Psycho-Oncology: Living With Cancer

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ABSTRACT

An interdisciplinary approach in oncology that includes psychiatric and psycho-oncological care has become essential due to the increasing number of newly diagnosed cancer cases and cancer-related deaths worldwide, as well as the increasing survival of cancer patients, It has been observed that approximately 50% of cancer patients have psychiatric disorders, including clinically significant emotional distress and/or undetected/untreated psychosocial conditions, during the course of their diseases. These psychiatric problems reduce patients' quality of life, disrupt their social relationships, contribute to poor treatment compliance and prolonged hospital stays. The International Psycho-Oncology Society (IPOS) Standards for Quality Cancer Care emphasize that psychosocial cancer care should be recognized as a universal human right, and stress should be assessed as the sixth vital sign after temperature, blood pressure, pulse, respiratory rate, and pain. Psycho-oncology is a multidisciplinary field that addresses the psychological, behavioral, and social dimensions experienced by individuals diagnosed with cancer and their families. Receiving a cancer diagnosis is not just a medical issue; it constitutes a psychological crisis. Therefore, the aim of psycho-oncology is to preserve the patient's psychological well-being and enhance quality of life at all stages of the illness. In this paper, we aimed to review the literature about psychiatric comorbidities and its pharmacological and non-pharmacological managements in cancer patients.

Key words; psycho-oncology, anxiety, depression, stress

INTRODUCTION

In the 1800s, a cancer diagnosis was considered equivalent to a death sentence, as there was no known cause or cure for the disease. Disclosing the diagnosis to the patient was seen as cruel and inhumane, based on the belief that the patient would lose all hope and might cope better if unaware of their illness. This was considered an acceptable "white lie." However, the patient's family was always informed. Tolstoy's story The Death of Ivan Ilyich strikingly portrays Ivan's sense of isolation in the 19th century; while his family and doctor claimed his severe abdominal pain was nothing serious, he was left alone with his suffering and the awareness of his terminal illness. In the 1970s, the word "cancer" was still stigmatized and not openly discussed. With the development and implementation of psycho-oncology, patients with cancer have been empowered to express their emotions regarding their illness [1].

A) Epidemiology And Conceptual Model

Cancer is one of the leading causes of death worldwide. According to 2022 Global Cancer Observatory (GLOBOCAN) data, the number of newly diagnosed cancer cases is 19.9 million, the number of deaths due to cancer is 9.7 million, and the 5-year case prevalence is around 53.5 million. The data indicates that approximately one in five men or women will develop cancer in their lifetime, while one in nine men and one in 12 women will die from cancer [2]. By 2040, new cancer diagnoses are projected to increase by 50%, with an estimated 28.4 million new cancer cases diagnosed annually. The most frequently diagnosed cancer type in 2022 was lung cancer (12.4%), with one in every eight cancer cases being lung cancer. The second most frequently diagnosed cancer type is breast cancer, with a frequency of 11.6% [3].

Psycho-oncology is a multidisciplinary approach to supporting the mental health of cancer patients. Approximately 50% of cancer patients experience emotional distress due to the physical symptoms of their illness and social stressors, while one-third meet the diagnostic criteria for psychiatric disorders, particularly adjustment disorder, anxiety, and depression. The presence of comorbid mental illnesses in cancer patients leads to prolonged hospital stays and frequent emergency room and outpatient clinic visits. In addition, patients with comorbid anxiety and depression are 4.4 times more likely to require inpatient treatment than those without. Therefore, psychological comorbidity in cancer patients is associated with increased use of healthcare resources [4].

1- The Relationship Between Stress and Cancer

Animal models of disease have demonstrated that stress can significantly influence tumor initiation and progression through various mechanisms [5–7]. It has found that that chronic stress can cause tumor formation and promote cancer development in studies about cancers such as prostate, breast, stomach, lung and skin cancer [8].

