



# Mental Health Prior to Hematopoietic Cell Transplantation

# 38

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## Introduction

The estimated annual combined incidence of leukemia, lymphoma, and multiple myeloma in the United States (US) is about 173,000, which is approximately 10% of all cancers [1]. Myelodysplastic syndrome (MDS) consists of stem cell disorders characterized by ineffective hematopoiesis with cytopenias and progression to leukemia in one third of cases; MDS is diagnosed annually in about 10,000 people in the United States [2, 3]. These blood dyscrasias may affect children, young adults, and those older than 65 years of age. Over time, cure rates have increased as has prolonged survival due to novel treatment regimens that can accompany hematopoietic cell transplant (HCT). HCT, which is discussed in Chaps. 37 and 40, is a potentially curative treatment involving the transplantation of stem cells from a donor (allogeneic) or from the patient (autologous). Approximately 20,000 HCTs are performed each year in the United States. The annual number of allogeneic transplant recipients has surpassed 8000 per year in the United States since 2013; the number of autologous transplant recipients has increased at a faster rate due to transplants being performed with reduced intensity regimens for plasma cell and lymphoproliferative disorders in older adults [4, 5]. Psychosocial distress and comorbid psychiatric symptoms and/or disorders in individuals with blood dyscrasias are common and may be greater in severity than the general population without cancer. Distress is a term used to describe the array of psychiatric symptoms and psychosocial issues that transplant recipients experience specific to the disease and transplant. Symptoms of distress are assessed to be the most intense before transplantation and over time can improve or resolve [6]. Adjustment, depressive, and anxiety disorders are most common in patients with cancer [7]. Of

notable concern is worsening of psychiatric symptoms in individuals with preexisting psychiatric disorders who develop hematologic malignancies and need to undergo HCT. In this patient population, there is particular consideration for medication nonadherence, drug-drug interactions, and drug-disease interactions [8].

Individuals with psychiatric issues are at risk for worse health outcomes, longer hospitalizations, and increased mortality [9, 10]. In patients undergoing HCT, mental health stability is of paramount importance given the associated physical and psychological factors associated with HCT and post-transplant sequelae, such as infection and graft versus host disease (GVHD). Psychological distress and alterations in thinking are common in these patient population who are often in isolation in the hospitalized setting [11]. Patients experience additional disruptions to their lives when being separated from their support systems, experiencing financial problems, having housing concerns, and dealing with other life stressors in the setting of illness. Among psychosocial risk factors, those associated with negative outcomes following transplantation include limited social support, history of poor adherence, comorbid untreated psychiatric disorder, use of avoidance-based coping, and active substance use [12]. Therefore, given the wide range of distress with which individuals may present, the screening, diagnosis, treatment of psychiatric symptoms, and disorders should be routinely provided to this patient population by a cross-disciplinary collaborative approach.

## Psychiatric Symptoms and Disorders

### Anxiety

While anxiety disorders in the DSM-5 include their own diagnostic criteria, the shared feature is heightened distress related to a threat and efforts to avoid or flee from the perceived danger [13]. The prevalence of anxiety in patients with cancer varies from approximately 10–30% given variable assessment

