

CHEMOTHERAPY INDUCED COGNITIVE IMPAIRMENT

What is Chemotherapy induced Cognitive impairment?

Chemotherapy induced cognitive impairment (CICI) is an adverse effect experienced by some patients during and after chemotherapy treatment for cancer. It is characterized by difficulty with thinking, remembering, concentrating and word retrieval as well as difficulty in efficiently processing information secondary to receiving chemotherapy. It has been defined as “the impairment of patients’ memory, learning, concentration, reasoning, executive function, attention, and visuospatial skills during and after discontinuation of chemotherapy.”¹ CICI is also known as, “chemo fog, chemo brain, chemotherapy-related cognitive impairment or cognitive dysfunction”.² Long and/or short term quality of life (QOL) can be negatively affected by CICI. Study results vary but have shown CICI to affect 16-75% of cancer survivors.¹ CICI is a diagnosable condition that is increasing in prevalence with increased survivorship. Physical Therapy can improve QOL for cancer survivors with CICI.

Risk Factors for CICI¹⁻⁴

- Radiation therapy to the brain
- Higher doses of chemotherapy or radiation
- Multi-agent chemotherapy combined with radiation
- Brain cancer
- Chemotherapy combined with whole-brain radiation
- Chemotherapy given directly to the central nervous system
- Hormone changes or hormone treatments
- Immune related dysfunction
- Genetic predisposition for genes associated with Alzheimer’s Disease
- The cancer itself
- Tiredness (fatigue)
- Sleep problems
- Other illnesses, such as diabetes or high blood pressure
- Drugs such as steroids, anti-nausea, or pain medicines. Drugs used during surgery (anesthesia),
- Depression
- Low blood counts
- Age
- Infection
- Nutritional deficiencies
- Stress, anxiety, worry, or other emotional pressure
- Younger age at time of cancer diagnosis and treatment

Common Symptoms of CICI³

- Forgetting things that are usually easy to recall (memory lapses)

- Trouble concentrating (can't focus, have a short attention span, may "space out")
- Trouble remembering details like names, dates, and sometimes larger events
- Trouble multitasking, like answering the phone while cooking, without losing track of one task (they are less able to do more than one thing at a time)
- Taking longer to finish things (disorganized, slower thinking and processing)
- Trouble remembering common words (unable to find the right words to finish a sentence)

Chemotherapy Medications Commonly Associated with CICI ^{1,5-7}

Cancer survivors on some chemotherapy medications may experience CICI. While this list is not comprehensive, some common medications associated with CICI are adriamycin, cyclophosphamide, methotrexate and 5-Fluorouracil. Cisplatin, BCNU, and cytarabine. These medications carry an increased risk of CICI by damaging neural progenitor cells. Risk escalates with increased dose and length of exposure. Pain medications, sedatives, and anti-nausea medications also increase the risk of CICI.

PT Examination and Assessment of CICI⁸

According to the APTA Guide to Practice – Principles of Physical Therapist Client Management– “Systems Review. After organizing the available history information, the physical therapist begins the hands-on component of the examination. The systems review is a brief or limited examination of (1) the anatomical and physiological status of the cardiovascular/pulmonary, integumentary, musculoskeletal, and neuromuscular systems and (2) the communication ability, affect, cognition, language, and learning style of the individual. The physical therapist especially notes how each of these last 5 components affects the ability to initiate, sustain, and modify purposeful movement for performance of an action, task, or activity that is pertinent to function.

The systems review includes the following:

“.....Cognition is one component of the systems review examination. "For communication ability, affect, cognition, language, and learning style: the assessment of the ability to make needs known, consciousness, orientation (person, place, and time), expected emotional/behavioral responses, and learning preferences (eg, learning barriers, education needs) ...”

Questionnaires and tests are frequently used to assess CICI in patients with a cancer diagnosis. These questionnaires and tests can also be employed to create a baseline measurement to track a patient's experience with CICI. However, a patient's self-report of symptoms are paramount in determining if a patient is experiencing CICI. The table below lists commonly used tools for measurement of cognitive impairment. Some of the

questionnaires and tests have been validated in CICI; others have not been validated in CICI, but provide important information to inform clinical treatment.