Under chronic stress, sustained activation of the hypothalamus produces corticotrophin-releasing factor (CRF). CRF is transported to the pituitary gland and stimulates the release of adrenocorticotropic hormone (ACTH). Sustained ACTH secretion also leads to corticosteroid synthesis. Chronic stress also activates the central nervous system (CNS) stimulating the release of important neurotransmitters such as norepinephrine (NA) and adrenaline (Ad). Stress hormones promote the formation and development of cancers by triggering DNA damage, increasing p53 degradation, and regulating the tumor microenvironment. Chronic stress can create an inflammatory tumor microenvironment by activating the inflammatory response and the interaction between inflammatory and cancer cells, thus supporting all stages of tumorigenesis. Chronic stress can also selectively suppress type 1 helper T cells (Th1), suppress cytotoxic T cell (CTL)-mediated cellular immunity and interferon production, and impair immune surveillance and other processes, thereby increasing the risk of cancer invasion and metastasis and reducing the effectiveness of antitumor therapy. Also, elevated glucocorticoid levels mediate the inhibition of p53 which can initiate DNA repair, cell cycle arrest, aging, and apoptosis, are related to the body's ability to inhibit tumor formation and respond to various types of cancer treatment [8].

Another system affected by chronic stress is the immune system, which leads to a decrease in the number and function of immune cells and a shift in the type 1/type 2 cytokine balance. All of these contribute to the persistent low-grade inflammation closely associated with chronic diseases, including cancer. Conversely, cancer itself creates an inflammatory environment with systemic manifestations, altering the activation of the hypothalamic-pituitary-adrenal axis and the appropriate stress-induced cortisol secretion [9].

2- Biopsychosocial model

More than a chronic disease requiring medical treatment, cancer is often recognized as a traumatic life event associated with significant psychosocial impacts across all levels of well-being. Cancer survivors may experience numerous cancer-related psychosocial problems, including, but not limited to, depression, anxiety, post-traumatic stress disorder, persistent fear about cancer recurrence, changes in sexuality and fertility, difficulty finding or maintaining employment, altered body image, survivor guilty, post-traumatic growth, and physical impairment related to the side effects of cancer treatment and related stressors. The biopsychosocial model is particularly relevant for cancer survivors because the intertwined biomedical and psychosocial impacts of cancer may not be adequately understood when assessed individually. Quality of life assessment is one of the most widely used biopsychosocial assessment tools in cancer care [10]. Screening scales such as the "Distress Thermometer," which is similar to the Hospital Anxiety and Depression Scale, are other biopsychosocial assessment tools that can be applied in busy clinics [11]. When evaluated within the framework of the biopsychosocial model, there are studies reporting that screening for distress in cancer patients enables people to share their feelings about their illness with their oncologists more easily and increases satisfaction with the treatment they receive [12]. As a result, evaluating cancer from a biopsychosocial framework allows for personalized interventions and creates a common language between the clinician and the patient.

B) Psychiatric Comorbidities In Cancer Patients And Interventions

Pain and Fatigue in Cancer Patients

One of the most common causes of physical distress in cancer patients is pain [13]. There is evidence suggesting that emotional distress, depression, anxiety, uncertainty, and hopelessness are associated with pain. Psychological and cognitive-behavioral therapies have been shown to reduce pain intensity and improve functioning; this has been demonstrated in multiple meta-analyses. Cognitive-behavioral therapy, psychoeducation, hypnosis, relaxation techniques, yoga, and exercise have been proven effective at various stages of the disease [14–18]. Among cancer patients, fatigue is reported as one of the main symptoms impairing quality of life, with prevalence rates ranging from 17% to 56% [19]. In these patients, depression, anxiety, insomnia, or pain may also cause or contribute to fatigue [20)].

