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Palliative Care-Main Role of Nursing: An Updated Review Article for Palliative Care in Brain Disorders with Focus on Biochemical Brain Markers.

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Abstract

Background: Brain disorders, including high-grade gliomas, Alzheimer's disease, amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), and Parkinson's disease, are associated with severe physical, cognitive, and psychosocial challenges that impact quality of life for both patients and their caregivers. Palliative care, with a central role played by nursing, addresses these complex needs, focusing on symptom management, psychological support, and improving quality of life through targeted interventions.

Aim: This review aims to examine the role of nursing in palliative care for patients with brain disorders, highlighting specific nursing interventions, symptom management, caregiver support, and adherence to clinical guidelines. Special attention is given to the need for early palliative involvement, end-of-life support, and approaches tailored to neurocognitive and psychiatric symptoms.

Methods: A comprehensive literature review was conducted, analyzing studies published on nursing interventions in palliative care, focusing on clinical practice guidelines, healthcare service utilization, and common challenges encountered by patients with brain disorders. Key domains included pain management, symptom control, simulation-based education for nurses, and support for families and caregivers.

Results: The findings highlight that nurses play an essential role in symptom management and emotional support, especially in managing pain, neurocognitive symptoms, epilepsy, fatigue, psychiatric symptoms, and end-of-life needs. Nurses also facilitate adherence to clinical practice guidelines and support home-based palliative care, which can reduce hospital admissions and improve end-of-life quality. Simulation-based education was found to enhance nurses' competencies in delivering high-quality palliative care.

Conclusion: Effective nursing-led palliative care interventions can substantially improve the quality of life for patients with brain disorders. Nurses' specialized skills in managing neurological symptoms and offering psychological support are critical for addressing both patient and caregiver needs. Early integration of palliative care is recommended to improve outcomes, particularly in managing neurocognitive decline and other complex symptoms associated with brain disorders.

Keywords: palliative care, nursing, brain disorders, symptom management, quality of life, caregiver support, clinical guidelines, neurocognitive symptoms.

1. Introduction

In order to provide tailored end-of-life care (EoLC), which aims to improve patients' quality of life and lessen their suffering, primary care providers—including general practitioners (GPs) or family doctors (henceforth referred to as GPs) and general practice nurses (GPNs)—are crucial [1]. Primary care is defined as the first, easily accessible, ongoing, all-encompassing, and coordinated level of medical care that is available when needed and puts the patient's long-term health ahead of the brief length of an illness. It coordinates any additional specialists that patients

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may need and handles common health issues in the community [2]. In order to develop therapeutic connections that support a thorough grasp of the requirements of patients and caregivers, general practitioners (GPs) are expected to be skilled in general medicine [3]. Additionally, they need to know about the social and health services in the area [3]. EoLC is an essential part of primary care in many modern healthcare systems since most people see a general practitioner (GP) on a regular basis [4][5] and many GPs consider caring for patients who are terminally ill to be a core role [6]. Over 80% of general practitioners in Australia said they have given EoLC to at least one patient in the previous 12 months [7].

As more people approach the end of their lives, the approach to end-of-life care is changing significantly due to an aging population, which calls for adjustments in the way care is provided [8]. The majority of people will die from non-malignant causes, such as several coexisting disorders or particular organ failures, even though specialized palliative care (PC) usually targets cancer patients [9]. Heart failure, cerebrovascular disorders, late-stage respiratory diseases [10], multimorbidity, frailty, and dementias [11][12] are among the common causes of mortality that entail predictable EoL trajectories. Primary care physicians and other medical experts offer the majority of EoLC for these illnesses. Numerous people spend their last year of life at home, frequently receiving care from spouses or adult children who may be responsible for their own family or health [13][14]. Since EoLC spans more than only the last days or weeks of life, which PC is frequently thought to represent, it is used instead of PC to reflect this change.

As the importance of interdisciplinary teams in healthcare has become more widely acknowledged, GPNs' roles have grown considerably. Primary care is defined by the WHO as the first point of contact and the supplier of all-encompassing care for community members [2]. The partnership between a GP and a GPN is a key component of a primary care team [2]. The WHO's view that high-quality EoLC is a fundamental human right [1][16] is consistent with Murray et al.'s claim that PC should be widely available, inclusive of all human elements and situations, and across all diseases [15]. Active primary care engagement on a global scale is necessary to achieve this. Identifying patients who require future EoLC, effectively managing comorbidities to reduce problems, addressing psychosocial issues, and coordinating with family and healthcare professionals while respecting the patient's EoL wishes and caregiver needs are all necessary for general practitioners to provide high-quality EoLC [15]. A multidisciplinary strategy combining hospital specialists, inpatients, and community services is frequently required [17]. These services may be coordinated or led by GPs and GPNs.

Efforts have been undertaken to better understand the role of GPs and GPNs in EoLC in order to increase their capability in community-based PC. A systematic assessment assessing GPs' ability to provide EoLC was published in 2002 [3], the only attempt to gather international research on GP performance in this area. But since then, a wealth of studies on the EoL role of primary care has surfaced worldwide. The extent of primary PC is influenced by national health systems, however certain fundamental duties are shared internationally. In order to improve the ability of general practitioners and GPNs to provide PC in communities, we have compiled the body of research on general practice PC produced since 2002. Two main concerns are addressed by this systematic review, which covers studies conducted between 2000 and October 2017: (1) To what extent do GPNs and GPs provide EoLC? and (2) What are the factors that facilitate and hinder their participation in EoLC? The usefulness of created EoLC models in general practice is examined in this paper, which concludes a five-part series [6][19–21].

Definitions:

Moreover 30% of Americans still die in acute care hospitals, despite the fact that most of them say they would prefer to die at home or in a similar environment [22]. In addition to preventing needless extension of the dying process, severely sick patients frequently express a desire for meaningful connections with loved ones, appropriate pain and symptom management, and a sense of control [23]. Similarly, caregivers look for care that guarantees their loved ones' comfort and is consistent with their ideals. For terminally ill patients, hospice care helps to fulfill these preferences [24, 25]. For those with life-limiting illnesses, hospice provides a kind, quality-driven approach that includes expert medical care, pain and symptom management, and personalized emotional and spiritual support. Hospice also offers families emotional support, including during the grieving process. The structure, delivery, expansion, and difficulties surrounding the use of hospice care in the US will all be covered in this chapter. Dame Cicely Saunders founded the hospice movement with the primary goal of alleviating the suffering of the terminally ill. Saunders established the fundamentals of hospice care that now influence hospice policy and practices worldwide when he created St. Christopher's Hospice in South London in 1967. Inspired by St. Christopher's Hospice, Connecticut Hospice was the first hospice program in the United States, established in 1974 by Florence Wald, RN. Inpatient settings were used for both of these early initiatives [26]. In order to help patients die at home, hospice organizations in the US now emphasize in-home care. Medicare, Medicaid, and almost all private insurance plans have covered hospice treatments since 1983, making them more accessible to a greater number of Americans.

