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# Race is associated with completion of neoadjuvant chemotherapy for breast cancer☆

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ABSTRACT

*Background:* Completion of prescribed neoadjuvant chemotherapy for breast cancer is paramount to patients obtaining full benefit from the treatment; however, factors affecting neoadjuvant chemotherapy completion are not known. We hypothesized that race is a predictor of completion of neoadjuvant chemotherapy in patients with breast cancer.

*Methods:* All patients with breast cancer treated with neoadjuvant chemotherapy 2009–2016 at a single institution were stratified by completion of neoadjuvant chemotherapy and by race. Univariate analysis and multivariable logistic regression were used to identify patient and tumor characteristics that affected the rate of neoadjuvant chemotherapy completion.

*Results:* A total of 92 (74%) of 124 patients completed their prescribed neoadjuvant chemotherapy. On univariate analysis, white patients were more likely to complete neoadjuvant chemotherapy than non-white patients (76% vs 50%, $P = .006$). Non-white patients were more likely to have government insurance and larger prechemotherapy tumors (both, $P < .05$), but these factors were not associated with rates of neoadjuvant chemotherapy completion. After controlling for age, insurance status, tumor size, and estrogen receptor status, whites remained associated with completion of neoadjuvant chemotherapy (OR 3.65, $P = .014$).

*Conclusion:* At our institution, white patients with breast cancer were more likely than non-white patients to complete neoadjuvant chemotherapy. Further investigation into the underlying factors impacting this disparity is needed.



## Introduction

Breast cancer is the most common cancer in women, representing 30% of all female cancers and leading to more than 40,000 deaths per year in the United States.[1] In select breast cancer patients, the survival benefit of chemotherapy is well established. Multiple studies have shown equivalent survival among patients who receive neoadjuvant or adjuvant chemotherapy.[2] Many patients with large primary tumors or locally advanced breast cancer are treated with neoadjuvant chemotherapy (NACT), which has the potential benefit of downstaging the tumor, allowing for a less extensive operation. The use of NACT also allows for early assessment of the efficacy of systemic therapy and in some cases can lead to a pathologic complete response (pCR) in which no residual tumor is found in the resection specimen. Pathologic complete response acts as a surrogate for risk of recurrence and overall survival, particularly in estrogen receptor (ER)- negative and human epidermal growth factor receptor 2 (HER2)-positive breast cancers.[3,4]

Racial disparities in outcomes for multiple malignancies including breast cancer have been described extensively, with worse survival for non-white patients compared with white patients.[5–9] The racial differences observed in outcomes of breast cancer have been attributed to many factors, including different tumor biology, less frequent screening, less aggressive treatment, and failure to seek medical care and follow-up.[9–11] While NACT leads to improved outcomes for patients with locally advanced breast cancer, the factors that affect whether patients complete their prescribed NACT regimens are not known. The objective of this study was to assess the impact of race on completion of NACT at our institution. Given the benefits of NACT and the known racial disparities in outcomes, we hypothesized that race would be a predictor of completion of NACT in patients with breast cancer.

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## Methods

### *Patient population*

All patients with breast cancer who were treated with NACT at the University of Virginia Health System (Charlottesville) from January 1, 2009, through December 31, 2016, were identified using an institutional clinical data repository (CDR). The CDR contains patient demographics, including age, body mass index, sex, race, insurance, medical comorbidities, tobacco use, and genetic mutations. Using CDR data, patient race was categorized as white or non-white (which included black, Hispanic, Asian, and other). Insurance status was defined as private, government (Medicaid, Medicare), or no insurance. Tumor characteristics (stage, size, pathology, hormone receptor status, HER2 status, and multifocality), type of operation, and details concerning the chemotherapy were abstracted by review of the electronic medical record. The institutional review board at the University of Virginia approved waiver of consent for this study (Protocol #18801).

### *Data analysis*

Univariate analyses were used to compare preoperative factors and postoperative outcomes by both NACT completion status and race. Data were compared using the $\chi^2$ test for categorical variables and appropriate parametric and nonparametric tests for continuous variables. Patients were then divided based on completion of prescribed NACT regimen, and a multivariable logistic regression model was created to identify independent predictors of NACT completion. Dependent variables were chosen a priori based on clinical factors shown previously to affect NACT completion and included at a rate of 1:10 for events in the population. A $P$ value $< .05$ was used for statistical significance. SAS version 9.4 (SAS Institute, Inc, Cary, NC) was used for all analyses.