Sleep Disorders

Sleep disorders and various sleep-related conditions (e.g., insomnia, hypersomnia, obstructive sleep apnea syndrome [OSAS]) are common and significant complaints among cancer patients [21]. Sleep disturbances are often associated with physical illness, pain, hospitalization, and specific medical treatments, along with the psychological effects of cancer. Altered sleep negatively affects emotional well-being and daytime performance and may be an early indicator of delirium in oncology settings. In the general population, chronic insomnia has been associated with an increased risk of developing clinical anxiety or depression [22] . Sleep disturbances are among the most common reasons for consultations requested for cancer patients [23]. Numerous large randomized trials and meta-analyses have demonstrated the effectiveness of cognitive behavioral therapy (CBT) for insomnia, not only in cancer patients but also in non-cancer populations [23,24]. In cases where CBT is unsuccessful or when patients have comorbidities contributing to sleep disturbances (such as pain, hot flashes, depression, etc.), pharmacological treatment may be necessary. Several types of medications are used in the treatment of disrupted sleep, including non-benzodiazepine benzodiazepine receptor agonists, benzodiazepines, melatonin receptor agonists, antihistamines, sedating antidepressants and antipsychotics, as well as melatonin itself . Melatonin's use in the treatment of insomnia in cancer patients has been shown to improve antineoplastic treatment response and reduce toxicity. Studies have reported its use as an adjuvant in radiotherapy. It has been reported to be beneficial in alleviating acute reactions due to radiation therapy through its effects on signaling pathways that play a role in DNA repair, inflammation, and cell survival. In addition, melatonin can regulate inflammation and redox activity that play a role in normal tissue damage and tumor resistance, improve DNA repair in normal cells, and promote apoptosis in cancer cells through the attenuation of prostaglandins. For the above reasons, it can be concluded that the treatment of sleep and its disorders is of fundamental importance for the prevention and treatment of different types of tumors; in this case, management of circadian rhythm disorders and insomnia is particularly crucial for regulating endogenous melatonin production. Among the new treatment options, it has been discovered that orexin (hypocretin) may play a therapeutic role not only in the field of sleep disorders but also in the treatment of some types of tumors. Orexin is relevant to narcolepsy because it helps stabilize wakefulness. Orexin receptors have been found specifically in gastrointestinal tumors (colon, liver, stomach), prostate, cervix and their metastases, and hematological malignancies, and these tumors are frequently seen in patients with hypersomnia. This link may be due to orexin, but further studies are needed to clarify this [25,26].

Anxiety Disorders

Common anxiety-related symptoms observed in cancer patients include palpitations, panic attacks, muscle pain, fatigue, dizziness, fear of death, irritability, difficulty concentrating, and a sense of tension. These symptoms may develop not only due to the stress of illness but also as side effects of medications used in cancer treatment. Anxiety symptoms tend to increase when patients experience uncertainty regarding the disease or when the treatment response is inadequate. Effective communication strategies can help alleviate patients' anxiety.

A current or past diagnosis of an anxiety disorder, a history of substance use disorder, pessimism, avoidant personality traits, and low levels of social support are considered risk factors for the development of anxiety disorders in cancer patients [27].

In the treatment of anxiety in cancer patients, low-dose benzodiazepines, buspirone, low-dose antidepressants, beta-blockers, and hydroxyzine are commonly used. In addition to pharmacological treatments, psychotherapy, relaxation techniques, and breathing exercises can also be beneficial [27,28].

Depressive Disorders

Depression is estimated to affect approximately one in four cancer patients, and the likelihood of experiencing depression in this population is five times higher than in the general population [29]. Depression can occur at any stage of the illness [30]. Cancer patients may not identify themselves with the term "depression"; therefore, asking whether their mood or morale is low may be a more practical approach. It is especially important to consider the possibility of depression in patients who appear withdrawn or have difficulty engaging in treatment [31].

Walker and colleagues, in a study conducted between 2008 and 2011 involving 21,151 patients undergoing routine depression screening, found the prevalence of major depression to be 13.1% in lung cancer, 10.9% in gynecological cancers, 9.3% in breast cancer, 7% in colorectal cancer, and 5.6% in genitourinary cancers. In this study, the high-risk groups for major depression included younger patients, those with low social support, and female patients with lung or colorectal cancer [32].

A meta-analysis conducted in 2015 identified the Hospital Anxiety and Depression Scale (HADS) as the most recommended and critically evaluated tool for screening depression in cancer patients [33]. The risk of suicide in cancer patients is 1.95 to 2.8 times higher compared to the general population. In patients with advanced cancer, 17% reported wishing they were dead [34]. Risk factors for suicide in cancer include depression, a history of suicide attempts, psychiatric history, hopelessness, the first year after diagnosis, physical symptoms, male gender, and advanced stage of the disease [34].

In the treatment of depression in cancer patients, antidepressant medications are commonly used. In general, selective serotonin reuptake inhibitors (SSRIs) are considered to have a favorable side-effect profile, and there is broad consensus regarding their safety [31]. However, certain antidepressants—such as paroxetine, fluoxetine, duloxetine, and bupropion—which inhibit the CYP2D6 enzyme, can reduce the efficacy of tamoxifen. Therefore, these medications should be avoided in patients taking tamoxifen. The use of paroxetine during tamoxifen therapy has been associated with an increased risk of mortality from breast cancer [35].

A recent study conducted in our country found that difficulties in emotion regulation, depression, and low psychological resilience were associated with prolonged grief disorder in breast cancer patients [36].