Role of Nursing:

Clinical Support Interventions

A palliative care (PC) telephone advisory service in the Netherlands, predominantly utilized by general practitioners (GPs), reported receiving inquiries mainly for managing pain (49%), delirium (20%), nausea and vomiting (16%), and dyspnea (12%). Additionally, 14% of consultations addressed end-of-life (EoL) matters, specifically terminal sedation (11%) and euthanasia (3%) [27]. In France, approximately one-third of GPs actively engaged in EoL decisions within hospital settings, with 60% reporting that they were consulted by phone prior to decisions regarding withdrawal of treatment [28].

Pain and Symptom Management

Efforts to control pain and other symptoms yielded varied outcomes. For instance, a home-shared care program in the United States demonstrated enhanced pain control [29], as did a structured pain management protocol in rural Japan [30]. Conversely, an educational program aimed at GPs did not yield significant improvement in pain management [31]. Similarly, mixed outcomes were observed in managing non-pain symptoms. While case conferences prolonged functional capacity [31] and improved physical and mental well-being during the last month of life [32], a shared care program involving GPs and PC providers helped reduce patient anxiety, depression, fatigue, and loss of appetite. However, a geriatric-PC integrated service did not show consistent benefits across various parameters [33]. Furthermore, routine telephonic communication between GPs and a head and neck cancer care team did not prevent nearly half of the patients from experiencing unresolved symptoms, although GPs reported satisfaction with the care provided [34]. A facilitation service in the UK did not increase GP confidence in managing symptoms [35].

Home Deaths

In the UK, 69% of patients whose GPs participated in the Gold Standards Framework (GSF) for PC achieved their desired place of death, with nearly half of these being home deaths [36]. Similarly, half of Dutch GPs involved in a regional head and neck support program were able to facilitate home deaths [37].

Adherence to Clinical Practice Guidelines

Structured programs such as the GSF and other EoL care pathways have been associated with better adherence to PC guidelines, as has a rural Japan pain management protocol [38]. The GSF emphasizes the importance of early identification of patients at risk of dying as central to improving EoL care. Nevertheless, most individuals on the UK PC registers (a core element of the GSF) had cancer, despite this group representing a smaller fraction of patients dying in general practice settings [39]. Additionally, GPs often relied on intuition rather than formal tools for identifying individuals approaching EoL [39].

Healthcare Service Utilization

Case conferences for a PC population (90% with cancer) in Australia resulted in approximately a 30% reduction in hospital admissions. Another study reported marked reductions in emergency department visits, hospital admission rates, length of stay, and associated costs. In contrast, there was no significant change in healthcare utilization among patients under a combined PC/geriatric service in the United States. No studies were identified that reported outcomes specifically related to general practice nurses (GPNs).

Case Studies:

This review examined interventions aimed at enhancing primary care involvement in end-of-life (EoL) care since 2002. Most interventions focused on either information sharing or collaborative care models between specialist services and primary care practitioners. While some studies demonstrated clear clinical improvements, outcomes were inconsistent across all studies. The review suggests that patient outcomes improved when general practitioners (GPs) actively participated in decision-making and direct care. However, many interventions lacked randomized controlled trial (RCT) designs, limiting the generalizability of results. Only three RCTs were conducted, with one study successfully reaching its sample target of 461 participants. This trial demonstrated significant reductions in hospitalizations and improved patient functional status, aligning with similar findings from Temel et al., who showed that early specialist palliative care (PC) for advanced lung cancer patients enhanced quality of life and survival compared to standard oncology care (40). Three key lessons emerge from the review. First, outcomes improved when GPs were actively engaged in integrated planning and care, which could also yield economic benefits. Without direct GP involvement in clinical planning, patient outcomes often mirrored usual care. This aligns with findings from a systematic review of primary care integration in advanced stroke management, showing that active GP collaboration nearly doubled the chances of patients being alive and residing at home compared to passive information-sharing approaches (41, 42). Second, a majority of the studies focused on cancer patients, which is common in specialist PC services. However, this focus overlooks the diverse needs of patients with non-malignant conditions, such as those with end-stage multimorbidity or dementia. These conditions often follow a prolonged and unpredictable trajectory, differing from the generally time-limited course expected in cancer-focused palliative care models. It is essential to explore whether these findings extend to non-cancer populations, given the unique challenges they face in EoL care.

The dying process and end-of-life (EoL) demands have been better understood thanks to a wealth of research, yet it is still difficult to incorporate these discoveries into community-based care approaches. In EoL care, general practitioners (GPs), who frequently treat fragile elderly patients, will remain essential. GPs should be seen as vital resources in the provision of end-of-life care, with the necessary training to support their duties, given the aging population and the anticipated rise in the demand for palliative care (PC). The kinds of interventions that are possible in EoL care are greatly influenced by the structure of national health systems. Care duplication, unclear treatment objectives, and possible misunderstanding for fragile, multimorbid patients are problems that systems with a strong expert emphasis may encounter. GPs may feel uncertain due to poor EoL care training, and specialists may not be familiar with GP competencies, making primary care integration in such settings difficult. Nonetheless, GPs are more likely to have the fundamental abilities required for EoL management in systems where primary care serves as a gatekeeper, as is the case in the UK. at line with Starfield's findings that primary care spending is associated with better population health outcomes, capitation payment systems may potentially fund national initiatives that raise the probability that patients would pass away at their preferred location (43, 44). Furthermore, there is little study on general practice nurses' (GPNs') participation in end-of-life care, despite their critical role in managing chronic diseases. Long-term condition management inevitably gives way to end-of-life care as a result of the changing patterns of death brought about by population aging. Since GPs and GPNs are currently involved in EoL-related tasks, research that includes anticipatory planning for patient deterioration and gives GPNs the resources they need to improve their participation in EoL care is necessary. By bridging the gap between EoL care and chronic disease management, this strategy may promote a more all-encompassing paradigm for aging population support.