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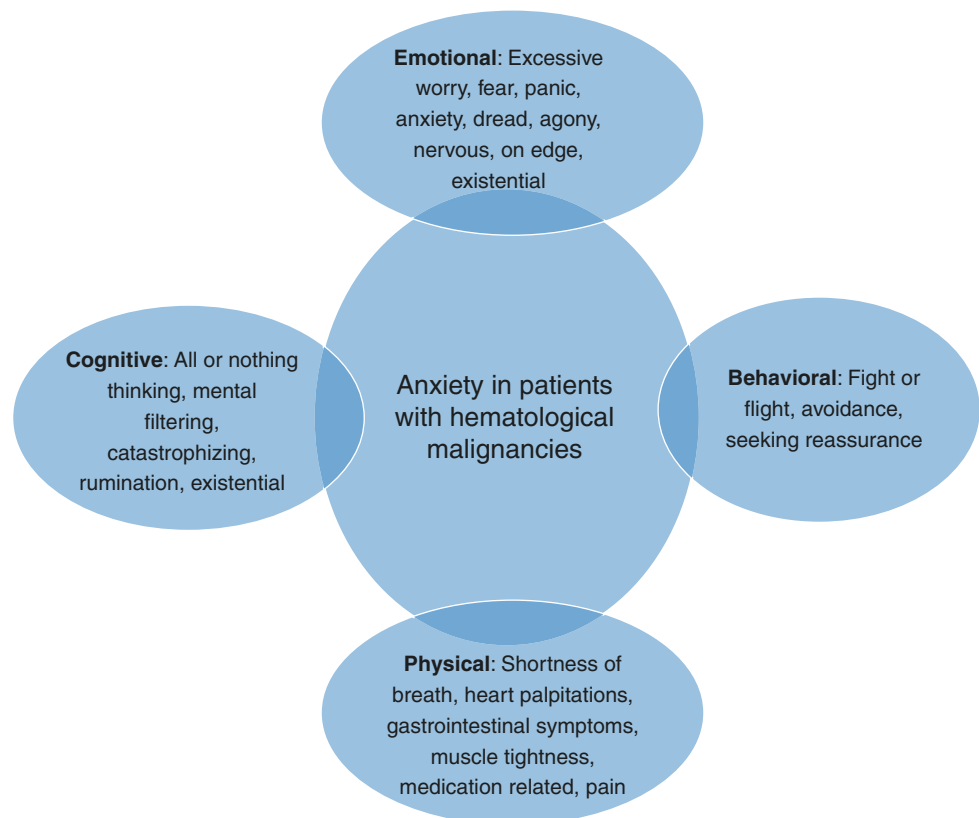
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methods [14]. People may experience anxiety symptoms from the onset of diagnosis and throughout the illness experience with shifts in roles, changes in functioning, financial stressors, and existential inquires. Anxiety may present as new symptom in these transitions or be reactivated from the past with the diagnosis of cancer [15]. Furthermore, patients with cancer may experience many factors related to the disease and associated with the treatment. In addition, medications, such as corticosteroids and antiemetics, as well as comorbid medical problems, such as a pulmonary embolism, may present as anxiety. Irrespective of the etiology, the presence of anxiety, especially in the form of a disorder, may negatively impact patients' quality of life (QOL) and treatment outcomes (Fig. 38.1). Thus, the screening, assessment, and treatment of anxiety disorders in patients with hematological malignancy is critical to comprehensive cancer care both for hospitalized patients and those undergoing outpatient evaluations for HCT. In a large 3-year prospective study of hospitalized patients undergoing HCT using the Hospital Anxiety and Depression Scale (HADS), anxiety was found to be the highest at the beginning of the hospitalization. This was related to the uncertainty and the fear undergoing the HCT, an aggressive medical therapy [16]. Guidelines from the American Society of Clinical Oncology recommend periodic screening for anxiety in patients with cancer with the use of screening tools and referral to mental health providers as clinically indicated [17] (Table 38.1).

## Depression

In a survey by the World Health Organization (WHO), 9.3–23% of participants with one or more chronic medical problem also had comorbid depression; depression had the largest impact on worsening mean health scores and increasing disability compared with other chronic conditions [18]. In a meta-analysis of 94 studies, the prevalence of depression in the cancer setting was 38% [14]. Depression in cancer is associated with greater physical, social, and existential distress and with measurable reductions in QOL [19]. Furthermore, depression in patients with advanced cancer may be associated with higher symptom burden [20].

Many factors may contribute to depression in patients with hematological malignancies. These include poor symptom control (e.g., mucositis), comorbid neurological disorders (e.g., cognitive impairment), and metabolic disorders (e.g., thyroid dysfunction). Cytotoxic therapies, disruptions in the hypothalamic pituitary adrenal axis, increases in pro-inflammatory cytokines, and paraneoplastic syndromes may also contribute to depressive symptoms in this patient population. Thus, it is important to note that comorbid medical disorders and/or treatments or symptoms associated with hematological malignancies (e.g., weakness, fatigue) can make it difficult to diagnose depressive disorders. Therefore, identifying risk factors for depressive disorders in this patient population is important for prevention and early diagnosis



**Fig. 38.1** Domains of Anxiety in Patients with Hematological Malignancies

**Table 38.1** Categories of anxiety disorders in patients with hematological malignancies

Anxiety disorders in hematological malignancies	
Primary psychiatric disorders	Generalized anxiety disorder Panic disorder Agoraphobia and other phobias Social anxiety disorder Obsessive-compulsive disorder Acute stress disorder Post-traumatic stress disorder Adjustment disorder with anxiety
Substance-induced anxiety disorder	Corticosteroids Antiemetics Stimulants Anticholinergics Withdrawal from nicotine, alcohol, benzodiazepines
Anxiety disorders due to medical condition	Somatic symptoms: Nausea, vomiting, pain Thyroid dysfunction Electrolyte derangements (e.g., hypercalcemia) Pulmonary embolism Pulmonary effusions

