Psychiatric Disorders in Advanced Cancer

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BACKGROUND. Emotional distress and psychiatric disorders are common among patients with advanced cancer. Oncologists play an important role in screening for these conditions, providing first-line treatment and referring patients for further evaluation and treatment when indicated.

METHODS. The literature on psycho-oncology was reviewed, focusing on the epidemiology, assessment, and treatment of psychiatric disorders (adjustment disorders, major depression, anxiety and post-traumatic stress, personality disorders, substance abuse, and major mental disorders such as schizophrenia and bipolar disorder) in patients with advanced cancer. Communication skills and the role of the oncologist in dealing with end-of-life issues were also reviewed. Relevant data were summarized from the most recent systematic reviews, epidemiological studies, and intervention trials. Clinical recommendations are provided.

RESULTS. About 50% of patients with advanced cancer meet criteria for a psychiatric disorder, the most common being adjustment disorders (11%–35%) and major depression (5%–26%). Both psychosocial and pharmacological treatments are effective for anxiety and depression, although existing studies have methodological limitations. Collaboration with mental health specialists is recommended for patients with personality disorders, major mental illness, and substance abuse problems. Effective communication involves active listening, exploring emotion and meaning, addressing prognosis, and discussing end-of-life issues when relevant.

CONCLUSIONS. Treating psychiatric conditions improves quality of life in patients with advanced cancer. Oncologists play a key role in screening for psychiatric disorders, initiating first-line treatments for depression and anxiety, and communicating with patients and caregivers about prognosis and end-of-life issues. ***Cancer* 2007;110:1665–76.** © *2007 American Cancer Society.*

KEYWORDS: cancer, terminal illness, anxiety, depression, distress, coping, communication, end of life.

Advanced cancer is distressing for both patients and their caregiver(s). In addition to suffering mounting physical debility, patients have to deal with the emotional impact of their illness and poor prognosis. Although most manage to cope effectively with these challenges, some do not. For instance, most terminally ill patients report having some positive feelings (65%),[1] but a few (3%) have frequent suicidal thoughts, which is a marker for distress.[2] Also, some patients have pre-existing psychiatric disorders that are exacerbated in the context of advanced disease, whereas others develop new symptoms of anxiety or depression during the course of their illness. And, all patients will eventually have to face the difficult task of preparing for death.

Not surprisingly, data show that emotional distress and psychiatric disorders are common among patients with advanced cancer

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and adversely affect quality of life.[3–6] However, oncologists frequently fail to recognize emotional distress and depression in patients.[7,8] Less than half of palliative-care patients who have moderate to severe depressive symptoms are on antidepressants, even though depression moderates desire for hastened death even more than pain does,[9] and even though depression and other psychiatric conditions are generally treatable, even in terminally ill patients.[10]

This article will help oncologists assess common psychiatric disorders in advanced cancer, initiate pharmacotherapy for symptoms of anxiety and depression, reduce patients' emotional distress through effective communication and routine emotional support, and make appropriate referrals to support groups and mental health professionals. It will also review the evidence for both pharmacological and psychosocial treatments for psychiatric disorders in advanced cancer, which comprises some randomized, controlled trials, but these findings do not yet contain strong evidence from systematic reviews of multiple high-quality studies.

Epidemiology of Psychiatric Disorders in Advanced Cancer

Prevalence rates for common psychiatric disorders in advanced cancer are summarized in Table 1. These data are compiled from a selection of well-designed recent studies that focused on advanced disease, terminal illness, and patients with high symptom burden (as in head an neck cancers and patients facing bone marrow transplantation).[3,6,11–15] In breast cancer, data show no significant differences in prevalence rates for early versus advanced disease.[3,4] Overall, about 50% (or more) of patients with advanced cancer meet criteria for a psychiatric disorder when the diagnosis of adjustment disorder is included, and psychiatric comorbidity is common (7.5%–35%).[3,6]