Nurses and Simulation-Based Education for palliative Care:

It has been demonstrated that simulation-based learning (SBL) improves healthcare professionals' comprehension of interpersonal skills, interdisciplinarity, and teamwork in palliative care. After SBL, participants in two studies expressed a greater appreciation for collaboration and the multidisciplinary aspect of end-of-life (EoL) care [45, 46]. They had a greater understanding of the roles played by different healthcare professionals and the value of working in multidisciplinary teams as a result of the training, especially during emergencies when interdisciplinary coordination is crucial [45, 46]. According to a different study, training in multicultural groups was beneficial for participants, who felt more at ease and confident in team-based palliative care settings.

Additionally, SBL increased participants' readiness and self-assurance in managing emotionally taxing discussions. Participants reported greater competence and satisfaction in addressing patients' emotional needs at EoL, as well as enhanced communication skills during challenging interactions [47-49]. Even in difficult situations, the training improved their capacity to discuss delicate subjects with patients and their families [49]. One study indicated better ability to explain advance care planning discussions and found a significant improvement in confidence after the workshop, especially in treatment that addressed patients' existential concerns [51]. Nonetheless, during a family conflict-focused session, a few participants expressed feeling overburdened, highlighting the emotional difficulties involved [47]. Additionally, SBL improved participants' clinical practice, especially in the area of communication. Following the training, participants in three trials reported feeling more patient, prepared, and sympathetic while interacting with patients in the real world [50]. The COMFORT model was deemed useful by participants for everyday communication and as a tool to manage patient contacts, leading to a better comprehension of patient requirements [49]. Additionally, they indicated interest in adding useful elements of pain and symptom management to the SBL curriculum. Future practice insights from the training included enhanced communication abilities, attentive listening, and a heightened focus on the emotional experiences of patients and their families during end-of-life decision-making [47]. In general, participants acknowledged the importance of reflection in SBL for self-evaluation and personal development, which gave them the bravery and fortitude required for palliative care. Taking on the role of a family member in these circumstances offered fresh insights, emphasizing the vulnerabilities families face and reaffirming the value of emotional support and empathy in EoL care [50].

Common Brain Disorders:

Palliative care is increasingly recognized as essential in managing symptoms, improving quality of life, and providing support for patients with serious brain disorders. While palliative care is traditionally associated with end-of-life care, it is now applied earlier in the disease trajectory for many neurological conditions. Common brain disorders that frequently require palliative care include high-grade gliomas, Alzheimer’s disease, amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), and Parkinson’s disease (**Figure 1**).

1. High-Grade Gliomas

High-grade gliomas, including glioblastoma, are aggressive brain tumors with a poor prognosis. Symptoms such as headaches, seizures, cognitive decline, and personality changes can cause significant distress for patients and their families. Palliative care in high-grade glioma focuses on symptom management, psychological support, and assistance with complex decision-making due to the rapid progression of the disease and its impact on cognitive and physical functioning. Studies suggest that early palliative care integration in glioma patients improves quality of life (QoL) and helps patients and caregivers navigate the challenges of an advanced cancer diagnosis. Advanced care planning (ACP) is particularly emphasized, as the cognitive decline associated with these tumors may eventually impair decision-making capacity, necessitating timely discussions around treatment preferences and end-of-life care options (Sherwood et al., 2016).

2. Alzheimer's Disease and Other Dementias

Dementia, particularly Alzheimer's disease, is one of the most common neurological conditions that requires palliative care. Patients with Alzheimer's experience progressive cognitive decline, leading to difficulties with memory, language, and daily functioning. As the disease advances, patients may suffer from behavioral changes, incontinence, feeding difficulties, and immobility. Palliative care in Alzheimer's disease focuses on maintaining comfort, managing symptoms such as pain, agitation, and anxiety, and supporting caregivers. Given the chronic and progressive nature of dementia, palliative care interventions may span several years and are aimed at enhancing the QoL of both patients and their families. The role of palliative care is particularly crucial during the later stages of the disease, where decisions about feeding methods, use of antibiotics, and comfort measures become prominent (Van der Steen et al., 2014).

3. Amyotrophic Lateral Sclerosis (ALS)

ALS is a neurodegenerative disease characterized by the progressive loss of motor neurons, leading to muscle weakness, paralysis, and eventually respiratory failure. Most patients diagnosed with ALS have a life expectancy of 3 to 5 years from symptom onset, although disease progression varies. As ALS progresses, patients require extensive assistance with breathing, mobility, and communication. Palliative care in ALS is aimed at addressing complex symptom management, including pain, respiratory difficulties, and swallowing problems. Palliative care teams also provide support for psychological symptoms such as anxiety and depression, which are prevalent in ALS patients due to the debilitating nature of the disease. ACP and decisions around the use of ventilatory support and feeding tubes are essential components of palliative care in ALS, as these decisions profoundly impact the patient's QoL and end-of-life experience (Mitsumoto et al., 2014).

4. Multiple Sclerosis (MS):

MS is a chronic autoimmune disorder that leads to demyelination and damage to the central nervous system, resulting in physical, cognitive, and emotional challenges. Patients with advanced MS may experience severe fatigue, pain, mobility issues, and cognitive impairment. Palliative care for MS patients is often supportive and addresses both physical and psychosocial needs. Since MS can have a relapsing-remitting course or progressive deterioration, palliative care needs may fluctuate, requiring flexible and individualized care plans. For patients with advanced or progressive MS, palliative care can provide relief from debilitating symptoms, assist with decision-making regarding invasive treatments, and support caregivers. Psychological support is particularly important, as MS patients may suffer from depression, anxiety, and social isolation due to the chronic and unpredictable nature of the disease (Solari et al., 2013).

5. Parkinson's Disease

Parkinson's disease is a neurodegenerative disorder that primarily affects movement but can also impair cognition, mood, and autonomic function as it progresses. Advanced Parkinson's disease can lead to severe motor disability, communication issues, and complications such as dysphagia and dementia. Palliative care for Parkinson's patients focuses on managing these complex symptoms to improve QoL and supporting patients and families in navigating disease progression and treatment options. Effective management of symptoms such as tremor, rigidity, pain, and non-motor symptoms like depression and constipation is essential in palliative care. ACP in Parkinson's is also critical due to the disease's progressive nature and the eventual risk of complications that may require decisions around life-sustaining interventions (Tuck et al., 2015). Palliative care for brain disorders is crucial in managing the significant physical, cognitive, and psychosocial symptoms associated with these conditions. For disorders like high-grade gliomas, Alzheimer's disease, ALS, MS, and Parkinson's disease, early integration of palliative care can provide symptom relief, facilitate decision-making, and improve overall QoL for patients and their families. The unique and complex challenges of brain disorders necessitate a multidisciplinary approach to palliative care, involving specialists in neurology, psychiatry, nursing, and social work. Future research should continue to refine palliative care models for these conditions, with an emphasis on early intervention, patient-centered care, and support for caregivers.