and treatment of depression. Additional contributory factors can be categorized into two groups: (1) general predisposing factors for depression and (2) psychosocial and personality factors. Past history of depression, family history of depression, and poor social support are among general predisposing factors for depressions. These have been associated with inflammatory responses in the brain. Personality factors also have been studied; Type D personality, characterized by negative affectivity and social inhibition, has been associated with worse mental health. However, studies have shown variable association between these biological and nonbiological factors [21]. In a recent multicenter study, a diagnosis of pre-HCT depression was associated with lower overall survival, higher risk of acute GVHD, and less days spent alive and out of the hospital during the first 100 days after HCT. These findings highlight the impact of pre-HCT depression on post-HCT outcomes and further identify the need for psychosocial assessments of patients with hematological malignancies prior to undergoing HCT [22].

## Demoralization

Demoralization is a term and concept introduced many years ago by Jerome Frank that recently has been described as a specific clinical entity in the oncology setting. Demoralization is characterized by existential despair, hopelessness, helplessness, and a subjective personal failure to achieve one's goals. It is associated with the loss of meaning and purpose in life. As a syndrome, it must persist for at least 2 weeks without the presence of a major psychiatric episode. Demoralization may be viewed as a spectrum that

encompasses disheartenment, despondency, despair, and fulminant demoralization syndrome, the last of which causes significant functional impairment [23–25]. There are two dominant measures of demoralization: a structured interview called the Diagnostic Criteria for Psychosomatic Research (DCPR) and the Demoralization Scale (DS), which is a self-report questionnaire [23,24]. Validation of the DS has allowed the estimation of demoralization among cancer patients to be 16% [26].

More recently, the Demoralization Scale-II was created as a self-report measure of demoralization consisting of 16 items and 2 subscales (meaning and purpose, distress and coping ability) [27]. Demoralization is clinically separate from depressive disorders, has a high prevalence in medical disorders, and, therefore, needs to be evaluated, measured, and treated during the course of the cancer illness experience. Differentiating between demoralization and depressive disorders is important for treatment planning and alignment of goals between providers and patients. Analyses of current measures of demoralization demonstrate that demoralization should be considered as a significant clinical entity in cancer settings to improve QOL [28]. In a longitudinal study of patients with acute leukemia evaluating physical and psychological well-being, depression, hopelessness, and demoralization were distinguished, and further investigation was recommended to evaluate, diagnose, and manage this distress in patients with leukemia [29]. With respect to demoralization in patients with cancer, a recent study showed an association with a significantly increased risk for suicidal ideation, further highlighting the importance of psychiatric evaluations of patients with hematologic malignancies [30].

## Suicide

Compared to the general population, individuals with cancer are at higher risk of suicide [31]. In a retrospective cohort study, there was a two times higher incidence of suicide in those with cancer compared to those without cancer. Patients were 13 times more likely to commit suicide within 1 week of receiving a cancer diagnosis. Patients were three times more likely to commit suicide within 1 year of cancer diagnosis than the general population [32]. Studies including individuals with hematological malignancies also have reported an increased risk of suicide [31, 33]. The risk of attempted and completed suicide was evaluated in a large population-based Swedish cohort study of over 40,000 patients diagnosed with lymphoma, myeloma, and leukemia. Patients with a hematological malignancy had a two times higher risk of completed suicide compared to those without cancer. A history of severe mental illness and a history of attempted suicide before diagnosis were associated with higher risk, although the overall greater risk of suicide was

not isolated to this group. The risk was highest within the first 3 months following diagnosis, and a 1.7-fold increase in risk of completed suicide remained after the first year of diagnosis. The findings of this study suggest an increase in suicidal intent in those with hematological malignancy [34].

In another large population-based study, patients with hematological malignancies were again found to be at increased risk for completed suicide and suicide attempt, particularly those with preexisting depressive disorders and alcohol use disorders [35]. Therefore, early identification of high-risk patients immediately after diagnosis and during follow-up is important as a preventative measure for suicide risk. These findings emphasize the need for multidisciplinary teams, psychiatric evaluations, and treatment to improve QOL measures and also to decrease the risk of suicide in patients with hematological malignancies.

## Delirium

Delirium is a neurobehavioral syndrome characterized by alterations in awareness, attention, cognition, language, and perception that is an abrupt change from the person's baseline due to a variety of endocrinologic, immunologic, neuroinflammatory, neurologic, and/or metabolic effects [36]. It is associated with increased morbidity and mortality, longer length of hospitalization, higher health-care costs, and distress among patients and their families. Delirium is a very common neuropsychiatric presentation in patients with cancer. Despite a prevalence of 10–30%, delirium continues to be underdiagnosed and untreated in patients hospitalized with cancer [37].

