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The cognitive processes of cancer patients in advanced stages: Navigating terminal realities

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Abstract

Cognitive impairment in late-stage cancer is an increasingly seen but underappreciated aspect of terminal care. This review integrates recent findings on the multifactorial etiology and expression of cognitive impairment in terminally ill cancer patients, considering data from neuroimaging, psychopharmacology, theoretical psychology, and palliative medicine. Structural and functional alterations—detected by modalities like CT, MRI, and fMRI—correlate with impairments in executive function, memory, attention, and emotion regulation. These deficits are further influenced by existential distress, cultural background, spiritual thought, and psychological resilience. Therapeutic interventions—ranging from cognitive behavioral therapy and meaning-centered psychotherapy to pharmacologic agents and caregiver-spiritual support—can maintain dignity and foster emotional balance, even in the face of irreversible neurological deterioration. This review article highlights the importance of an integrated, patient-oriented approach to cognitive care in cancer, supporting early identification, interdisciplinary interventions, and culturally sensitive support that respects the patient's mind, identity, and values at the end-of-life.

Keywords Cognitive, cancer, patients, advanced stages

1. Introduction

In addition to being a medical condition, cancer, especially when it is advanced, is a profound existential experience [1]. Patients experience a complex psychological journey as their lives draw to a close, characterized by declining physical abilities, intense emotional reactions, and notable changes in cognitive function [2, 3]. Although tumor reduction and life extension have historically been the main goals of oncological care, there is growing awareness that cognitive and emotional well-being must be given just as much attention in the final stages of illness [4, 5]. Compassionate, person-centered care is informed by an understanding of the cognitive processes of terminal cancer patients, which is not just an academic pursuit but also a humanitarian necessity [6].

A number of variables, including tumor burden, neurological metastases, systemic inflammation, drug side effects, emotional distress, and the psychological burden of facing death, can cause subtle or noticeable, temporary or progressive cognitive changes in cancer patients nearing the end of their lives [7-10]. These alterations frequently show up as emotional dysregulation, concentration issues, short-term memory loss, and impaired executive function [10, 11]. These cognitive symptoms can significantly impact autonomy [12], quality of life [13], and decision-making skills when exacerbated by psychological stressors such as anticipatory grief, fear of dependency, unresolved trauma, or spiritual questioning [14].

The foundations of these cognitive declines have started to be clarified by modern neuroscience. Patients with cancer-related cognitive impairment (CRCI) have shown altered patterns of brain activation in functional neuroimaging, especially functional magnetic resonance imaging (fMRI), especially in areas linked to attention, memory, and emotional regulation. Computed tomography (CT) and other structural imaging techniques frequently show signs of brain metastases or cortical atrophy [15, 16]. In the context of terminal illness, cognitive dysfunction is not solely a biological phenomenon, though. The patient's psychosocial identity, cultural values, religious beliefs, family dynamics, and the overarching narratives of hope and despair are all interwoven with it. For many people, the last stage of life turns into a period of introspection, which is a cognitive process in and of itself [17]. During this time, patients try to find meaning in their experiences, revisit unresolved conflicts, and affirm personal values.

Depending on how they are handled, these existential thoughts can either be a burden or a buffer, and they frequently influence how people feel about dying [18].

When incorporated into a multidisciplinary palliative care model, psychosocial and spiritual interventions can be extremely effective in reducing cognitive distress [19, 20]. Even in the face of irreversible decline, it has been demonstrated that spiritually integrated care, meaning-centred psychotherapy, mindfulness-based techniques, and cognitive behavioural therapy (CBT) increase patients' sense of agency and foster resilience [21, 22]. These interventions can enhance mental clarity and promote emotional equilibrium when combined with the prudent use of pharmaceutical agents, such as selective serotonin reuptake inhibitors (SSRIs) for depression or psychostimulants for cognitive fatigue [23, 24].