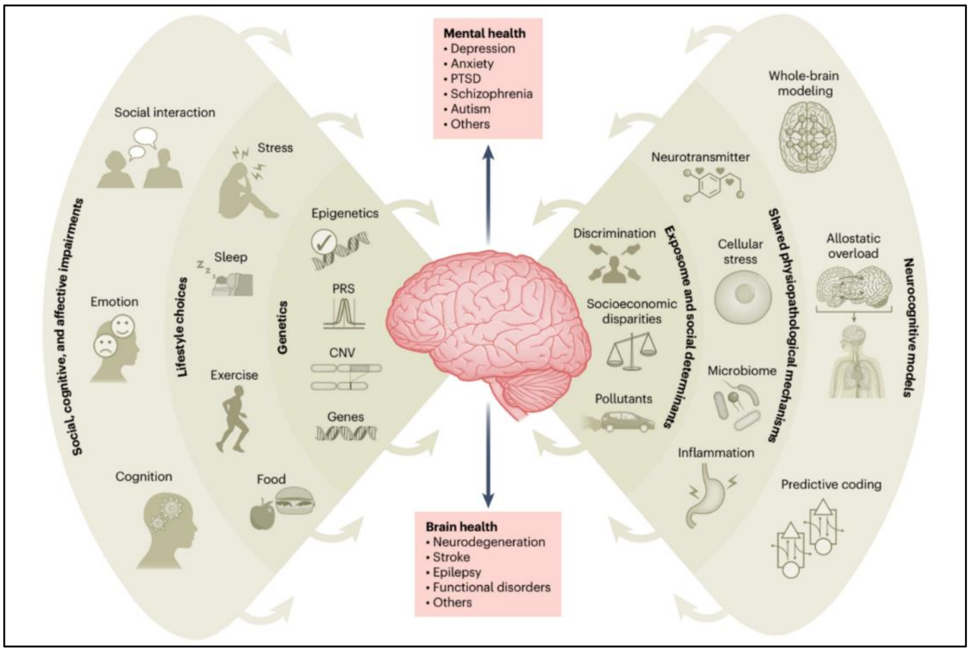
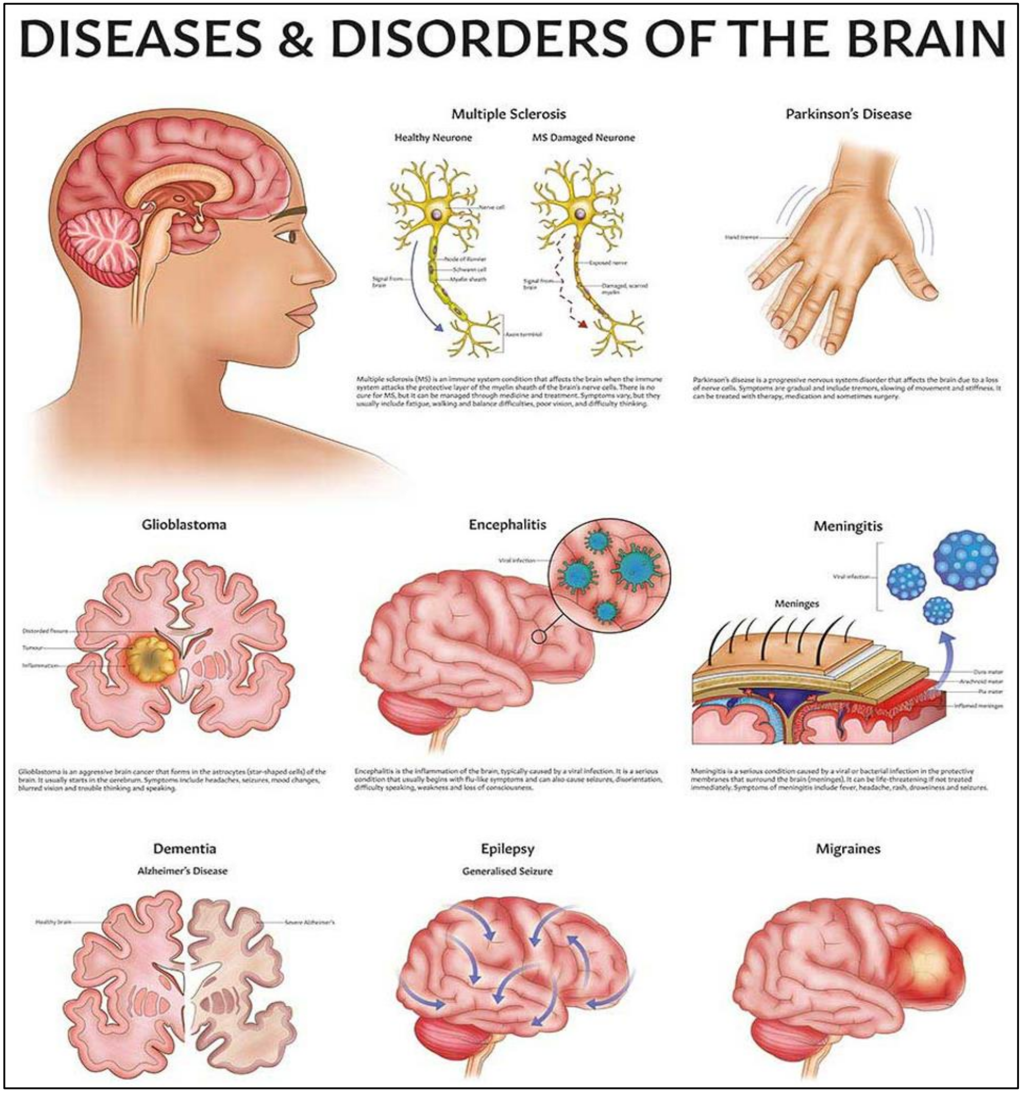


Figure 1: Common Factors affecting brain and mental health.



Multiple sclerosis (MS) is an immune system condition that affects the brain when the immune system attacks the protective layer of the myelin sheath of the brain's nerve cells. There is no cure for MS, but it can be managed through medicine and treatment. Symptoms vary, but they usually include fatigue, walking and balance difficulties, poor vision, and difficulty thinking.

Parkinson's disease is a progressive nervous system disorder that affects the brain due to a loss of nerve cells. Symptoms are gradual and include tremors, slowing of movement and stiffness. It can be treated with therapy, medication and sometimes surgery.