In patients with hematological malignancies, several pre-transplantation risk factors for delirium have been identified. These include lower pre-transplant renal, hepatic and cognitive functioning, acute leukemia, total body irradiation, and prior substance use. Additionally, chemotherapy-related hormonal changes in females and hypermagnesemia have been associated with a higher delirium risk. The diagnosis and treatment of delirium prior to HCT may reduce the risk and severity of delirium after HCT [38]. In a study by Fann, et al., potentially modifiable pre-transplantation risk factors were liver dysfunction, dehydration, and renal dysfunction. Pain control and judicious use of opioid medications were associated with lower risk of delirium. Identifying risk factors for delirium symptom severity is important in decreasing the morbidity from delirium before, during, and after HCT [39].

## Somatic Symptoms

### Pain

In cancer, pain is a multidimensional experience of physical symptoms, personality factors, cognition, and social and behavioral relations. The experience of pain may change

over the course of the cancer illness experience. A patient with cancer who has pain can be best treated when all of the different aspects of the pain are considered and addressed [40]. In patients with hematological malignancies, oral mucositis is among the most debilitating side effects of myeloablative therapy prior to HCT. Mucositis results from damage to mucosal epithelium of the mouth and throat with activation of proinflammatory cytokines in the submucosa, leading to oral ulceration. Oral mucositis can impact all aspects of QOL and interfere with daily activities, such as talking, eating, swallowing, and sleeping. The Oral Mucositis Daily Questionnaire (OMDQ) is a valid and reliable tool that can be used to measure mucositis severity. Treatment of mucositis includes basic oral care, anti-inflammatory agents, anesthetic agents, coating agents, and antimicrobials [41, 42]. Other types of pain in patients with blood dyscrasias include bone pain, paresthesias, treatment-related pain, infection-related pain, and skeletal lesions. Both preventative and interventional measures should be implemented to optimize the pain management of patients prior to undergoing HCT. Nonpharmacological and pharmacological treatments can be of particular benefit, and patient-related variables, such as performance status, comorbidities (including psychiatric illness), and concurrent medications should be considered when making clinical decisions about treatment [43, 44]. Research over the years has demonstrated that depression, anxiety, distress, and lower QOL are associated with greater levels of pain in patients with cancer. Using a biopsychosocial approach when evaluating pain can elicit such contributory factors and better delineate pain management options [45].

### Fatigue

Fatigue in cancer is a persistent, subjective experience of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment which is disproportionate to activity and interferes with usual functioning. Fatigue is a highly distressing symptom of cancer and is associated with decreased QOL and significant psychological and functional morbidity [46]. Severe fatigue has been reported more frequently in patients with hematologic malignancies than in those with solid tumors. Fatigue may be a presenting symptom at time of diagnosis of a hematologic malignancy; “B” symptoms of lymphoma include fatigue. A major contributor to increased fatigue and diminished QOL is anemia related to both the disease state and treatments. Other mechanisms, such as endocrine changes, physical deconditioning, impaired sleep, and alterations in cytokines, also have been proposed [47]. Physical exercise has been studied and recommended as an intervention for patients who will undergo HCT to improve physical activity, performance status, and quality of life [48, 49]. Managing psychiatric symptoms, anemia, metabolic derangements, and any nutritional deficiencies can improve

the severity of fatigue. Psychopharmacologic agents should be considered, particularly in cases where a patient's functional status is compromised prior to transplant [46, 50].

### Sleep

Sleep disorders, such as difficulty falling asleep, difficulty maintaining sleep, early awakening, and daytime sleepiness, are prevalent among patients with cancer. Sleep in patients with cancer may be impacted by a number of factors, including anxiety, depression, pain, and fatigue and may be related to biochemical changes associated with cancer and antineoplastic treatment [51].

Reasons for sleep disorders include thinking, pain or discomfort, concerns about health, concerns about family or friends, cancer diagnosis, physical effects of cancer, and concerns about finances [52].