Using knowledge from neuroimaging, psychopharmacology, psychological theory, and palliative care, this manuscript aims to synthesize the state of our knowledge regarding the cognitive processes that terminal cancer patients go through. It draws attention to the necessity of compassionate, integrated interventions that take into account the entirety of the dying person's experience [25, 26]. We hope to expand the conversation about what it means to think, feel, and be in the last stages of life by investigating the relationship between the brain, mind, and spirit in terminal illness.

2. Neurocognitive decline in advanced cancer

Patients with advanced-stage cancers are increasingly being identified as having cognitive impairment as a serious clinical concern. Cancer's effects on brain integrity worsen with time, leading to symptoms that impair executive functioning, language, memory, attention, and emotional control [27, 28]. During terminal care, neurocognitive decline, which has historically received little attention, has become a significant factor in determining patient autonomy, quality of life, and psychosocial well-being. Designing successful interventions and guaranteeing thorough, compassionate end-of-life support require an understanding of its pathophysiological foundation [29, 30].

Multiple factors contribute to neurocognitive dysfunction in advanced cancer, including secondary effects of systemic treatments and physiological decline in addition to primary oncological effects on the central nervous system (CNS). Primary brain tumors, leptomeningeal carcinomatosis, or brain metastases can all cause direct infiltration or compression of the brain [31]. Depending on the size and location of the lesion, brain metastases, which are frequently caused by cancers of the breast, lung, skin, and kidney, cause focal deficits and cognitive disorientation. In addition to causing widespread neurologic symptoms like seizures and cranial neuropathies, leptomeningeal carcinomatosis disrupts the flow of cerebrospinal fluid [32, 33]. Glioblastoma and other primary brain tumors cause edema and mass effect, which worsen cognitive impairment [34].

Despite being less frequent, paraneoplastic neurological syndromes (PNS) play a major role in cognitive impairment. Hippocampal inflammation in limbic encephalitis, which is usually associated with ovarian tumors or small cell lung cancer, results in confusion and memory loss. Through autoimmune-mediated neuronal damage, paraneoplastic cerebellar degeneration further deteriorates motor memory and coordination [35].

Chemotherapy-induced neurotoxicity, commonly referred to as "chemo brain," is caused by endothelial damage, oxidative stress, neuroinflammation, and the suppression of hippocampus neurogenesis. Reduced executive function, mental haze, and forgetfulness are some of the symptoms. These might not go away even after treatment, especially in patients with breast or hematologic cancers. Radiation therapy is risky as well. Whole-brain radiation is useful in treating metastases, but it can also result in early fatigue and memory loss, as well as long-term progressive white matter damage, demyelination, and cognitive decline [36, 37].

Cancer patients nearing the end of their lives frequently experience widespread and upsetting cognitive symptoms. Short-term memory loss, poor executive function, diminished attention, confusion, and emotional instability are typical symptoms. Damage to the prefrontal cortex and hippocampal regions is usually the cause of memory impairments. Patients may have trouble remembering new information, miss appointments, or forget recent conversations [38, 39].

Focus, problem-solving, and multitasking are all hampered by reduced executive function. These deficiencies are associated with inflammation interfering with neurotransmitter systems and dysfunction of the prefrontal cortex. Disorientation, which can be brought on by metabolic abnormalities or brain lesions, frequently manifests as confusion about time, location, or identity. Rapid mood swings, indifference, or irritability are signs of emotional lability, which is frequently caused by dysregulation of the limbic system [40-42].

Effective palliative care delivery requires an understanding of these symptoms. Disorientation may impede spiritual closure, memory loss may impede the creation of a legacy, and poor attention may impede last discussions. In order to ensure early detection and interdisciplinary intervention, clinicians must treat cognitive symptoms as modifiable targets of care [43].

3. Neuroimaging correlates of cognitive decline: fMRI and CT insights

The understanding of cognitive decline in terminal cancer has been revolutionized by neuroimaging techniques. Because of their speed and accessibility, CT scans are extremely useful in palliative settings. They show ventricular enlargement, cortical atrophy, and lesions from ischemic episodes or metastases. These structural alterations are frequently seen in the frontal, parietal, and temporal lobes, and they are associated with behavioral and cognitive deficits [44].