Glioblastoma is an aggressive brain cancer that forms in the astrocytes (star-shaped cells) of the brain. It usually starts in the cerebrum. Symptoms include headaches, seizures, mood changes, blurred vision and trouble thinking and speaking.

Encephalitis is the inflammation of the brain, typically caused by a viral infection. It is a serious condition that usually begins with flu-like symptoms and can also cause seizures, disorientation, difficulty speaking, weakness and loss of consciousness.

Meningitis is a serious condition caused by a viral or bacterial infection in the protective membranes that surround the brain (meninges). It can be life-threatening if not treated immediately. Symptoms of meningitis include fever, headache, rash, drowsiness and seizures.

Figure 2: Common Brain Disorders that Require Palliative Care.

Palliative Care in Brain Tumors:

Neurocognition:

Neurocognitive functioning is a critical concern for patients with brain tumors, as it directly affects their ability to process information and perform daily activities. This includes deficits in attention, executive functioning, language, and memory, with nearly 90% of patients with malignant brain tumors exhibiting deficits in at least one of these areas at diagnosis. These neurocognitive impairments are often attributed to a combination of factors, including the tumor itself, treatments like radiotherapy, and medications such as antiseizure drugs (ASDs) (52-54). Several studies have explored interventions to manage or mitigate neurocognitive decline. Tumor resection has been shown to improve attention, language, learning, and memory, although it can negatively impact executive functioning, particularly in the immediate postoperative period. Additionally, awake surgeries have demonstrated positive effects on neurocognitive domains. Radiation therapy's effects on cognition are not fully understood, especially in primary brain tumor patients. However, for patients with brain metastases, whole brain radiotherapy (WBRT) has been a primary focus, though its neurocognitive toxicity is a significant concern. High-level evidence on how to mitigate these side effects is still evolving. Studies suggest that stereotactic radiosurgery (SRS) may cause less neurocognitive deterioration than WBRT, both immediately post-treatment and at 6 months, without affecting overall survival . Additionally, the combination of hippocampal avoidance during WBRT (HA-WBRT) with memantine has been shown to reduce the risk of cognitive decline while maintaining similar overall survival. Pharmacological interventions aimed at improving neurocognitive function have been tested, though results have been mixed. Donepezil, an acetylcholinesterase inhibitor, did not show significant improvements in overall cognitive functioning, despite some improvements in specific cognitive domains for patients with more severe deficits. Similarly, dexamphetamine, a stimulant, did not lead to improvements in neurocognition for brain tumor patients. Non-pharmacological approaches such as exercise or yoga have been explored as potential therapies, but the evidence supporting their effectiveness on cognitive outcomes remains limited. In summary, managing neurocognitive decline in brain tumor patients involves a multifaceted approach, incorporating surgical interventions, radiation therapy modifications, pharmacological agents, and potential non-pharmacologic therapies. However, despite some promising strategies, significant challenges remain in preserving and improving neurocognitive function in this patient population.

Epilepsy:

Patients with brain tumors frequently experience seizures, albeit the frequency varies according to the type of tumor. Throughout the course of the disease, the incidence varies from around 15% to 30% in patients with brain metastases to about 80% in those with grade 2 gliomas (55, 56). Antiseizure medication (ASD) primary prophylaxis is discouraged in current guidelines for seizure-naïve individuals with brain tumors (57). Nonetheless, because non-enzyme-inducing ASDs have little or no interactions with other drugs, such as corticosteroids and systemic treatments, their usage following a first seizure is highly advised (58). The most often prescribed first-line treatment for patients with brain tumors is levetiracetam, a non-enzyme-inducing ASD (59).

Phenytoin, pregabalin, and levetiracetam were the most effective monotherapy agents, with levetiracetam exhibiting the lowest treatment failure rate among the agents examined in a recent systematic review evaluating the effectiveness of ASDs in glioma patients with epilepsy (60). In 1,435 glioma patients with epilepsy, a retrospective analysis comparing first-line levetiracetam to valproic acid found that levetiracetam was considerably more effective while having comparable levels of toxicity. Levetiracetam is not advised for patients with a history of mental illnesses like anxiety or depression, though, as nearly half of the unacceptable side effects in glioma patients were of psychiatric origin (61). Brivaracetam, an analog of levetiracetam, has been demonstrated to be well-tolerated and effective in lowering seizure frequency in patients with brain tumors, and it seems less likely to cause psychiatric side effects (62, 63). Due to uncontrollable seizures despite monotherapy, approximately one-third of glioma patients with epilepsy need more than one ASD. In these situations, it is advised to combine ASDs with various modes of action (64). Lacosamide and perampanel have been shown to be effective and tolerable in a number of studies evaluating their use as adjuncts for patients with brain tumors and uncontrollable seizures. A shared decision-making strategy may be used to explore discontinuing ASD in patients with low-grade gliomas who have long-term seizure independence following anticancer therapy (65). In the last stages of life, seizures are more common and frequently result in hospitalization. Seizures should be administered as usual in these situations, with alternatives such as subcutaneous or oral levetiracetam, buccal clonazepam, or intranasal or subcutaneous midazolam for patients who have trouble swallowing (66, 67).

Fatigue

Up to 90% of patients with malignant gliomas experience fatigue at some point during the course of their disease, making it one of the most prevalent symptoms among patients with brain tumors (68). Fatigue is probably caused by a combination of factors, such as the tumor itself, symptomatic treatments (such ASDs), and anticancer treatments (like radiation). There is no proof that either non-pharmacologic or pharmaceutical treatments considerably reduce fatigue in brain tumor patients, according to a 2016 Cochrane systematic review.

However, a number of follow-up studies have assessed different therapies. Glioma patients who engaged in aerobic training sessions at home 20–45 minutes, three times per week) demonstrated reduced tiredness in comparison to a waitlist control group in a pilot randomized controlled trial (RCT). Glioma patients who participated in a complete nursing program that included cognitive-behavioral therapies also reported less symptoms of fatigue than those in a control group that got regular nursing follow-up for three months. But among patients with brain tumors, non-pharmacologic treatments like yoga (69), educational programs (70), and online courses in problem-solving therapy (a type of cognitive behavioral therapy) did not significantly reduce fatigue. Phase II (n = 54) and phase III (n = 328) double-blind, placebo-controlled trials have examined the pharmacological drug armodafinil in glioma patients in recent years, but they found no improvement in fatigue (71). The feelings of weariness were not alleviated by other pharmaceutical treatments, such as donepezil and dexamphetamine (72).