Sleep disturbances and insomnia co-occur in symptom clusters in patients with cancer. The presence of symptom comorbidity in cancer may be related to underlying inflammatory processes common to all of them. The maintenance of circadian rhythms and consistent sleep wake patterns can reduce depressive symptomatology, improve overall perception of quality of life, and potentially improve outcomes and survival. Individuals with insomnia demonstrate cognitive, physiological, and cortical hyperarousal, cognitive patterns, and attentional biases. Cognitive behavioral therapy for insomnia (CBT-I) is a multimodal intervention to address these contributory factors. CBT-I has five main components: sleep restriction, stimulus control, sleep hygiene, cognitive restructuring, and relaxation training. A review of the literature has showed that CBT-I is associated with statistically and clinically significant improvements in subjective sleep outcomes in patients with cancer. CBT-I also may improve mood, fatigue, and quality of life during and after cancer treatment [53]. Pharmacologic interventions for sleep have not been adequately studied in patients with cancer. While they should be offered when indicated, caution must be exercised when prescribing these agents due to the potential for increased sedation, drug-drug interactions, delirium, and/or dependency.

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## Evaluation and Diagnosis

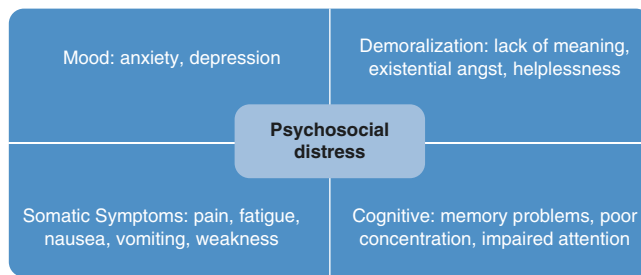
### Screening

Major depression, minor depression, anxiety disorders, and adjustment disorders are among the most common psychiatric presentations in patients with cancer. A clinically significant mood disorder can be predicted in four in ten patients early in their disease course [14]. Many patients also experience emotional difficulty after a cancer diagnosis but do not meet criteria for a DSM-V disorder. The concept of distress has garnered popularity as the sixth vital sign, following

temperature, blood pressure, pulse, respiratory rate, and pain. The National Comprehensive Cancer Network (NCCN) has established distress management guidelines and defined distress as the "multifactorial unpleasant emotional experience of a psychological (cognitive, behavioral, emotional), social, and/or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms and its treatment" [54, 55]. NCCN and other national guidelines promote the need for integrated psychosocial care and the use of psychometric assessments to help clinicians identify emotional problems in patients with cancers. Psychometric assessment would contribute to ruling out patients who do not need professional help (screening) and confirming the presence of a treatment psychiatric disorder (case finding). Psychometric assessment also would help quantify the severity of the disorder while monitoring for response to treatment [56].

The American College of Surgeons has established the Commission on Cancer's Cancer Program Standards which includes a process to integrate and monitor psychosocial distress screening and referral for the provision of psychosocial care. The standards require that all cancer patients be screened for distress a minimum of one time at a pivotal medical visit as determined by the program. The method of screening must utilize the expertise of physicians who can administer and interpret the screening tool. The tool used to screen should be a standardized, validated instrument. The distress screening then is to be discussed with the patient at the medical visit which may prompt a referral to a mental health provider [57].

Using the distress thermometer or asking a patient "are you worried?" or "are you depressed?" is a simple way to assess distress or anxiety [58, 59]. Screening for psychiatric symptoms and disorders in patients with cancer may include the use of a reliable, validated screening questionnaire or tool, of which there are many. The Generalized Anxiety Disorder-7 scale (GAD-7) and the Patient Health Questionnaire-9 (PHQ-9) are widely validated and used measures in medical populations [60, 61]. The Hospital Anxiety and Depression Scale (HADS) is the most extensively validated scale for screening emotional distress in patients with cancer. The thresholds for clinical decision-making vary widely, however, across studies [62]. A systematic review of assessment instruments to measure emotional distress in patients with cancer demonstrated the utility of both the HADS and the Center for Epidemiologic Studies Depression Scale (CES-D). The reviewers emphasized the importance of using short tools for screening of patients who undergo strenuous treatments, such as those with hematologic malignancies. Shorter tools may be better implemented in the setting of hospitalization prior to HCT [63]. While there are ongoing efforts to improve psychometric assessments for patients with cancer, such as the National Institute of Health project Patient-Reported Outcomes Measurement



**Fig. 38.2** Examples and sources of psychosocial distress

Information System network, the standard for psychosocial evaluation of patients with cancer continues to be structured clinical interviews (Fig. 38.2).