MRI offers high-resolution information on white matter integrity, particularly when paired with Diffusion Tensor Imaging (DTI). Microstructural degeneration in the frontal and temporal tracts is often revealed by DTI, and it is directly linked to cognitive deficits in processing speed and flexibility. In addition, MRI reveals post-radiation [44] chemotherapy [45] leukoencephalopathy and hippocampus atrophy, which are consistent with executive dysfunction and memory loss [46].

Real-time brain activity is investigated by functional magnetic resonance imaging (fMRI). The dorsolateral prefrontal and orbitofrontal cortices exhibit reduced activation in terminally ill patients, according to fMRI studies, which indicates compromised executive function [47]. The amygdala and hippocampus exhibit altered activity, which is indicative of limbic dysregulation and explains emotional instability and memory problems [48]. Mental exhaustion and poor autobiographical recall are associated with disruption in the Default Mode Network (DMN), particularly in the posterior cingulate and medial prefrontal cortex [49, 50]. By incorporating these imaging results into treatment, family conversations can be facilitated, prognostication improved, and patient symptoms validated. Neuroimaging research findings can help guide clinical reasoning and support personalized care planning even in situations where imaging is not practical.

4. Psychological and existential dimensions of cognitive processing

Beyond neurobiology, cognitive decline in terminal cancer is intricately linked to psychological responses and existential contemplation. Patients frequently use denial as a coping strategy to protect themselves from the emotional burden of their illness. Although protective at first, it might postpone involvement in care decisions. On the other hand, hope, whether rooted in personal objectives, treatment optimism, or spirituality, can inspire patients and lessen their suffering [50]. Many patients experience mood swings between hopelessness and rage, particularly when their sense of autonomy declines. These feelings could show up as blame, withdrawal, or irritability. When acceptance is attained, it promotes tranquility and enables patients to refocus their attention on their inner fulfillment, relationships, and legacy [51, 52].

Particularly prevalent are existential themes. Patients wrestle with unresolved relationships, consider the meaning of life, and face fears of being a burden or dying without dignity. How people understand their suffering and get ready to die is influenced by their cultural and spiritual backgrounds. Holistic care requires honoring these beliefs and encouraging narrative exploration.

5. Interventions for cognitive and emotional resilience

In the face of cognitive decline, resilience can be improved by a variety of therapeutic strategies. Patients who receive cognitive behavioral therapy (CBT) are able to confront their negative thoughts and create useful coping mechanisms. Even in cases of early cognitive impairment, modified versions of CBT are beneficial [53, 54]. In order to affirm their identity beyond illness, Meaning-Centered Psychotherapy (MCP) helps patients create personal narratives and discover purpose. Acceptance and Commitment Therapy (ACT) and Mindfulness-Based Stress Reduction (MBSR) provide strategies for cultivating presence and coping with distress. These methods help patients connect with their values, improve emotional regulation, and lessen anxiety [55].

Compensatory techniques like memory aids, task simplification, and environmental modifications are used in neurocognitive rehabilitation. These are essential for increasing independence and reducing annoyance. Caretakers should also receive interventions to help them better manage the difficulties of communication and providing care [56, 57].

6. Pharmacological management of cognitive symptoms

Pharmacological tactics can be used in conjunction with behavioral and psychological therapies. Methylphenidate and modafinil are examples of psychostimulants that improve alertness, focus, and decrease fatigue [58]. Patients with intact insight and declining motivation benefit most from these agents. SSRIs and SNRIs are two examples of antidepressants that treat mood-related cognitive symptoms. Other advantages of mirtazapine include better appetite and sleep. Because of the potential for delirium and sedation, benzodiazepines are used with caution [59, 60].

COX-2 inhibitors and omega-3 fatty acids are examples of new neuroprotective techniques that may lessen the neuroinflammation associated with CRCI. These substances have a promising supplemental role in maintaining cognitive function, but they are still being studied [61, 62].

7. Family, caregiver, and spiritual support

A terminally ill patient's cognitive decline has a significant impact on their emotional health and family relationships [63]. By managing everyday needs, promoting communication, and offering emotional support, caregivers develop into essential partners in care. They do, however, also experience a great deal of burden and grief in advance. Burnout among caregivers can be lessened by structured support networks, education, and respite care [64-66].