Pain and Headaches

Between 4% and 62% of individuals with brain tumors experience headaches, making them a prevalent symptom (73). Reducing intracranial pressure with medication or surgery can help relieve headaches that are sometimes caused by edema or the mass effect, which raises intracranial pressure (74, 75). The disruption of the blood-brain barrier caused by brain tumors and associated treatments can result in the extravasation of proteins and plasma fluid, which raises intracranial pressure and causes vasogenic edema. In patients with brain tumors, cerebral edema is a major cause of morbidity, resulting in symptoms such headaches, nausea, vomiting, seizures, and localized neurological impairments (76). Because of their great potency, extended half-life, and restricted mineralocorticoid effects, corticosteroids—in particular, dexamethasone—are frequently used to treat cerebral edema. However, prolonged use should be taken with caution as it can lead to negative effects like myopathy, hyperglycemia, immunological suppression with increased susceptibility to opportunistic infections, adrenal insufficiency, and neuropsychiatric effects (74). There was no discernible difference between the two treatment groups in a phase III, double-blind, placebo-controlled trial that compared dexamethasone to losartan, an angiotensin II receptor blocker, in 75 patients with newly diagnosed glioblastoma during radiation therapy (77). Although extensive prospective trials are still required to validate its effectiveness, bevacizumab, a VEGF inhibitor, has demonstrated promise as a corticosteroid substitute in lowering cerebral edema. Approximately 13% to 25% of people with brain tumors may have physical pain in addition to headaches. These patients get multimodal pain management that follows the World Health Organization's three-step analgesic ladder and is similar to that given to patients with systemic malignancies (78). About 85% of glioma patients surveyed said that cannabis-based therapies helped them with their pain (79), however another prospective study found that taking medicinal cannabis did not significantly reduce pain (80). In spite of this, there aren't much recent research looking at how to treat headaches or other physical pain in patients with malignant brain tumors.

Psychiatric Symptoms

Patients with brain tumors frequently experience neurobehavioral symptoms, such as mental health issues. About 25% of patients with gliomas experience anxiety, and 15% of patients have depression (81). While psychosis in glioma patients has been less thoroughly investigated and its frequency is still unknown, a systematic analysis found that the prevalence of behavioral and/or personality alterations in these individuals ranged between 8% and 67% (82). In recent years, a number of non-pharmacologic treatments for mental health issues have been assessed. Online problem-solving treatment, a low-intensity type of cognitive behavioral therapy, did not lessen depression in 115 glioma patients with depressive symptoms in a randomized controlled trial as compared to the waitlist control group. But in a different RCT with 150 glioma patients, those randomly assigned to a care program based on recollection therapy—which involved talking about prior experiences, events, and activities in a group setting—showed lower levels of anxiety and sadness than the control group. An RCT found that glioma patients who received a thorough nursing program based on cognitive-behavioral therapies experienced reduced levels of anxiety and depression. No high-quality research have particularly looked into pharmacological therapies for depression in people with brain tumors, according to a 2020 Cochrane comprehensive review. Moreover, improvements in affective symptoms were not observed in an RCT examining the effects of dexamphetamine on neurocognition, mood, and health-related quality of life (HRQoL) in patients with brain tumors.

Caregiver Needs

In addition to caring for patients with brain tumors, family caregivers also help patients' health-related quality of life (HRQoL) (84). Giving care for a loved one who has a brain tumor, however, may be a devastating and transformative experience. Caregivers may feel "mixed feelings of right and wrong, patience and guilt, hope and despair" as a result of the patient's changed conduct and personality (85). Neuro-oncology caregivers frequently encounter numerous unmet demands, and the stress of caregiving in the context of brain tumors is multifaceted (86). High levels of distress, anxiety, and depression (89–93); low HRQoL (94); a lack of information about care and resources (95); insufficient tools to address caregiver burnout, end-of-life care for the patient, and caregivers' psychological and bereavement needs (88); and fear of recurrence of the patient's brain tumor, which highlights the importance of including caregivers in psychotherapeutic support when appropriate (87). Cultural or national variations did not significantly affect caregiver issues, according to qualitative research including small caregiver cohorts from the United States and the Netherlands. According to the majority of caregivers, problems started early in the course of the illness, which made them more in need of assistance (96). Research on coping in dyads of patients and caregivers with high-grade gliomas showed that coping mechanisms had a direct impact on HRQoL elements. In particular, the use of avoidance techniques was linked to worse HRQoL, whereas the use of social support by caregivers early in the disease trajectory was linked to improved HRQoL. Similarly, when caregivers used social support coping methods, patients' HRQoL improved. By concentrating on these networks, evaluating caregivers' social networks offers a chance to meet their support needs (97). It has been suggested that web-based applications can be helpful in facilitating social support interventions (98). Small feasibility studies have examined interventions like yoga, meditation, and exercise for patients and caregivers, with varying degrees of success. In general, participants gave positive assessments, and the researchers thought the interventions were practicable (99). Furthermore, it has been shown that early interventions utilizing a palliative care strategy, administered by a nurse or cancer care coordinator, are beneficial in assisting caregivers along the course of the illness. Additionally, a palliative care strategy has been developed to support glioma patients and caregivers, attending to their needs during times of transition, such as bereavement.

Early Palliative Care

The following five phases of the disease were identified in a 2017 framework for palliative and supportive care for patients with high-grade gliomas: (1) time of diagnosis, (2) completion of initial radiation treatment, (3) tumor recurrence, (4) deterioration leading to death, and (5) post-death care. Each phase has unique needs for the patient and caregiver. In order to promptly address the needs of patients and caregivers throughout these stages, advance care planning, or ACP, is essential. "Enabling individuals to define goals and preferences for future medical treatment and care, to discuss these goals and preferences with family and healthcare providers, and to record and review these preferences if appropriate" is how the European Association for Palliative Care defines ACP (100). Because malignant brain tumors can affect neurocognitive functioning, communication skills, consciousness, and other neurological and psychiatric symptoms, making it difficult to make decisions, ACP is especially crucial for patients with these conditions. According to a number of studies, glioma patients' and their caregivers' assessments of the prognosis and treatment objectives may be erroneous (101). Therefore, in order to help patients and their families participate in decision-making and make their treatment choices clear, communication tactics must be tailored to the cognitive limitations of the patients. For patients with glioblastoma, a disease-specific ACP program has been created that addresses issues like present health condition, worries about everyday chores, supportive treatment options, and chosen locations for care and death. The clinical application of this program is presently being assessed (102). For patients with advanced cancer, the American Society of Clinical Oncology (ASCO) has developed clinical practice recommendations that advocate for early palliative care engagement within 8 weeks of diagnosis (103). Only over half of the patients in a retrospective study with brain metastases obtained a consultation for palliative treatment (104). ACP documentation rates were 11%, 29%, and 54%, respectively, according to a different study that evaluated ACP in glioblastoma patients at three different stages of the illness trajectory: before diagnosis, within six months of diagnosis, and at the last follow-up (105). Early palliative care is rarely incorporated into the routine care of patients with brain tumors, and its implementation is frequently uneven, especially in systemic cancer care, despite compelling evidence that it improves HRQoL, lowers depression, increases care satisfaction, decreases the use of chemotherapy near the end of life, and increases survival in cancer patients (106, 107).