### Psychiatric Interview and Exam

Once a patient with a hematologic malignancy is determined by having signs of emotional distress, depression, anxiety, or another psychiatric symptom, a psychiatric assessment is considered the next step. Many dimensions of a person's psychological symptoms may be explored further with a clinical interview. The aim of a standard psychiatric interview and exam would be to establish whether or not there is a psychiatric disorder or another condition requiring clinical psychiatric and/or psychosocial attention. During the exam, clinical data is collected to support a differential diagnosis and a comprehensive formulation. The formulation may include the clinical diagnosis which can be derived from the DSM-V. There also may be a discussion about other variables in the patient's presentation, including coping and attachment, vulnerabilities, strengths, history of life events, and social support. Factors affecting the individual with cancer distinct from the clinical diagnosis may describe further the individual's psychosocial suffering [64].

### Quality of Life

Several domains of health-related QOL have been studied in patients treated with auto-HCT and allo-HCT. These include biomedical functioning (symptoms, disease, treatment), physical functioning (activities of daily living, sleep, fatigue), psychological functioning (cognitive, emotional, psychiatric symptoms), social functioning (social relations, support, education, socioeconomic status, work), and sexual functioning. Low social support and psychological distress prior to HCT have been identified to be predictors of diminished health-related QOL following HCT. Therefore, identifying factors that predict health-related QOL following HCT is important in understanding the ways patients may adapt to the consequences of the disease and treatment, such as resulting GVHD [65]. QOL assessments completed by patients before HCT have shown a strong association with

post-transplant physical and psychological functioning and also shown to be a strong independent predictor of post-HCT self-reported recovery through the first year [66]. Associations among psychosocial distress, coping responses, and QOL indicate that poor psychosocial functioning pre-HCT increases the likelihood of impaired QOL across the illness experience. Therefore, those who are more vulnerable should be identified and offered interventions earlier to help influence post-HCT outcomes [67]. A longitudinal study of QOL and physical and psychological symptoms experienced by patients with hematologic malignancies hospitalized for HCT and also their caregivers demonstrated the importance of addressing pre-HCT QOL, anxiety, depression, and fatigue in patients and offering psychiatric interventions where indicated. Additionally, the distress experienced by patients' caregivers was highlighted as another opportunity for supportive care interventions [68].

### Social Support

The role of social support on the impact of illness has been extensively studied. Social support is believed to affect health in three ways: (1) regulating thoughts, feelings, and behaviors to promote health, (2) fostering an individual's sense of meaning in life, and (3) facilitating health-promoting behaviors. Supportive relationships have been identified in the literature as an important component in the adjustment and psychosocial functioning of patients with cancer. In patients who undergo HCT, social support has been associated with significantly better psychosocial adjustment [69]. The use of the Psychosocial Assessment of Candidates for Transplantation (PACT) scale has been studied in patients with hematological malignancies undergoing allo-HCT. "Family or support system availability" was identified as an important subscale and associated with a decreased risk of mortality [70]. Social support, self-efficacy, and optimism before HCT have been associated with health-related QOL after HCT. Prior to HCT, patients may be offered a list of support groups, educational resources, and online support and also be encouraged to identify family, friends, and existing members of their community for support [71].

Caregivers for patients with hematologic malignancies are expected to provide extensive support throughout the illness and transplant. Caregivers and patients may experience changes in employment, housing, and shifts in roles. Caregivers are tasked with a variety of responsibilities related to providing medical support (e.g., monitoring and administering medications) and navigating logistical challenges (e.g., transportation). A review of the literature demonstrated that psychosocial distress among HCT caregivers is highest pre-HCT and decreases over time. Factors associated with this distress include being a female caregiver, higher levels of subjective burden, and higher symptom distress in the patient. Caregivers for patients undergoing HCT experience

uncertainty while adapting to changing roles and needing to balance their own needs with the patients' needs [72].

Studies suggest that rates of distress for caregivers following HCT may be the same as or greater than that of the patients in the immediate post-HCT period. Offering educational interventions and problem-solving therapy has demonstrated benefit in reducing caregiver distress and dyadic distress between the patient and his/her caregiver [73]. In a multicenter longitudinal study, the dyadic coping of patients with hematologic malignancies and their partners was investigated using the SF-12 questionnaire for QOL and the Dyadic Coping Inventory (DCI). Baseline QOL was the strongest predictor of physical and mental QOL for patients and their partners. Analyses of the DCI suggested the importance of incorporating patients' partners in a systematic way to help improve understanding of illness, improve compliance, and strengthen psychosocial adjustment [74].

