater among Black women than White. Our team, and others, have challenged the notion that dosing disparity in ESBC treatment is patient driven. There are dosing alteration decisions in response to patient's specific symptoms and/or overall distress made by the clinical staff. These dosing alterations then lead to racial differences in RDI of ESBC chemotherapy.

In this related research article, Hu and colleagues explored toxicity during ESBC chemotherapy through a descriptive study, following a cohort of Black and White women diagnosed with stage I–III, hormone receptor–positive breast cancer from a large cancer center in 2007–2015, reporting symptoms among this cohort at baseline, during and after chemotherapy. They found racial disparity primarily focused on physical symptoms.

Among 1,273 patients, they found Black women ($n = 405$) were more likely to report one-SD increase in general physical symptoms (55.6% vs. 48.2%, $P = 0.015$), treatment side effects (74.0% vs. 63.4%, $P < 0.001$), and acute distress (27.4% vs. 20.0%, $P = 0.015$) than White women. Interestingly, among this cohort, Black and White patients did not have differences in scores at baseline but over time, when comparing symptom changes from

baseline, 55.6% of Black women reported a one-SD increase compared with 48.2% of White women ($P = 0.015$; ref. 9).

A study led by Madison and colleagues, following a cohort of 195 women ($n = 163$ White, $n = 32$ Black) from shortly after breast cancer diagnosis to 6 and 18 month survival reported more emotional distress among Black than White women as they advanced through early stage breast cancer treatment. Additionally, the symptoms did not abate as readily for Black women as compared to White. Black women experienced greater cancer-related distress ($P = 0.004$), intrusive thoughts about cancer diagnosis and treatment ($P = 0.002$), perceived stress ($P = 0.04$), and emotional fatigue ($P = 0.01$). In fact, White women reported an increase in distress-related symptoms from diagnosis to 6 months post treatment with stability through the remaining post treatment period, while Black women had persistently elevated distress even 18 months into survivorship (10).

Racial differences in the symptom management experience were explored through both the Cancer Health Accountability for Managing Pain and Symptoms (CHAMPS) study (11) and the Breast Cancer Treatment Symptom Experience, Management and Outcomes According to Race (SEMOARS) study (12). The CHAMPS study explored symptom management through focus groups ($n = 3$ Black and $n = 3$ White). Both Black and White racial groups felt that symptom management could be improved. In the CHAMPS focus groups, White survivors were not satisfied with symptom information and did not feel enough reassurance was offered, while Black patients felt that symptoms were not well addressed proactively, nor managed without the patient needing to advocate for themselves. Our current study, (1R01MD012245) The Breast Cancer Treatment SEMOARS study is exploring the chemotherapy symptom experience, management, and dose intensity received/prescribed according to race during ESBC (12). The SEMORS study utilizes close symptom monitoring, before and after each chemotherapy cycle, and audio recordings of clinical encounters prior to each chemotherapy visit. The study, which just completed data collection, includes an in-depth assessment of patients as they begin, and matriculate through chemotherapy, fully documenting the symptom experience, reporting, and management that is inherent in the chemotherapy experience. An important component of this study is to correlate the symptom experiences with dose modifications. This correlation increases the significance of the racial differences in the ESBC chemotherapy symptom experience to include not only racial differences in patient distress, but also differences in the dose intensity of the early-stage chemotherapy received.

In essence, although there are some conflicting reports, racial disparity in the symptom experience during ESBC chemotherapy is established, as is racial disparity in chemotherapy dose intensity. The missing piece in the knowledge is our complete understanding of the relationship between the treatment toxicity and subsequent dosing modifications leading to less than-optimal RDI during ESBC chemotherapy and how that differs by race. Important components of symptom management involve the communication of symptoms, the self-care abilities of the patient, the patient's perception of the clinical encounter, and the patient centeredness of the clinical encounter. Racial differences in the symptom reporting, the clinical "reception" and response to symptoms, the prescribed management, and the patient adherence to symptom management requires further investigation. The lifetime experience

of Black patients living with structural and institutional racism must also be considered as contributing factors to symptom inequity (13).

Ensuring full RDI in ESBC is quality care (14). Research moving forward must provide not only descriptive racial comparisons of symptoms and dose alterations during ESBC chemotherapy, but also identify the exact interventional targets to proactively assess provide appropriate mitigation. Optimal and equitable ESBC chemotherapy without undue patient symptoms or distress is the goal.

Authors' Disclosures

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