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Chemotherapy-related cognitive impairment in older patients with cancer



Kah Poh Loh^{a,*}, Michelle C. Janelins^a, Supriya G. Mohile^a, Holly M. Holmes^b, Tina Hsu^f, Sharon K. Inouye^{d,e}, Meghan S. Karuturi^f, Gretchen G. Kimmick^g, Stuart M. Lichtman^h, Allison Magnuson^a, Mary I. Whitehead, Melisa L. Wong^j, Tim A. Ahles^h

^aJames P Wilmot Cancer Institute, University of Rochester, United States

^bUniversity of Texas Health Science Center at Houston, United States

^cThe Ottawa Hospital Cancer Centre, Canada

^dHarvard Medical School, Beth Israel Deaconess Medical Center, United States

^eHebrew Senior Life, United States

^fUniversity of Texas MD Anderson Cancer Center, United States

^gDuke University Medical Center, United States

^hMemorial Sloan Kettering Cancer Center, United States

ⁱHelen Diller Family Comprehensive Cancer Center, University of California, San Francisco, United States

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ABSTRACT

Chemotherapy-related cognitive impairment (CRCI) can occur during or after chemotherapy and represents a concern for many patients with cancer. Among older patients with cancer, in whom there is little clinical trial evidence examining side effects like CRCI, many unanswered questions remain regarding risk for and resulting adverse outcomes from CRCI. Given the rising incidence of cancer with age, CRCI is of particular concern for older patients with cancer who receive treatment. Therefore, research related to CRCI in older patients with cancers is a high priority. In this manuscript, we discuss current gaps in research highlighting the lack of clinical studies of CRCI in older adults, the complex mechanisms of CRCI, and the challenges in measuring cognitive impairment in older patients with cancer. Although we focus on CRCI, we also discuss cognitive impairment related to cancer itself and other treatment modalities. We highlight several research priorities to improve the study of CRCI in older patients with cancer.

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* Corresponding author at: James P. Wilmot Cancer Center, 601 Elmwood Avenue, Box 704, Rochester, NY 14642, United States. Tel.: +1 413 306 9767.

E-mail address: kahpoh_loh@urmc.rochester.edu (K.P. Loh).

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1. Introduction

Evidence suggests that cancer treatments can cause cognitive impairment that is subjectively reported or objectively measured using neuropsychological tests.^{1–4} Patients with cognitive impairment may encounter challenges in daily functioning, decision-making and treatment adherence, leading to decreased quality of life and possibly shorter survival.^{5–7} Cognitive impairment can also increase caregiver burden. Prevention of cognitive impairment in patients with cancer undergoing treatment is therefore especially important in older patients, given the increasing long-term survival with new treatments and the increasing numbers of older patients living with cancer as a chronic condition.

Cross-sectional and longitudinal studies often do not include enough older patients with cancer to evaluate the interactions that exist among cancer, its treatment, aging and effects on cognition. Assessing cognitive impairment is challenging in the clinical trial setting given lack of routine use of standardized, brief and accurate neuropsychological testing. When cognitive impairment is detected in clinical practice, oncologists are often unprepared to manage the abnormal results. Additionally, there is a lack of evidence-based preventive measures or interventions when cognitive impairment is detected in the cancer population. A study suggested that patients were less likely to accept treatments that may worsen their cognition, but it is unclear how the presence of cognitive impairment in a patient with cancer affects oncologists’ decision-making process.⁸ As a result, controversy exists regarding the benefits of screening patients for cognitive impairment in clinical practice. Therefore, the National Cancer Institute (NCI) has designated chemotherapy-related cognitive impairment (CRCI), often called “chemo brain” or “chemo fog,” as a high-priority area of research. In this manuscript, we discuss current gaps in research and highlight research priorities for the study of CRCI in older patients with cancer, with some mention of cognitive impairment related to cancer itself and also to other treatment modalities given that they frequently overlap.

The research gaps and priorities were initially discussed during a National Institute on Aging (NIA)/NCI sponsored U13 conference. The U13 conference provides a forum for a multi-disciplinary team of investigators in geriatrics and oncology to review the present level of evidence in geriatric oncology, identify areas of highest research priority, and develop research approaches to improve clinical care for older adults with cancer. The research gaps were then further refined during monthly calls with the expert group over a 4-month period. The expert

group is composed of 6 geriatric oncologists and 2 geriatricians who have expertise in the care of older adults with cognitive impairment and/or have conducted research in the area, 2 researchers with expertise in cognitive effects of cancer treatments and 1 patient advocate. We performed a literature search on PubMed using the keywords “cognition”, “cancer”, “prevalence” and “chemotherapy”. For research gap 1, relevant studies which described prevalence of CRCI and included older adults with cancer were selected from the search results. For research gap 4, studies evaluating treatment and preventive strategies for CRCI were selected if they were randomized trials or pre- and post-intervention in design (keywords “cognition”, “cancer”, “chemotherapy” and “treatment or prevention”). The studies were presented to the group of experts in cognition who selected the ones to be included in the manuscript. The studies were chosen with the purpose of illustrating research gaps rather than providing a comprehensive review of the literature.

2. Research Gaps

2.1. Gap 1: Very Few Studies Focus Exclusively on the Prevalence of CRCI in Older Adults With Cancer

CRCI has been reported in up to 12–75% of patients with cancer and is associated with cancer type, treatment, duration of follow-up, type of study design and definition of cognitive impairment.^{1,2} Most of these published studies assessed prevalence of CRCI in a heterogeneous group of patients, including both young and old patients, illustrated by first three studies in Table 1.^{9,10,11} However, since the impact of chemotherapy on cognition in older adults with cancer may be more significant given the higher prevalence of pre-existing cognitive impairment in this age group, studies that include older patients exclusively would provide more relevant information. Little is known about how chemotherapy influences the prevalence of cognitive impairment in older patients with cancer.

To date, there are only a few studies that focused on prevalence of CRCI in older patients with cancer (29–51% in Table 1). The limited number of studies may be because researchers are reluctant to study CRCI in older adults due to challenges in study accrual and high dropout rates compared to their younger counterparts.^{12,13} Older adults are also more reluctant to participate in clinical trials due to comorbidities, economic constraints, communication issues such as impaired hearing and eyesight, cultural divisions, language barriers, physical immobility with constraints in transportation and lack of social support.¹⁴

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