TABLE 1
Prevalence of Psychiatric Disorders in Advanced Cancer

	Advanced disease	Terminal illness	Caregivers
Adjustment disorder	14%–34.7%	10.6%–16.3%	—
Anxiety disorders			
Generalized anxiety	3.2%–5.3%	5.8%	3.5%
Panic disorder	4.2%	5.5%	8.0%
Post-traumatic stress	2.4%	0%	4.0%
Unspecified	—	4.7%	—
Any	6%–8.2%	13.9%	—
Depressive disorders			
Major depression	15%; range, 5%–26%	6.7%–17.8%	4.5%
Minor depression	7.2%–25.6%	2.1%	—
Dysthymia	—	4.5%	—
Any	14.1%–31%	20.7%	—

Adjustment Disorders

The most common psychiatric differential diagnosis confronted by oncologists is between an adjustment disorder and major depression.

Definition

The American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, 4th edition, (DSM-IV) defines an adjustment disorder as emotional and/or behavioral symptoms that are in excess of what would normally be expected from exposure to a given stressor.[16] This definition is vague in the oncology setting; thus alternative diagnoses (eg, demoralization syndrome) are currently being evaluated.[17,18] However, it is useful to think of an adjustment disorder as symptoms of situational anxiety or depression that are distressing enough to warrant treatment but that are not so strong and pervasive as to meet criteria for a full anxiety or depressive disorder. Symptoms of situational anxiety include insomnia, worry, muscle tension, restlessness, occasional shortness of breath, palpitations, sweating, trembling or shaking ("the jitters"), and feeling dizzy or lightheaded. Symptoms of situational depression include irritability, mood swings, tearfulness, poor concentration, social withdrawal, and transient spells of hopelessness or demoralization. Both types of symptoms can cause increased dependence on caregivers for emotional support.

Epidemiology

Adjustment disorders are the most common psychiatric syndromes that oncologists will encounter. Prevalence rates for patients with advanced disease are listed in Table 1.

Assessment

Adjustment disorders can present with symptoms of anxiety, depression, or both. The oncologist should inquire about the symptoms listed above, fluctuation in symptom severity, behavior at home and work, how the patient is coping, and cancer-related concerns. Pain and worry about changing tumor markers can fuel psychological distress,[19,20] as can concerns about work, finances, parenting, marital and family relationships, loss of independence, sexual function, and end-of-life issues. Tearfulness that is cathartic (ie, experienced as an emotional release) suggests an adjustment disorder, whereas depressive crying is draining and unrelieving. Although there is no ideal questionnaire for diagnosing adjustment disorders in cancer patients, the Hospital Anxiety and Depression Scale (HADS) is a brief, self-report instrument that can be used to assesses and monitor distress in

TABLE 2
Psychiatric Medications for Use in Patients With Advanced Cancer

Agent	Starting dose, mg	Normal dose, mg	High dose, mg	Schedule	P-450 inhibition	Advantages	Side effects	Warnings
Antidepressants								
SSRIs							All SSRIs & SNRIs:	All SSRIs & SNRIs:
Escitalopram	5	10	30	qD or HS	2D6	least side effects	GI distress, nausea, anorexia insomnia, drowsiness, headaches, tremors, sexual dysfunction, can activate anxiety	rare hyponatremia, serotonin syndrome, bleeding risk, and seizures in epilepsy
Citalopram	10	20	40–60	qHS	(2D6)*	mildly sedating, generic		
Sertraline	25–50	100	200	qD	(2D6, 1A2, 3A3/4)*	neutral, generic		
SNRIs								
Venlafaxine XR	75	150–225	300	qD or BID	none	can help hot flashes	tachycardia, dry mouth, urinary hesitancy/ retention	missed-dose withdrawal, rare hypertension
Other								
Mirtazepine	7.5	15–30	45	qHS	none	improves sleep, appetite, nausea, anxiety		occasional heavy sedation
Stimulants								
Methylphenidate	2.5–5	10	20	8 AM & noon	none	rapid onset of action, "gold standard," can get sustained-release forms	anxiety, tremors, insomnia, dry mouth, palpitations, irritability, dizzyness, arrhythmia	cardiac decompensation in elderly or heart disease; confusion in cognitively impaired
Anxiolytics & Sedatives								
Benzodiazepines							All benzodiazepines:	
Lorazepam	0.5	1	2	BID or TID	none	mostly widely used, anti-emetic	sedation, confusion, tolerance, abuse, disinhibition, gait instability	
Alprazolam	0.25	0.5	1	BID or TID	none	least sedating benzo, used only for that reason		withdrawal due to short half-life
Other								
Trazodone	25	50–100	200	qHS	none	nonhabit-forming	sedation	rare priapism
Antipsychotics (for nausea, delirium, anxiety)								
Olanzapine	2.5–5	5 or 10	15	qHS	none	very well tolerated, stimulates appetite	sedating at high dose	All antipsychotics: CVA in dementia-related psychosis, metabolic syndrome, NMS, QTc prolongation
Quetiapine	25	25–50	200	qHS	none	sedating	heavy sedation	
Haloperidol	0.5	0.5–1	2	BID	none	generic, low sedation, paid for by hospice	EPS (akathesia, dystonia)	

