American Heart Journal Plus: Cardiology Research and Practice 38 (2024) 100353

Contents lists available at ScienceDirect

American Heart Journal Plus: Cardiology Research and Practice

journal homepage: www.sciencedirect.com/journal/american-heart-journal-plus-cardiology-research-and-practice

Research paper

# Rate of adverse cardiovascular events in breast cancer patients receiving chemotherapy and targeted therapy: Impact of frailty

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ARTICLE INFO

*Keywords:*
Cardio-oncology
Frailty
Cardiotoxicity
Electronic health records

Approximately 80 % of breast cancer cases are diagnosed at or beyond the age of 50 years, from which the risk of chronic illnesses begins to increase [1]. Frailty is an age-related risk factor that has received increasing scientific attention as a potential explanation for adverse health outcomes in older adults [2]. Breast cancer patients often receive adjuvant therapies to enhance the cure rate and minimize recurrences [3]. Nonetheless, these treatments can lead to cardiotoxicity, a serious adverse effect that contributes to mortality among breast cancer survivors [4]. Breast cancer patients with a higher burden of pre-existing frailty who undergo adjuvant therapy may be at higher risk for cardiotoxicity given their poorer prognosis compared to their healthier counterparts. However, there is a lack of studies that examine how frailty impacts cardiotoxicity risk in breast cancer patients, especially studies based on real-world data such as electronic health records (EHRs).

EHR Data from breast cancer patients treated with chemotherapy and targeted therapy between 2012 and 2022 were extracted from the OneFlorida+ Clinical Research Network. We defined cardiotoxicity as cardiovascular events that occurred during adjuvant therapy or within 90 days after the last dose of adjuvant therapy. Frailty was measured using EHRs frailty index (eFI) score based on data from the 12 months before the first chemotherapy or targeted therapy. eFI contains information from 45 items (termed deficits) in EHRs, including 30 diagnoses (e.g., depression), 12 laboratory testing results (e.g., hemoglobin), and 3 vital signs (e.g., underweight). eFI was categorized into no deficits, prefrailty, and frailty [5]. We calculated cardiovascular event rates by eFI and built multivariable Cox proportional hazard models to examine the association of multiple factors with cardiotoxicity.

Of the 11,054 breast cancer patients identified, 10.2 % ($n = 1127$) experienced any cardiovascular events after chemotherapy or targeted therapy. The cardiotoxicity rate in the cohort of no deficits, prefrailty, and frailty cohort were 9.1 %, 12.5 %, and 15.9 %, respectively ($p < 0.001$). In the Cox regression analysis, we found that prefrail (hazard ratio [HR] = 1.2, 95 % confidence interval [CI] = 1.01–1.42; $p = 0.038$) and frail patients (HR = 1.35, CI = 1.01–1.80; $p = 0.044$) were more likely to experience cardiovascular events than no deficits patients, adjusting for age at breast cancer diagnosis, race-ethnicity, insurance coverage, adjuvant treatment type, zip-code level rurality and poverty, history of hypertension and diabetes, and number of inpatient or outpatient visits.

Overall, results from this study showed that the percentage of cardiotoxicity among breast cancer patients receiving chemotherapy or targeted therapy was 10.2 %, which aligns with rates from previous studies [6]. Our analysis revealed that cardiovascular events were more likely to occur in frail cancer patients compared to non-frail cancer patients. The findings suggest that assessing frailty may help identify breast cancer patients who are at a higher risk of cardiotoxicity and may benefit from interventions to mitigate this risk. Further research is needed to better understand the underlying mechanisms linking frailty to cardiotoxicity and to explore potential interventions that may mitigate these risks in breast cancer patients.

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https://doi.org/10.1016/j.ahjo.2023.100353
Received 5 September 2023; Received in revised form 30 November 2023; Accepted 3 December 2023
Available online 7 December 2023

## Ethics statement

No animal of human studies are reported in this publication.

## Funding acknowledgments

This symposium was funded by the University of Florida Cancer Center, the University of Florida College of Pharmacy Department of Pharmacotherapy and Translational Research, and the University of Florida College of Pharmacy Center for Pharmacogenomics and Precision Medicine.

YG is supported by a Scientific Research Grant from the Florida Breast Cancer Foundation and NIH grants 5R01CA246418, 3R01CA246418-02S1, 1R21CA245858-01A1, 3R21CA245858-01A1S1, and 1R21CA253394-01A1.

## CRediT authorship contribution statement

**Shuang Yang:** Data curation, Formal analysis, Investigation, Writing – original draft, Writing – review & editing. **Yi Guo:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Writing – review & editing.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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