Sexual Functions

In recent years, as a result of advancements in cancer diagnosis and treatments, the survival rates have increased, leading to a rise in studies evaluating the quality of life of patients. Sexuality, along with the pleasure and satisfaction derived from it, is one of the dimensions used to assess quality of life [37].

The frequency of sexual dysfunction in cancer patients varies depending on the patient group. Prevalence rates for sexual problems associated with cancer and cancer treatment are reported to range from 40% to 100%. This variation in prevalence depends on the primary diagnosis, treatment method, and type of sexual problem [38] . Another study found that 59% of men and 79% of women reported a decrease in sexual activity and complaints related to sexual functioning [39].

In cancers where the genital organs are directly affected, erectile dysfunction, orgasm disorders, and dyspareunia are commonly observed. Damage to the germinal epithelium of the testes due to chemotherapy and radiation can lead to temporary or permanent oligospermia/azoospermia [37].

After radical prostatectomy, it has been found that decreased libido, erectile dysfunction, ejaculation difficulties, impaired urinary functions, and reduced intimacy with the partner are common [40]. Erectile dysfunction has been observed in approximately 80% of male patients with a history of prostate cancer, with no significant difference in the development of erectile dysfunction between those undergoing radical prostatectomy and those receiving radiotherapy [41].

In a study evaluating long-term sexual functions after rectal cancer treatment, it was reported that in men, nerve damage, radiotherapy, and the presence of a stoma led to erectile dysfunction and ejaculation difficulties; while in women, radiotherapy and the presence of a stoma caused dyspareunia and vaginal dryness [42].

Another important factor affecting sexual functions in oncology patients is the change in body image and self-esteem experienced during this process. In a study conducted with women receiving treatment for breast cancer, those who reported negative thoughts about their body image had more complaints related to sexual functioning compared to those who did not. Vaginal dryness, satisfaction with sexual intercourse, and stigmatizing thoughts related to the body were found to be the most significant predictors of sexual function [43)]. In a study, it was observed that breast cancer patients who underwent breast reconstruction after mastectomy had a better perception of body image and exhibited fewer symptoms of depression compared to those who did not undergo reconstruction [44]. Another study involving 110 patients receiving chemotherapy for breast cancer found a statistically significant correlation between sexual desire and body image, social support, and medication side effects ($P = .000$). Among these, body image perception was identified as the most influential parameter affecting sexual desire [45].

Similarly, male patients undergoing or having undergone cancer treatment associated the loss of sexual function with a perceived loss of "masculinity." In a survey study, it was found that men who perceived a greater loss of masculinity after cancer treatments experienced more erectile dysfunction, independent of the severity of sexual dysfunction [46].

Regarding pharmacological approaches, in women with symptoms of vaginal and/or vulvar atrophy, lubricants in addition to vaginal moisturizers may be tried as a first-line option. In some cases, low-dose vaginal estrogen, lidocaine, and dehydroepiandrosterone may also be considered. In men, phosphodiesterase type 5 inhibitors may be considered, and in the presence of symptoms refractory to medical treatment or complications, surgical options may be considered. Both men and women experiencing vasomotor symptoms should be offered interventions aimed at symptomatic relief, including behavioral options such as cognitive behavioral therapy, slow breathing, and hypnosis, and medications such as venlafaxine and gabapentin [38].

To improve sexual function problems in cancer patients, it is advisable to inform patients about the potential sexual side effects associated with their treatment before therapy begins. During and after treatment, sexual issues that may be distressing and impact the patient's quality of life should be more frequently addressed. It may also be necessary to discuss the difficulties experienced during the cancer treatment process with the sexual partner. Couple-based interventions have been shown to positively affect both the cancer treatment process and sexual adjustment between partners when compared to individual counseling [39].

Delirium and Its Management in Cancer Patients

Delirium is a syndrome of acute brain failure that develops as a direct pathophysiological consequence of an underlying medical condition or toxic exposure. According to the DSM-5, it is characterized by an acute onset and fluctuating course of disturbances in attention, awareness, and cognitive functioning [47] . Global impairments can be observed in cognitive functions such as memory, orientation, language, perception, and visuospatial abilities. Additionally, changes in the sleep-wake cycle, alterations in psychomotor activity, and emotional instability may also accompany the condition. Delirium is the most commonly observed psychiatric syndrome in hospitalized patients. Its prevalence ranges from 11% to 42% in general medical wards and reaches up to 87% in intensive care units [48,49].