### Financial Burden

The national cost of cancer care is expected to increase due to adoption of more expensive targeted treatments as standard of care. Additionally, as the population ages, the impact on cancer prevalence may exceed the impact of declining cancer incidence rates for some cancers. This will result in an increase in both the number of cancer survivors and cancer expenditures [75]. As the number of patients with cancer in the United States increases, the numbers of patients with cancer who are treated with chemotherapy and diagnosed with neutropenia are also expected to rise. In patients with hematologic malignancies, patients face hospitalizations for cancer-related neutropenia and associated infections. Hospitalizations related to neutropenic complications result in significant medical costs, longer lengths of hospital stay, morbidity, and mortality [76].

The term "financial toxicity" is used to describe the financial hardship as a result of cancer diagnosis and treatment. Financial toxicity encompasses adverse economic consequences due to medical treatment that may result in nonadherence and lifestyle changes for patients, impacting their QOL and increasing the morbidity and mortality of treatments. Higher costs of newer treatment, more out of pocket costs, barriers in communication about costs, and medical comorbidities are cited as sources of increased financial toxicity in patients with hematological malignancies. One area of intervention, therefore, may be increasing communication between providers and patients to influence shared decision-making, health behaviors, and health outcomes [77].

### Unmet Psychosocial Needs

A particular area of importance in patients with hematologic malignancies is unmet psychosocial needs. Psychosocial needs relate to a desire or requirement for support or help that underlies a patient's emotional or psychological welfare.

Examples include maintaining a sense of identity, body image, spirituality, relationships, social support, or practical issues related to a patient's illness experience. These needs are underreported to clinicians and may be left unacknowledged. In patients with hematological malignancies, the manner and setting in which treatment is received can differ from those diagnosed with solid tumors. Treatment is intensive, carries a high burden of illness, and can impact a patient's social, occupational, and family functioning. Data shows that fear of recurrence, needs relating to information, psychological needs, and fertility issues are unmet psychosocial needs in patients with hematological malignancies [78]. Currently, there is a lack of randomized trials of psychosocial interventions to address unmet psychosocial needs of these patients. Challenges are related to underutilized screening guidelines and tools in addition to lack of time allocated for managing these unmet needs. Increased efforts to screen for unmet needs in this population of patients would contribute to developing evidence-based interventions [79].

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## Special Considerations

### Sexuality and Fertility

Patients with hematologic malignancies undergo treatments that affect body image, sexual function, hormone levels, and reproductivity. Myeloablative regimens cause loss of ovarian function and sexual dysfunction. High-dose conditioning regimens of HCT cause gonadal and hormonal dysfunction [73]. The deterioration in fertility potential may be temporary or permanent. Fertility issues and difficulties related to sexuality span the illness experience and thus may impact the mental welfare of patients who are pre-HCT. Biological factors (e.g., treatment related), behavioral factors (e.g., medical prohibitions on sexual activity), relational issues (e.g., partner response to sexual changes), and psychological factors (e.g., sexual esteem) all contribute to compromised sexuality. The review of literature demonstrates that those who will receive HCT may experience long-term sexual problems, including decreased libido, decreased sexual activity, genital changes, erectile and/or ejaculatory dysfunction, and altered sexual appearance. Measures should be considered for sexual health counseling and fertility preservation in patients with hematological malignancies [80–82].

### Substance Use Disorders

All aspects of the cancer illness experience can be impacted by the use of substances and substance use disorders (SUD). Illicit drug or alcohol use disorders can cause nonadherence to potentially life-saving treatments. SUD can affect pain

management and increase morbidity and mortality. It has remained a challenge to diagnose SUDs in patients with cancer partly due to underdiagnosis. Patients with cancer with historic or current SUD may participate in aberrant drug-taking behavior which may prompt a treatment team to consult a psycho-oncologist. Prescription drug abuse, including opioids, may complicate pain management and compromise both medical and psychiatric stability. Tobacco use disorders have been shown to impact HCT outcomes, thus inferring the need for tobacco use cessation. A multidisciplinary approach for pain and symptom management is recommended in patients with cancer who have SUD [83–85].

## Decision-Making Capacity

Patients with cancer may have comorbid cognitive difficulties, dementia, or delirium related to a premorbid history of neuropsychiatric problems or as a consequence of the cancer and associated treatment. While screening measures and assessment tools are available, a diagnostic evaluation by a trained expert, such as a psychiatrist, would facilitate clinical decision-making, particularly in cases where decision-making capacity is of concern. Decision-making capacity consists of the patient's ability to understand relevant information, appreciate the situation and its consequences, manipulate information rationally, and communicate choices. Decision-making capacity can fluctuate with changes in patients' underlying medical or psychiatric problems, fatigue, or medication-related effects. Therefore, there may be a need to evaluate decision-making capacity more than once. In patients being evaluated for HCT, consideration of the afore-

mentioned factors is important when assessing decision-making capacity to assent to or to refuse a proposed treatment or intervention [86].

