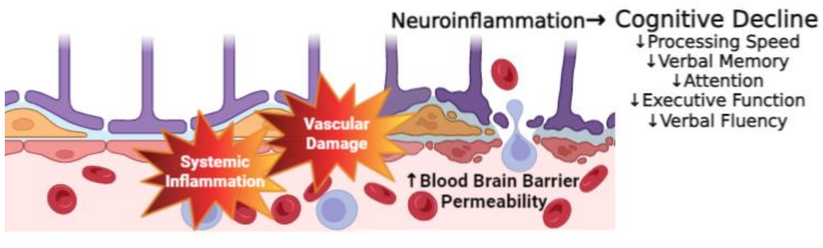
Relationships between Inflammatory Vascular Function Markers and Cognitive Function in Patients with Breast Cancer in a Nationwide Cohort Study

Michelle Janelsins[1], Eva Culakova[1], Zac Werner[1], Mark Gallagher[1], Sara Alberti[1], Emma Bentley[1], Nikesha Gilmore[1], Jeremy McGuire[1], Adedayo Onitilo[2], Steven Corso[3], Jamal Misleh[4], Allison Magnuson[1], Luke Peppone[1], Michael Sohn[1]
[1]University of Rochester, Wilmot Cancer Institute, Rochester, NY, [2]Wiscnoncin NCORP, Wisconsin, MN, [3]Upstate Carolina Consortium Community Oncology Research Program, Greer, SC, [4]Delaware/Christiana Care NCORP, Newark, DE

Background

- CRCI is an important clinical problem encompassing difficulties in attention, memory, and executive function
- Interventions for CRCI during chemotherapy have not been established
- Inflammation is associated with CRCI [1,2]
- We hypothesized that indicators of vascular damage are associated with CRCI

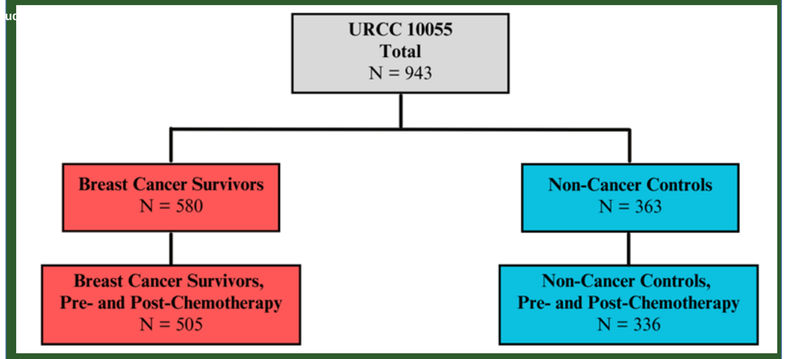


The goal of our study is to assess how vascular biomarkers change with chemotherapy in patients with breast cancer compared to a control group of those without cancer, and relationships with cognitive function.

Methods

- Participants were recruited through NCI Community Oncology Research Program (NCORP) sites nationwide in collaboration with the URCC NCORP Research Base.
- Serum levels of d-dimer, soluble(s) ICAM-1, sP-Selectin, sVCAM-1, and SAA were assessed in 2 groups: 526 females with breast cancer before (T1; mean age = 53.4) and after chemotherapy (T2) and 340 females without cancer (controls; mean age= 52.8) at equivalent times.
- To assess changes over time in markers in patients and controls, linear mixed effects models with group, time and group x time interaction as fixed effects, participants as random factor, and age and race as covariates were used.
- Repeated measures correlation assessed each biomarker and each cognitive test (verbal memory (e.g., word recall, COWA) and working memory (e.g., Digits Backward)) at all timepoints.
- Regression analysis including all markers and the same adjusting covariates was also used to assess predictors of each T2 cognitive score, and also changes in cognitive scores from T1 to T2. Statistical tests were conducted at α=0.05.