The prevalence of delirium varies depending on the stage of cancer and ranges from 10% to 85%. In oncology patients, delirium may result from direct involvement of the cranial nervous system by the cancer itself (e.g., cranial tumors, metastatic cranial tumors), as well as from side effects of medical treatments (e.g., electrolyte imbalances, dehydration, organ failure, vascular complications), and paraneoplastic syndromes. Immunotherapeutic agents such as vincristine, corticosteroids, and interferon, as well as supportive care medications commonly used in cancer patients—such as opioids, antiemetics, and benzodiazepines—can precipitate delirium [50].

In the management of delirium, non-pharmacological interventions and the resolution of underlying medical conditions are prioritized to prevent its onset. In a study reviewing non-pharmacological strategies to prevent delirium, various methods were applied, including therapeutic interventions to enhance cognitive function, early mobilization, minimizing the use of psychoactive medications, preventing sleep deprivation, ensuring access to necessities such as glasses and hearing aids, and increasing communication with the patient. Compared to the group where these interventions were not implemented, the incidence of delirium was lower; however, these interventions did not alter the severity or duration of delirium [51].

The primary goal in treating delirium is to identify and address the underlying causes. Although psychiatrists are often consulted for delirium management, they collaborate with other specialists to coordinate the treatment and monitoring of delirious patients.

It is important to promptly recognize and treat reversible causes such as hypoxia/anoxia, hypoglycemia, hyperthermia, hypertension, and thiamine deficiency. Pain management, especially in cancer patients, should also be considered as a key element in delirium prevention [50,51].

Haloperidol, a high-potency dopamine antagonist with minimal anticholinergic and cardiovascular side effects, is the first-choice antipsychotic for the treatment of delirium. During antipsychotic treatment, extrapyramidal side effects such as tardive dyskinesia and neuroleptic malignant syndrome may occur. There is evidence that intravenous administration of antipsychotics reduces this risk.

Studies have shown that intravenous haloperidol can prolong the QT interval. Although this is associated with high doses (>35 mg/day).Many studies recommend 1–2 mg of haloperidol every 4 hours; however, for elderly patients, a lower dose of 0.25–0.50 mg every 4 hours as needed is suggested. In patients with significant psychomotor agitation, the dose may be increased accordingly. Olanzapine, risperidone, and quetiapine may also be beneficial in the treatment of delirium [52].

Psychosocial interventions

Adjustment to cancer is associated with six distinct challenges as defined by Faulkner and Maguire (1994):

1. Coping with uncertainty about the future,
2. Searching for meaning,
3. Dealing with loss of control,
4. Needing clarity,
5. Emotional support,
6. Medical support [53].

Failure to manage these challenges can lead to psychosocial difficulties. Psychological interventions are generally initiated to help patients cope with these problems and adapt to their illness.

The range of psycho-oncological interventions is quite broad, ranging from relaxation therapies to music therapy. Psychoeducation is the primary intervention, aiming to increase the patient's awareness of their condition. Commonly used therapies in cancer care include psychodynamic psychotherapy, systemic therapy, and cognitive behavioral therapy [54,55].

Besides individual psychotherapy, group therapies have also been found effective in improving survival among oncology patients. Self-help groups play an important role as they provide peer support in resolving common personal and social problems. These groups create opportunities for individuals to express their feelings, share coping experiences, and find emotional support. For such groups to continue successfully, several conditions must be met, including voluntary membership, bonding around shared issues, commitment, fostering hope, and group cohesion. Examples of such groups among cancer patients include those composed of women who have undergone mastectomy and individuals who have had stoma surgery.

Techniques such as relaxation methods, systematic desensitization, and hypnosis can help relieve symptoms related to treatment side effects, such as tension, pain, nausea, and vomiting [56].

Group Psychotherapies

Group psychotherapy has several advantages for patients diagnosed with cancer, distinct from individual psychotherapy. Through social support in group therapy, patients experience a reduction in feelings of loneliness. In this way, they have the opportunity to meet others who are going through similar processes. Compared to individual therapy, group therapy is more cost-effective [57]. Supportive, cognitive-existential, meaning-centered group therapies, and psychoeducational groups are among the group psychotherapies studied in the field of oncology [58]. Meaning-centered group therapy helps patients with advanced cancer to rediscover their primary sources of meaning, create new meanings for themselves, and reduce the sense of hopelessness at the end of life [59].

Declaration of Interests

The authors declare that they have no known competing personal interests that could have influenced the work reported in this paper.

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