Evidence Based Measurement Tools That Are Used for CICI

Title	Description	Reliability and Validity	Validated for use with CICI?
Functional Assessment of Cancer Therapy-Cognition (FACT-COG)	37-item questionnaire; 6 domains: memory, concentration, mental acuity, verbal fluency, functional interference, and multi-tasking ability. Noticeability and “effect of perceived cognitive impairment on QOL,” are two additional subscales. ⁸	Cronbach α = 0.707–0.929), & test–retest reliability was satisfactory for both versions (Intraclass correlation coefficient [ICC] = 0.76 and 0.70, respectively. ⁹	Yes
High Sensitivity Cognitive Screen (HSCS)	25 minute paper/pen test for pts 14-70 years. Assesses verbal memory, language, visual-motor, spatial, attention, concentration, self-regulation & planning. Classifies pts as normal, borderline, mild, moderate, or severe	Test-retest validity (0.78-0.80); inter-rater reliability (0.98). Overall accuracy-compared to comprehensive neuropsychological testing is 93% & Pearson product - moment correlation coefficient (0.71). ⁴	Yes
Mini Mental State Examination (MMSE)	May not detect CICI. (O’Shaughnessy) 11 questions, 5-10 minutes to administer. ⁹	R=0.89; concurrent validity=0.66-0.78. ¹⁰	No
Trail making Test	Results based on time required to connect 25 circles in a specific order. (Should accomplish part A in 90 seconds and part B in 3 minutes. ¹¹	R= 0.72. ⁴	No
Stroop Color Word Test	Pts are asked to look at 3 pages and read words or name ink colors as quickly as possible. Score is calculated from number of items completed on each sheet. ¹²	reliability = 0.75-0.91 ¹³	No
Montreal Cognitive	30 point scale;10 minutes examines visual/spatial abilities,	Test-retest reliability= 0.79-.92 ^{14,15} (nasreddine, gill)	No

Assessment	executive functions, naming, memory, recall, and orientation. ¹²⁻¹⁶	Cronbach's alpha= 0.78-0.83 ^{14,16}	
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PT Interventions for CICI

EXERCISE:

Although exercise for treatment of CICI is a new area of study, Fitzpatrick et al. found that physical activity increased, “cognitive health and quality of life for those on chemotherapy.”¹⁷ Evidence suggests that physical activity can also help patients with cancer combat fatigue,¹⁸⁻²⁰ enhance aspects of mood^{21,22}, and enhance QOL.²⁰ Exercise has also been well established to produce cognitive benefits in children^{23,24}, the elderly^{25,26}, and animal models^{27,28}. The Center for Disease control and Prevention (CDC) and ACS recommend that adults achieve 150 minutes of moderate intensity aerobic exercise per week and muscle strengthening activities on 2 or more days a week targeting all muscle groups.^{29,30} It is important to ensure patients diagnosed with cancer are educated about the benefits, risks, and safety measures involved with exercise. Individual exercise programs should be developed to meet the needs of specific patients diagnosed with cancer.

COGNITIVE STRATEGIES:

1. Recommend the use of memory aids such as a journal, detailed daily planner, smartphone app, or a calendar posted at home for easy visibility to keep track of appointments, schedules, “to do” lists, important dates, websites, phone numbers and addresses.
2. Provide home exercise program or other educational materials in writing and with pictures for ease of understanding and assistance in remembering.
3. Videotape home exercise program for survivors who prefer to use a computer to follow their exercise program.

REFERRAL TO OTHER HEALTHCARE PROFESSIONALS (HCP):

It is important to determine the HCP available in your organization or local community that treat CICI. Neurologists, Psychologists, Neuropsychologists, Occupational Therapists, and Speech Language Pathologists evaluate and treat varying aspects of CICI. However, within each organization referral procedures vary. Often physical therapists will screen survivors for CICI and forward the results to the primary care physician or oncologist, who will then refer the survivor to the appropriate specialist for evaluation and treatment. It is important to communicate with physicians and other HCP in your organization or community to determine the most appropriate and efficient referral source.

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The Chemotherapy Induced Cognitive Impairment Fact Sheet for Health Professionals is a public service from the Oncology Section of the American Physical Therapy Association. It is not intended to be a comprehensive overview of the subject.