Results



Study Demographics

Characteristic	Chemo N=580[1]	Control N=363[1]	p-value[2]
Age	53 (11)	53 (10)	0.3
Race			0.016
Black	47 (8.1%)	16 (4.4%)	
Other	16 (2.8%)	4 (1.1%)	
White	517 (89%)	343 (94%)	
Education			<0.001
<High School	11 (1.9%)	0	
High School/GED	131 (23%)	43 (12%)	
College	438 (76%)	320 (88%)	

[1]Mean (SD); n (%)
[2]Welch Two Sample t-test; Fisher's exact test

Table 1: Study Demographics

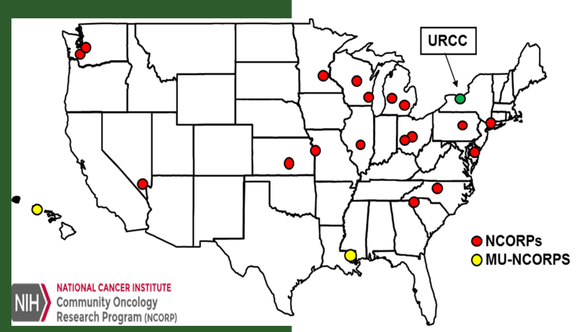


Figure 2: Participating NCORP Locations
M/U=minority/underserved

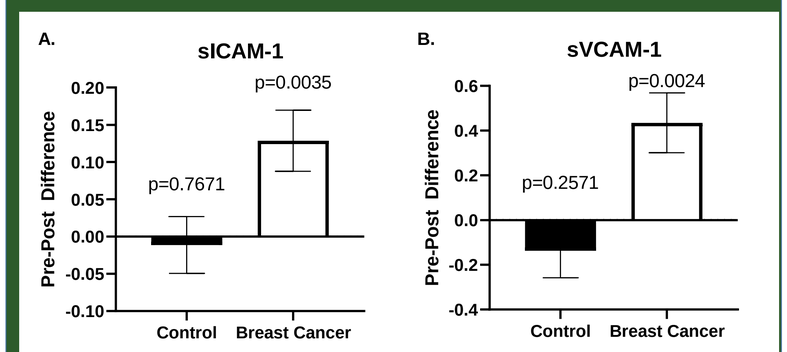


Figure 3: Change in serum expression of A) sICAM-1 and B_ sVCAM-1 from pre- to post-chemotherapy.

Results

Repeated Measures Correlation (Covariates: Age, Race, Group)

Cognitive Test	Biomarker	Correlation Coefficient	Lower limit of 95% CI	Upper limit of 95* CI
Verbal Recall	D-Dimer	-0.082	-0.123	-0.035
Verbal Recall	ICAM-1	-0.045	-0.081	-0.006
COWA	ICAM-1	-0.065	-0.094	-0.034
COWA	SAA	-0.084	-0.145	-0.026
Digits Backwards	D-Dimer	-0.076	-0.129	-0.022

Table 2: Relationship between biomarkers and cognitive measures (significant results from the multilevel models listed).

COWA

	Estimate	SE	p value
(Intercept)	2.086	0.515	0.00006***
Group-Chemo	-0.811	0.198	0.00004***
D-Dimer	0.002	0.002	0.088
ICAM-1	-0.032	0.017	0.045*
PSel	-0.003	0.029	0.882
VCAM-1	0.033	0.039	0.608
SAA	-0.0005	0.0007	0.168
Age	-0.023	0.009	0.001**
Race-Black	-0.387	0.47	0.41
Race-Other	0.671	0.721	0.352

Phone: Digits Backwards

	Estimate	SE	p value
(Intercept)	0.58	0.282	0.040*
Group-Chemo	-0.288	0.109	0.008**
D-Dimer	-0.0006	0.0008	0.488
ICAM-1	-0.021	0.01	0.026*
PSel	0.01	0.016	0.528
VCAM-1	0.027	0.021	0.211
SAA	-0.0004	0.0004	0.223
Age	-0.006	0.005	0.244
Race-Black	-0.237	0.258	0.358
Race-Other	-0.297	0.395	0.452

Table 3: Regression models for change in cognitive test scores (COWA, Digits Backward). Abbreviations: ICAM-1 (Intercellular Adhesion Molecule 1); PSel (P-selectin); VCAM-1 (Vascular Cell Adhesion Molecule 1); SAA (Serum Amyloid A).

Conclusions

- Chemotherapy increased vascular markers associated with inflammation.
- These biomarkers were weakly but significantly associated with worsening cognitive function.

References: [1]Belcher *et.al.*, JNCI 2022. [2]Janelsins *et. al.,* J Neuroimmunology 2022
Funding: R01CA231014, T32CA102618, UG1CA18996
Twitter: @MJanelsins, Department of Surgery, Division of Supportive Care in Cancer