Fears of dying, guilt, and meaninglessness are all addressed in spiritual counseling. Through rituals, introspection, and forgiveness, chaplains and spiritual advisors who are sensitive to cultural differences assist patients in finding inner peace. Through prayer, music, or sensory cues, even patients with cognitive impairments can participate [1, 67, 68].

By addressing cognitive symptoms in addition to physical and emotional suffering, palliative care integration

guarantees all-encompassing support. Multidisciplinary teams handle care coordination, ethical dilemmas, and neuropsychiatric symptoms. Palliative care helps patients with cognitive impairments maintain their dignity and makes sure that their final days are kind and well-organized [69, 70].

8. Expanding the scope of cognitive understanding

Our understanding of cancer-related cognitive impairment (CRCI) is being reshaped by new research from Megari and colleagues, which indicates that cognitive dysfunction goes far beyond the scope of chemotherapy or direct involvement of the central nervous system [16, 71, 72]. More and more cancer types, including those without metastatic brain disease, are being identified as having neuropsychological disorders like executive dysfunction and language impairment [73-75]. Even in early survivorship, these deficiencies impair personal identity, communication, and everyday autonomy [74]. This necessitates a more comprehensive, inclusive understanding of CRCI that takes into consideration the burden of cognitive symptoms, which are imperceptible but significant [76, 77].

The persistent nature of cognitive dysfunction following chemotherapy and the necessity of continuous, individualized rehabilitation are further highlighted by Megari's research. Structured interventions and cognitive screening ought to be viewed as necessities rather than extras in survivorship care [78]. Early intervention can protect critical functions like emotional expression, decision-making, and narrative coherence in the context of terminal illness, even in patients with a limited prognosis [79].

This changing viewpoint is further supported by recent comparative studies that show older cancer patients and orthopedic surgery patients have similar cognitive vulnerabilities [80, 81]. These results highlight how crucial it is to incorporate perioperative and geriatric cognitive care into palliative oncology [80, 82]. A multidisciplinary and age-informed approach can enhance end-of-life experiences and promote cognitive resilience in older adults with comorbid conditions.

9. Limitations

There are still a number of barriers to comprehending and treating cognitive decline in terminal cancer, despite advancements. In environments with limited resources, access to neuroimaging and cognitive rehabilitation is still restricted. Standardization is made more difficult by the wide variations in symptom presentations caused by the type of cancer, past medical treatments, and cultural background.

Because of high attrition and ethical issues, longitudinal studies are challenging, which reduces the body of evidence supporting late-stage cognitive care. Additionally, there is a chance that too many psychotropic prescriptions will be written, which, if not carefully controlled, could make symptoms worse. Innovation, education, and a dedication to fair, person-centered care are necessary to close these gaps.

10. Conclusion

Cognitive impairment in terminal cancer is a convergence of neurobiological decline, emotional nuance, and existential contemplation. These cognitive alterations—frequently including memory deficits, executive dysfunction, disorientation, and emotional lability—are at the core of the patient's lived experience, affecting autonomy, decision-making, relationships, and the capacity to find closure at life's end.

This review highlights that these symptoms should not be considered as unavoidable or marginal, but as clinically and ethically essential. Neuroimaging advancements yield objective markers of validity for patient experience and guide care. Meanwhile, psychological treatments, mindfulness training, spiritually integrated psychotherapy, and focused pharmacologic agents provide pragmatic avenues to maintaining lucidity, comfort, and selfhood.

In the end, an empathic, interdisciplinary care model—one in which cognitive functions are seen to be interlinked with the emotional, relational, and spiritual integrity of dying—becomes indispensable. From this perspective, the last chapter in life is not only a time of loss, but also one of deep meaning-making, relationship, and dignity.

Author Contributions

M.M.A. initially developed the research concept and conducted the literature review. J.J. contributed by reviewing and proofreading the manuscript to enhance its clarity and coherence.

Competing Interests

No conflicts of interest exist.

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