Biomarker Associations with Cognitive Impairment Following Chemotherapy in Older Cancer Patients: A Systematic Review

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Introduction

Background

- Chemotherapy-related cognitive impairment (CRCI) commonly affects memory, attention, and executive function, with older cancer patients being especially vulnerable due to age-related brain changes and reduced cognitive reserve. It can lead to poor treatment adherence, reduced quality of life, and increased dependence.
- Biomarkers help assess cognitive risk and guide personalized interventions, making them essential for improving care and outcomes in older adults.

Purpose

- To identify biomarkers that are associated with cognitive impairment in older adults with cancer to enhance nursing interventions and patient outcomes.

Methods

Design

- This systematic review was consistent with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guideline (PRISMA)

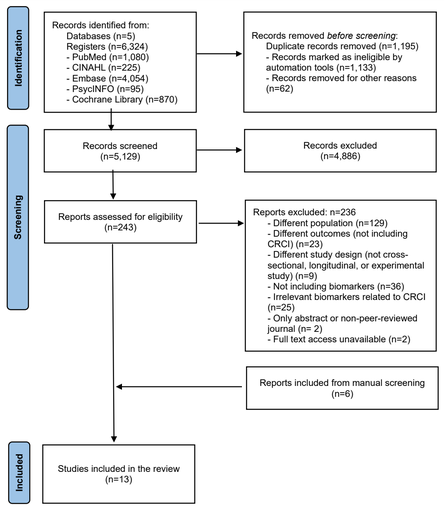

Figure 1. PRISMA Flow diagram. *CINAHL Cumulative Index of Nursing and Allied Health, CRCI chemotherapy-related cognitive impairment.*

Inclusion criteria

Table 1. Inclusion criteria

Population	Older patients (over 60 years) with cancer
Intervention	N/A
Comparisons	N/A
Outcomes	Cancer-related cognitive impairment and its biomarkers
Study design	Experimental studies (randomized controlled trials, quasi-experimental studies), cross-sectional studies, longitudinal studies

Result

Characteristics of included studies

Table 2. Description of the included studies (n=13)