## Treatment

### Psychopharmacologic

Psychotropic medications are frequently used in this patient population to treat psychiatric symptoms and disorders, as well as to manage nonpsychiatric conditions, such as fatigue, delirium, suppressed appetite, neuropathic pain, as well as nausea and vomiting. Optimal treatment of contributory medical problems, such as insomnia, with medications should be tried as a means to improve psychosocial health. While there is a spectrum of indications for psychopharmacologic agents, many agents may also increase the risk for hematopoietic dysfunction. Caution should be exercised to minimize adding to the burden of neutropenia, agranulocytosis, abnormal bleeding, and platelet dysfunction. Psychopharmacologic agents may interact with anticancer therapies, causing worsening gastrointestinal side effects, anticholinergic effects, and increased sedation. Psychotropic agents should be utilized as indicated, among other appropriate interventions, to improve the medical and psychiatric health of patients with hematologic malignancies prior to HCT, while monitoring for tolerance and side effects [73, 87]. See Table 38.2.

### Non-Psychopharmacologic

Different modalities of psychotherapy have demonstrated efficacy for managing mood symptoms in patients with cancer [88]. These include cognitive behavioral therapy, prob-

**Table 38.2** Psychopharmacologic agents commonly used in patients with hematological malignancies

Medication class	Uses	Risks	Interactions	Hematologic effects
Antidepressants	SSRIs and SNRIs: Depression, anxiety, panic Mirtazapine: Sleep, appetite, nausea Bupropion: Fatigue	SSRIs: GI disturbances, headache SNRIs: GI disturbances, headache, hypertension Mirtazapine: Rare risk of agranulocytosis Bupropion: Seizures	MAOI interaction (e.g., procarbazine) CYP450 2D6 and 3A4 interactions (e.g., fluoxetine, paroxetine)	Cytopenias, platelet, impaired platelet aggregation
Anxiolytics: Benzodiazepines	Anxiety	Sedation, delirium, fatigue, respiratory depression, misuse	Narcotics, other sedative hypnotics	Cytopenias, platelet, impaired platelet aggregation
Antipsychotics	Anxiety, delirium, sleep Olanzapine: Nausea	Orthostatic hypotension, akathisia, EPS	QT prolongation with other agents, higher risk of EPS with antiemetics	Cytopenias, eosinophilia (clozapine)
Mood stabilizers, Anticonvulsants	Anxiety, irritability, delirium Gabapentin: Neuropathic pain	Sedation, weight gain Valproic acid: Transaminitis, decreased platelet aggregation, hair loss	Possible additive one marrow suppression with cytotoxic therapy	Cytopenia, anemia
Psychostimulants	Fatigue, concentration, depression	Anxiety, headache	Increased stimulation with corticosteroids	Not available

SSRIs selective serotonin reuptake inhibitors, SNRIs serotonin norepinephrine reuptake inhibitors, MAOI monoamine oxidase inhibitor, EPS extrapyramidal symptoms



lem-solving therapy, interpersonal therapies, group intervention, and behavioral activation. Relaxation therapy, mindfulness-based therapy, meaning-centered therapy, and dignity therapy are other approaches with principles that may be used to manage different causes of emotional distress. Other therapies, such as existential and psychodynamic, may be helpful in the setting of advanced disease. These many therapeutic approaches may be applied as indicated to patients with hematological malignancies before, during, and after HCT [73]. Please refer to Chap. 43 for further psychotherapeutic interventions.

### Conclusions

The American Society for Blood and Marrow Transplantation HCT guidelines for clinical centers include a psychiatric/psychosocial assessment as part of the medical evaluation for all HCT candidates [89]. Improving a treating team's knowledge of a patient's psychosocial distress, psychiatric history, social support, and other important psychosocial factors can influence medical outcomes before, during, and after HCT. Standardized approaches, such as the PACT, have been developed in identifying psychosocial concerns before HCT. Associations have been shown between psychosocial health and QOL with adherence to treatment, length of hospital stay, morbidity, and mortality. Screening measures to complement clinical interviews and exams can offer valuable opportunities to intervene and improve psychosocial variables in patients with hematologic malignancies. While there are many future directions for research, the psychosocial assessment of this patient population remains of paramount importance in assessing the risks for HCT, which may be the only treatment option. Therefore, a multidisciplinary, collaborative approach to meet the psychosocial needs of patients with hematological malignancies can contribute to better HCT outcomes.

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