Association Between Cumulative Symptom Burden and Cognitive Difficulties Among Breast Cancer Survivors: A Cross-Sectional Study

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Background

- Cancer related cognitive dysfunction (CRCD) is a very common and distressing symptom among breast cancer survivors.
- Addressing CRCD requires recognizing its complex and multifaceted nature, with a focus on its comorbid symptoms.
- Most current studies conducted in general breast cancer survivors. Patients seeking care for CRCD remain understudied, highlighting the need to identify symptom profiles to inform targeted and effective interventions.

Aim

- To evaluate the prevalence of comorbid symptoms and their impact on subjective and objective CRCD among breast cancer survivors with self-reported insomnia and CRCD

Methods and Materials

- Baseline data from a 3-arm parallel randomized controlled trial ENHANCE (ClinicalTrials.gov identifier NCT04837820). It compares acupuncture against sham acupuncture and usual care among breast cancer survivors with insomnia-related moderate to severe CRCD. The Institutional Review Board at Memorial Sloan Kettering Cancer Center approved this trial.

Outcomes:

- **Patient-Reported Subjective Cognitive Difficulties**: Perceived cognitive impairment (PCI) subscale from the Functional Assessment of Cancer Therapy–Cognitive Function (FACT-Cog), version 3.
- **Standardized Objective Cognitive Performance:** The Hopkins Verbal Learning Test – Revised (HVLT-R) "Delayed Recall" score (<40: objective CRCD)

Covariates:

- **Comorbid Symptoms:** Insomnia – Insomnia Severity Index; Fatigue – Brief Fatigue Inventory Worst Fatigue; Pain: Patient-Reported Outcomes Measurement Information System – Global Health, Pain Item; Anxiety – Hospital Anxiety and Depression Scale – Anxiety; Depression – Hospital Anxiety and Depression Scale – Depression.
- **Cumulative Symptom Burden** – Cumulative Symptoms Score (CSS): Based on the severity of comorbid symptoms: 0 = no or mild, 1 = moderate, and 2 = severe. Total score, higher scores indicating a greater symptom burden.

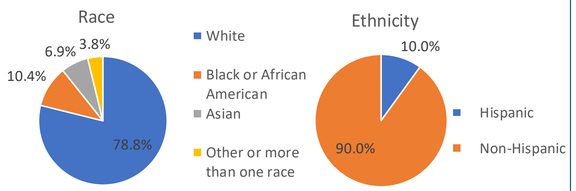
Statistical Analysis:

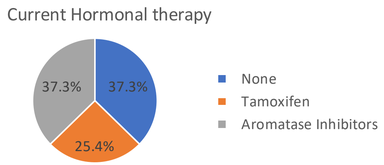
- Pearson correlations: Examine the relationship between each comorbid symptom and cognition.
- Linear regression models: Evaluate the association between CSS and both subjective and objective CRCD.

Results

Participant Characteristics (N=260):

- Age, mean (SD), years: 56.6 (10.4)
- Education at least a college education: N=195, 77.0%
- Previous chemotherapy: 139 (53.5%)
- Year since cancer diagnosis, mean (SD): 4.7 (2.8)

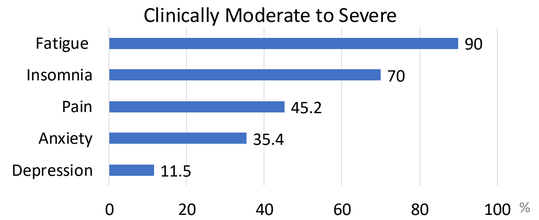




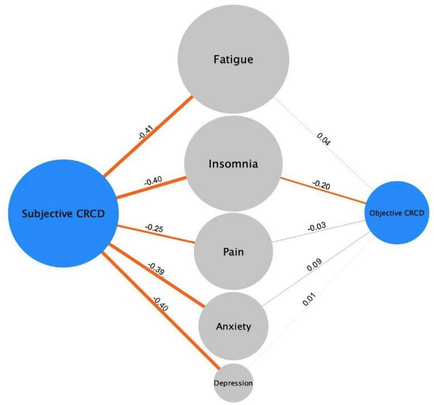
Subjective and Objective CRCD

There was no significant difference in FACT-Cog PCI scores between participants with objective CRCD (PCI = 36.2, SD = 13.1) and those without (PCI = 35.8, SD = 15.5) (p = 0.84).

Prevalence of Comorbid Symptoms



Correlation Between Comorbid Symptoms and Both Subjective and Objective CRCD



Size of the circles: the prevalence of each symptom. Thickness of the lines: the strength of the correlation between symptoms.

Cumulative Symptom Burden (CSS) and Its Association with Subjective and Objective CRCD

Subjective CRCD

Univariable linear regression analysis revealed a statistically significant association between CSS and FACT-Cog PCI (Coef. = -3.3, 95% CI = -3.9 to -2.7, p < 0.001).

Multivariate Logistic Regression: CSS Associated with FACT-Cog PCI, Adjusting Age and Chemotherapy

	Coefficient	95% CI	P-value
(Constant)	37.9	28.8-46.9	-
CSS	-3.0	-3.6- -2.4	<0.001
Age	0.2	0.1-0.4	0.001
Chemotherapy			
No	-		
Yes	-2.5	-5.4-0.4	0.097

Objective CRCD

Linear regression showed that the CSS score was not significantly associated with the HVLT-R delayed T-score (Coef. = -0.2, 95% CI = -0.9 to 0.5, p = 0.58), even after adjusting potential covariables (Coef. = -0.2, 95% CI: -0.9 to 0.5, p = 0.64).

Main Limitations

- Study population included individuals with insomnia and CRCD, so findings may differ from those with CRCD alone.
- Most participants had a college-level education or higher.
- We included only the HVLT-R as a measure of objective cognitive function.
- This study was conducted at a large, urban academic cancer center.

Conclusions

Cumulative symptom burden was associated with subjective but not objective CRCD. Comprehensive symptom management has the potential to improve subjective appraisal of CRCD. Sleep disturbance may be a therapeutic target for improving objective outcomes.

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