Author (year)	Country	Aim of the study	Study design (statistical methods)	Applicable participants (age [yr], n)	CRCI measures	Biomarkers	Outcomes associated with biomarkers: CRCI variables	Outcomes associated with biomarkers: Other dependent variables
Carlson et al. (2018)	US	To explore preliminary associations between serum markers of vascular aging and changes in cerebral blood flow with persistent cognitive symptoms in breast cancer survivors after CTx	Cross-sectional study (correlation, independent t-test)	Post-menopausal breast cancer survivors after 12–18 months of CTx (64.4±12.3, n=15)	- Objective Data: Severity of cognitive symptoms (MoCA)	<Blood> - IL-6, TNF-α, CRP, IGF-1 <Brain> - $rcSO_2$	- Severity of cognitive symptoms: IL-6 (–), TNF-α (–), CRP (–), low IGF-1 (+), laterality in $rcSO_2$ (+)	N/A
Chen et al. (2018)	US	To investigate the association between changes in brain volume and cognitive function in older breast cancer women after CTx	Longitudinal study (unconditional logistic regression; Fisher exact test)	Older women (over 60 years) with stage I–III breast cancer (67.0±5.39, n=16)*	- Objective Data: Neuropsychological score (NIH Toolbox Cognition Battery)	<Brain> - Brain volume (MRI scans)	- Oral reading recognition: Temporal (+), frontal (–), parietal (–), occipital (–) lobe volume	N/A
Chen et al. (2018)	US	To track changes in gray matter density using brain MRI scans in older patients with cancer undergoing CTx	Longitudinal study (repeated measures two-way ANOVA; voxel-wise regression analysis)	Older women (over 60 years) with stage I–III breast cancer (67.0±5.39, n=16)*	- Objective Data: Neuropsychological score (NIH Toolbox Cognition Battery)	<Brain> - Gray matter density (MRI scans)	- List sorting working memory: Gray matter density in left insula (–)	N/A
Chen et al. (2019)	US	To identify the associations between brain MRI parameters and cognitive function in older women with breast cancer undergoing adjuvant CTx	Longitudinal study (repeated measures two-way ANOVA; voxel-wise regression analysis)	Older women (over 60 years) with stage I–III breast cancer (67.0±5.39, n=16)*	- Objective Data: Neuropsychological score (NIH Toolbox Cognition Battery)	<Brain> - Brain activity: ALFF, fALFF, ReHo (MRI scans)	- Pattern comparison processing speed: ALFF (–), fALFF (–), ReHo (–)	N/A
Chen et al. (2020)	US	To detect alterations in white matter microstructure in older breast cancer patients receiving CTx	Longitudinal study (linear mixed models; voxel-wise & ROI-based analysis; Pearson correlation)	Older women (over 60 years) with stage I–III breast cancer (CTx group mean 66.6± 5.24, n=19)	- Objective Data: NIH Toolbox Cognition Battery	<Brain> - DTI metrics: FA, MD, RD, AD (MRI scans)	- Neuro-psychological function: FA(-), MD(-), RD(-), AD(-)	N/A
Chen et al. (2022)	US	To assess DMN connectivity alterations and their association with episodic memory in older breast cancer patients undergoing CTx	Longitudinal study (paired & two-sample t-tests; FDR correction; functional connectivity analysis; graph theory; correlation analysis)	Older women (over 60 years) with stage I–III breast cancer (CTx group mean 66.6± 5.24, n=19)	- Objective Data: NIH Toolbox Picture Sequence Memory	<Brain> - DMN, FNC (functional MRI scans)	- Episodic memory: DMN(-), FNC (+), ΔFNC(-)	N/A
Daniel et al. (2023)	US	To longitudinally assess brain cortical thickness in older survivors of breast cancer	Longitudinal study (linear mixed modeling; independent t-test; paired t-test; linear regression analysis)	Older breast cancer survivors who received CTx (73.5±5.06, n=20)†	- Objective Data: Neuropsychological score (NIH Toolbox Cognition Battery)	<Brain> - Cortical thickness (MRI scans)	- Neuro-psychological function: Cortical thinning (–)	N/A
Liu et al. (2022)	China	To identify the topological properties of the brain white matter network in patients with NSCLC before CTx	Cross-sectional study (independent t-test; false discovery rate)	People with NSCLC (60.08±4.15, n=24)‡	- Subjective Data: Memory, distractibility, blunders, names, total cognition (self-reported Cognitive Failure Questionnaire)	<Brain> - Brain activity: frontal, temporal, parietal, occipital, subcortical (functional MRI scans)	- Memory: lFGtriang.L region (+) - Blunders: ORBinf.L region (+), PUT.R region (+) - Total cognition: ORBinf.L region (+)	- Anxiety : ORBinf.L (+), ORBmid.L (+)
Loh et al. (2020)	US	To investigate changes in inflammatory biomark0ers during induction therapy for older adults with AML, and their associations with geriatric assessment and outcomes	Prospective observational study (paired t-test, Spearman correlation, Kaplan-Meier, Wilcoxon test)	Older adults over 60 years with newly diagnosed AML receiving induction chemotherapy (median 68.3, n=20)	- Objective Data: Physical function (SPPB), Cognition (3MS), Depression (CES-D), distress, ADL/IADL	<Blood> - IL-6, IL-6 sR, TNF-α, TNF-α sR1, IL-3, CRP	- Cognition: ΔIL-6 (-), ΔIL-6 sR(-), Δ TNF-α (-), ΔTNF-α sR1(-), ΔIL-3(-), ΔCRP(-)	- Physical function, depression, ADL : ΔIL-6(-), ΔIL-6 sR(-), Δ TNF-α (-), ΔTNF-αsR1(-), ΔIL-3(-), ΔCRP(-) - IADL: only ΔTNF-α sR1(+)
Koleck et al. (2017)	US	To explore associations between PTFs and variability in pre-adjuvant therapy cognitive performance in postmenopausal women newly diagnosed with breast cancer	Cross-sectional study (Wilcoxon-Mann-Whitney test; Multiple linear regression analysis; Cook's distance)	Postmenopausal women with stage I–III hormone-positive breast cancer starting anastrozole, possibly with CTx (61.05±5.98, n=329)	- Objective Data: Attention, concentration, executive function, mental flexibility, psychomotor speed, verbal memory, visual memory, visual working memory (cognitive function composite)	<Pathologic> - HER2 receptor, Estrogen receptor (ER), Progesterone receptor (PR), Oncotype DX® Breast Cancer Assay Recurrence Score®, Ki67 index	- Concentration: Ki67 (+) - Metal flexibility: Oncotype DX® Breast Cancer Assay Recurrence Score® (+) - Verbal memory: HER2 positive (+), PR (+) - Visual memory: HER2 positive (+) - Visual working memory: HER2 positive (+)	N/A
Mancuso et al. (2006)	Italy	To examine the relationship between Hgb levels and comprehensive geriatric assessment outcomes, including cognitive function, in older patients with lung cancer undergoing CTx	Longitudinal study (Spearman's rank-order [non-parametric] coefficient r)	Older lung cancer patients, aged 70 years and above and undergoing CTx (76.6±4.8, n=42)	- Objective Data: Cognitive function (MMSE)	<Blood> - Hgb	- Cognitive function: Hgb (+)	- QoL/fatigue, functional status, depression : Hgb (+) - Cumulative illness, required daily activities: Hgb (–)
Massa et al. (2006)	Italy	To investigate how increases in Hgb levels, following rHuEPO treatment, affect cognitive and functional outcomes in older patients with cancer receiving CTx	Experimental study (Student t-test)	Older patients aged 65 years and older who were receiving chemotherapy and had moderate anemia (71.4 [68–75], n=10)	- Objective Data: Cognitive function (MMSE)	<Blood> - Hgb	- Cognitive function: Hgb (+)	- Comprehensive geriatric health function: Hgb (-)
Zimmer et al. (2015)	Ger-many	To determine the influence of chemo-immunotherapy patients' cognitive function and on possible (neuro-) physiological factors	Cross-sectional study (independent t-test; Mann-Whitney U test; Spearman correlation test; ANOVA)	People with B-cell non-Hodgkin lymphoma (63±12.8, n=30: BR+R-CHOP group)§	- Objective Data: Correct responses, incorrect/omitted responses (Wiener test) - Subjective Data: Subjective perception of cognition (EORTC-QLQ-C30)	<Blood> - IL-6, BDNF <Brain> - iAPF (EEG recordings)	- Correct responses: IL-6 (–), BDNF (+); iAFE central region (+, only BR group) - Incorrect responses: iAFE central region (+, only BR group), iAFE frontal region (+, only R-CHOP group) - Omitted responses: iAPF parietal region (+) - Subjective perception of cognition: iAPF frontal region (+, only BR group)	- Subjective fatigue : IL-6 (+), BDNF (–) - Emotional functioning : IL-6 (–), iAPF frontal region (+)