End-of-Life Needs and Care

As they are near the end of their lives, patients with malignant brain tumors have substantial and frequently unmet care demands. According to data, these patients experience a wide range of symptoms during the terminal phase, such as fatigue, seizures, motor dysfunction (e.g., focal weakness and dysphagia), communication problems (e.g., aphasia and speech impairments), and pain, mostly headaches (108, 109). There is also a prevalence of existential and psychological anguish (110). Crucially, patients with brain tumors have different neurological symptoms than those of patients with cancers that do not affect the central nervous system, which makes their end-of-life care requirements distinct (111). These results emphasize the need for population-specific strategies in brain tumor patients' end-of-life care. Physicians generally agree that aggressive end-of-life care, such as hospitalization, intensive care unit (ICU) admission, and the administration of chemotherapy or radiation in the final weeks of life, may have a negative impact on HRQoL without offering significant benefits, despite the fact that there is considerable variation in how end-of-life care quality is evaluated across nations (112, 113). However, research shows that over one-third of patients with glioblastoma are admitted to the hospital in their final month of life, and late hospitalization and intensive care unit admissions are still frequent among patients with malignant brain tumors (114, 115). With rates ranging from 6% to 18%, chemotherapy is administered less frequently in the latter weeks of life (116, 117). In the United States, 24% to 37% of patients with malignant brain tumors are either recruited late (i.e., within the final 3 days of life) or not at all, despite the fact that prompt hospice referral and enrollment are stressed as crucial components of end-of-life care (118, 119). Perhaps as a result of regional variations in healthcare access and hospice service provision, hospice membership rates are substantially lower in Europe (19%) and Asia (8%), respectively (120). Formal palliative care consultations have been linked to higher hospice enrollment rates, according to several research (120). The timing of hospice referrals and the total hospice participation rate for patients with brain tumors may both be improved by initiatives to increase palliative care involvement, as palliative care services are still underutilized in neuro-oncology.

Common End-of-Life Biomarkers: Brain Biomarkers:

End-of-life biomarkers are critical tools in understanding the physiological changes and predicting the progression of terminal illnesses. In particular, brain biomarkers play a significant role in assessing the status of individuals nearing the end of life, especially in conditions such as neurodegenerative diseases, brain injuries, and various cancers. These biomarkers provide insights into brain function, disease progression, and potential response to treatment, and they help clinicians make informed decisions regarding patient care, pain management, and end-of-life interventions.

Brain Biomarkers in Neurodegenerative Diseases

Neurodegenerative diseases such as Alzheimer's disease (AD), Parkinson's disease (PD), and amyotrophic lateral sclerosis (ALS) are among the most common conditions that lead to end-of-life care, particularly in older adults. Brain biomarkers are instrumental in diagnosing these diseases at early stages and monitoring their progression.

1. **Amyloid-beta and Tau Proteins**: In Alzheimer's disease, amyloid-beta plaques and tau tangles are key pathological features. The presence of elevated levels of amyloid-beta in cerebrospinal fluid (CSF) is a significant indicator of early Alzheimer's disease and can predict cognitive decline. Tau, a protein involved in stabilizing microtubules in neurons, when hyperphosphorylated, forms tangles that disrupt cell function. These tau tangles are often used as biomarkers for assessing the severity of Alzheimer's-related dementia.
2. **Alpha-Synuclein**: In Parkinson's disease and related disorders, the accumulation of alpha-synuclein in the brain is a hallmark of disease progression. This protein aggregates in neurons, disrupting normal brain function. Elevated levels of alpha-synuclein in CSF or blood can be used to diagnose Parkinson's disease and monitor its progression toward the end of life.
3. **Neurofilament Light Chain (NfL)**: Neurofilament light chain (NfL) is a biomarker for neuronal injury and degeneration. Elevated levels of NfL in blood and CSF are associated with various neurodegenerative diseases, including Alzheimer's, Parkinson's, and ALS. NfL has shown promise in monitoring disease progression and can serve as a predictive biomarker for end-of-life stages in patients with these conditions.

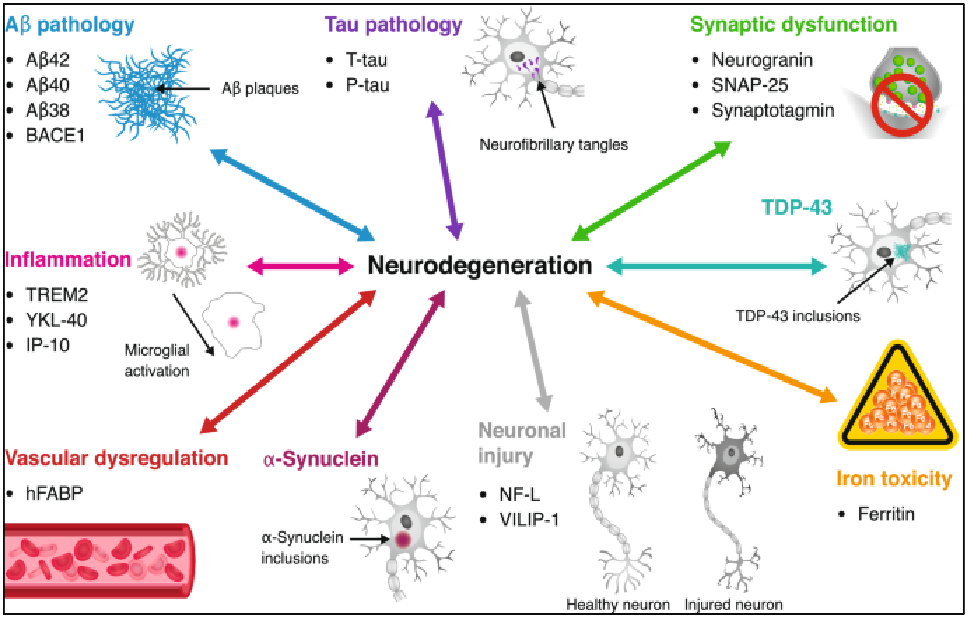


Figure 3: Biomarkers of Brain Neurodegenerative Disorders.