## Results

A total of 124 patients with breast cancer were treated with NACT throughout the 8-year study period at our institution. A total of 86 patients (69%) in the cohort were white and 38 (31%) were non-white; of the non-white patients, 31 (82%) were black. The differences in patient and tumor characteristics of those who completed NACT versus those who did not complete NACT are listed in Table 1. The differences in patient and patient tumor characteristics of white versus non-white patients are listed in Table 2. Of note, white patients were more likely to have ER-positive tumors than non-white patients (69% vs 45%; $P = .01$). Non-white patients were more likely to have government insurance and larger prechemotherapy tumors (both $P < .05$), but these factors did not affect rates of NACT completion. Overall, 92 patients (74%) completed NACT as prescribed. On univariate analysis, white patients were more likely to complete NACT than non-white patients (76% vs 50%, $P = .006$).

We found no differences in pCR between patients who did and did not complete NACT (32% vs 34%; $P = .77$). We also found no difference in local, regional, or distant recurrence based on completion of NACT ($P = .26$, .76, and .34, respectively). We found no difference in pCR rates between white and non-white patients (37% vs 21%; $P = .08$). Non-white patients were more likely to experience local, regional, and distant recurrences (all, $P < .01$). Outcomes stratified by NACT completion and by race are presented in Tables 3 and 4, respectively.

The most common reason for failure to complete NACT was chemotherapy toxicity, noted in 9 (60%) white patients and 11 (65%) non-white patients. Neurologic side effects were the most common toxicity in non-white patients and occurred in none of the white patients (24% vs 0%; $P = .038$). In white patients, the toxicity was most commonly gastrointestinal. Other factors included cancer progression, patient choice, and psychosocial issues. Reasons for lack of completion of NACT are presented in Table 5. We found no differences in chemotherapy regimens prescribed to white compared with non-white patients, and the majority of both white and non-white patients (64% and 71%, respectively) received Taxotere, Adriamycin, cyclophosphamide (TAC). Table 6 presents details of chemotherapy regimens by race.

A multivariable logistic regression analysis was performed to determine the independent contribution of race on completion of NACT (Table 7). After controlling for age, insurance status, tumor size, and ER status, white race remained associated with completion of NACT (OR 3.65, $P = .014$).

## Discussion

The present study aimed to investigate the effect of race on the completion of the prescribed course of NACT for breast cancer patients at a single academic institution. Through the use of a retrospective chart review, we found that white patients were more likely to complete prescribed NACT as compared with non-white patients; this difference remained after adjusting for insurance status. Although racial disparities in treatment of breast cancer and outcomes have been well documented, most studies examining rates of completion of chemotherapy in breast cancer have been focused on the completion of adjuvant chemotherapy. The racial disparity identified in the present study is consistent with previous findings that non-white patients are less likely to complete adjuvant breast cancer chemotherapy and are more likely to have dose reductions and treatment delays compared with white patients.[12–14]

No clear explanation is currently available for how race affects completion rates of NACT in patients with breast cancer, because prior studies are sparse and have yielded conflicting results.[15,16] Killelea et al[15] conducted a large retrospective study utilizing the National Cancer Data Base and found that NACT was utilized more frequently for black, Hispanic, and Asian women than for white women, but this observation was largely explained by those groups presenting with more advanced primary tumors as well as greater rates of triple-negative and HER2-positive disease. Although this study did report that non-white patients had a longer time from diagnosis to the start of NACT and from the start of NACT until surgery than did white patients, the authors did not examine NACT completion rates by race. In contrast, Andic et al[16] found no difference in the likelihood of completing prescribed NACT or in the timing of therapy completion between races; however, this was a smaller, retrospective review specifically evaluating women with inflammatory breast cancer; whereas the present study included all types of breast cancer.

In our study, it is important to note that the discrepancy in NACT completion among races persisted even after controlling for insurance status, which serves as a proxy for socioeconomic status. We therefore, cannot fully attribute the racial disparity found in this study to affordability of or access to oncologic care. A number of possible explanations exist for this finding, and the roles of social and health system barriers must be considered. Wheeler et al[17] described a variety of underlying factors affecting cancer care quality, including type and volume of the heath system, distance to care, availability of specialists, and provider preferences. Transportation and inability to work while undergoing treatment are some of the known barriers to cancer care. Our institution provides oncologic care to patients from the entire state of Virginia, which can necessitate substantial distances to travel for many patients, and the associated costs may be especially difficult for some patients.

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