Measurement of CRCI

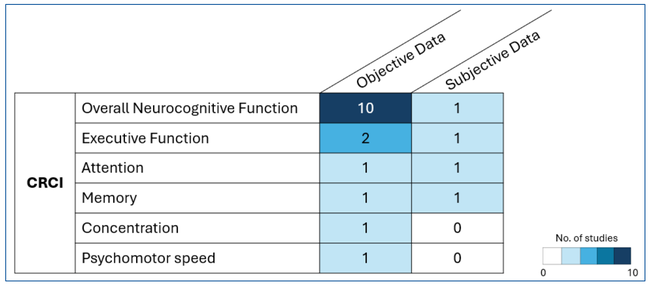

Figure 2. Number of studies assessing the Chemotherapy-Related Cognitive Impairment domain

Biomarkers related to CRCI

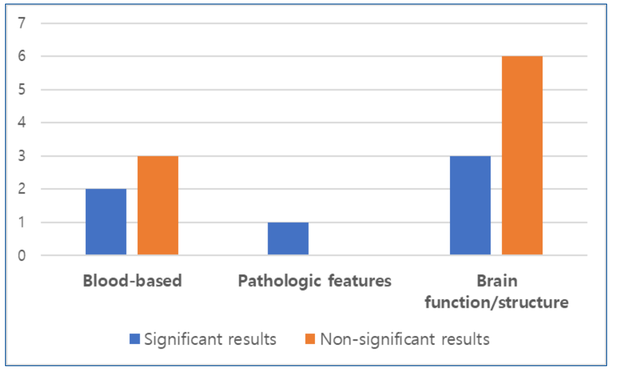

Figure 3. Association between biomarkers and the Chemotherapy-Related Cognitive Impairment domain

Conclusions

- This study provides critical insights into the manifestation of CRCI in older adults undergoing cancer treatment, highlighting specific biological pathways that may be amenable to intervention.
- Biomarkers derived from blood, pathological features, and brain structure and function illustrate the complex interplay between systemic biological processes and cognitive outcomes.
- These findings underscore the potential of biomarker-informed, targeted, and personalized approaches for the management and prevention of CRCI in geriatric oncology populations.

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References