Brain Biomarkers in Brain Injuries and Tumors

Brain injuries resulting from trauma or stroke, as well as brain tumors, represent significant causes of mortality in patients at the end of life. The identification and measurement of specific biomarkers can help assess the extent of damage and predict outcomes.

1. **S100B Protein**: The S100B protein, found in astrocytes, is released into the bloodstream following traumatic brain injury (TBI). Elevated levels of S100B are indicative of blood-brain barrier disruption and neuronal damage. It has been used to predict outcomes in TBI patients, particularly in assessing the potential for recovery and mortality.
2. **Glial Fibrillary Acidic Protein (GFAP)**: GFAP is another biomarker that is elevated in cases of brain injury, particularly in traumatic brain injury and stroke. It is a marker of astrocyte activation and is used to assess the extent of brain damage and predict the severity of the condition, especially in the critical or end-of-life stages.
3. **Circulating Tumor DNA (ctDNA)**: In patients with brain tumors, particularly glioblastomas, ctDNA can be used to detect tumor progression and genetic mutations associated with resistance to treatment. Monitoring ctDNA levels provides clinicians with critical information about tumor dynamics and can help guide end-of-life care decisions, such as transitioning to palliative care or providing more aggressive treatment options based on the genetic profile of the tumor. Brain biomarkers offer a wealth of information that can significantly enhance the care of patients at the end of life. By identifying the underlying causes of neurological decline and disease progression, biomarkers such as amyloid-beta, tau, alpha-synuclein, NfL, S100B, GFAP, and ctDNA help clinicians better understand the patient's condition, predict outcomes, and make informed decisions regarding treatment and care. The integration of these biomarkers into clinical practice promises to improve the accuracy of prognostication, personalize care plans, and support better decision-making at the critical end-of-life stages.
4.

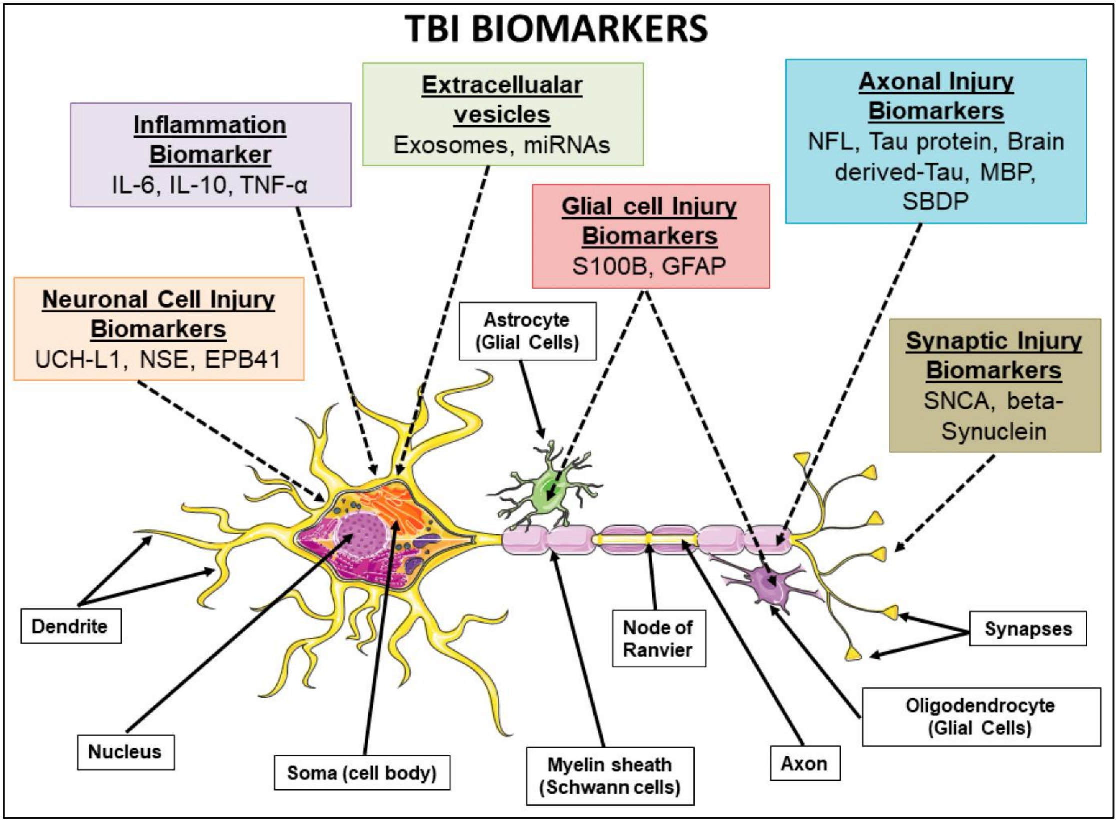


Figure 4: Common Biomarkers of Brain Injuries.

Conclusion:

This review underscores the critical role that nursing plays in providing palliative care for patients with brain disorders. As highly skilled practitioners, nurses are central to delivering compassionate, holistic, and evidence-based care that addresses the multifaceted needs of these patients and their families. Managing complex symptoms such as pain, fatigue, and neurocognitive decline requires not only technical expertise but also sensitivity to the emotional and psychological challenges these patients face. Nurses' contributions are essential across the disease trajectory, from initial diagnosis to the end-of-life phase, making them key advocates for patients' preferences and care goals. Early palliative care has proven benefits for brain disorder patients, particularly in terms of quality of life, symptom management, and reduced healthcare utilization. Nurses are positioned to implement early palliative interventions, providing tailored support that considers the unique needs of neuro-oncology and neurodegenerative disease patients. As disease progresses, nurses continue to play a pivotal role in managing symptoms, supporting ACP, and coordinating care that respects patient autonomy and dignity. The findings also reveal the importance of specialized training, including simulation-based education, to strengthen nursing competencies in palliative care. Equipped with these skills, nurses can better respond to challenges such as complex neurological symptoms, cognitive impairments, and caregiver support needs. Future research should prioritize developing standardized nursing protocols and educational programs tailored to the neuro-palliative care landscape. In conclusion, nursing in palliative care for brain disorders is vital to enhancing patient quality of life and meeting diverse clinical and psychosocial needs. Early, proactive nursing-led interventions in palliative care not only improve patient outcomes but also support caregivers, helping both patients and families navigate the challenges of brain disorders with greater resilience and dignity.

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