SSRI indicates selective serotonin reuptake inhibitor; SNRI, serotonin-norepinephrine reuptake inhibitors; NMS, neuroleptic malignant syndrome; qD, every day; HS, at bedtime; qHS, every night; BID, twice daily; TID, three times a day; CVA, cerebrovascular accident; EPS, extrapyramidal symptoms; QTc, corrected QT interval on electrocardiogram.
* Slight at high dose only.

patients with advanced disease. A combined score of 10 to 11 or higher suggests an adjustment disorder, whereas a score of 19 to 20 or higher suggests major depression.[21–23]

Treatment

Treatment of adjustment disorders is supportive and problem-focused. Educating patients, controlling physical symptoms, and maintaining effective communication are key strategies. Benzodiazepines can reduce anxiety symptoms and insomnia, whereas trazodone is a safe, effective, and nonhabit-forming sleep agent (see Table 2 for dosing).[24,25] Patients benefit from the opportunity to discuss their concerns about loved ones, meaning, future care options, and end-of-life issues; oncologists should listen for and encourage discussion of these issues when patients bring them up or allude to them. Evidence shows that using a multidisciplinary team approach and telephone monitoring reduces symptoms of psychological distress in patients with advanced disease.[26,27] Good collaboration and communication with mental

health providers about medical issues, prognosis, and patient concerns facilitate effective treatment.

Both support groups and individual counseling are effective for patients with adjustment disorders and advanced cancer. Supportive-expressive therapy focuses on current life problems, key relationships, challenges to effective coping, and expression of emotions in a receptive environment. Cognitive behavior therapy (CBT) encourages patients to identify overly negative or irrational interpretations (cognitions) they have about themselves, their illness, and life situation; to analyze how these thoughts are being translated into dysfunctional behaviors; and then coaches them to adopt more reasonable cognitions and more functional behaviors. CBT can also include training in relaxation techniques to manage stress. CBT and supportive expressive therapy have both been shown to reduce symptoms of anxiety and distress in advanced cancer.[28–31]

Major Depression

Definition

According to the DSM-IV, major depression is defined by persistent low mood, or anhedonia (pervasive loss of interest or pleasure), that lasts for 2 weeks or more and is accompanied by at least 4 of the 9 following symptoms: sleep disruption (especially early morning insomnia), weight loss or change in appetite, psychomotor retardation or agitation, fatigue or loss of energy, feelings of worthlessness or excessive guilt, diminished ability to think or concentrate, and recurrent thoughts of death or suicidal ideation.[16] Because many neurovegetative (physical) symptoms of depression can be caused by cancer or side effects of treatment, different approaches to diagnosis have been proposed.[32] Given evidence about the bidirectional relation between fatigue and depression in cancer patients,[33] and the finding that inflammatory cytokines may cause both depression and the cancer "sickness syndrome,"[34,35] we favor including all neurovegetative symptoms as indicators of depression in patients with advanced disease.

Epidemiology

See Table 1. The highest rates of depression are seen in patients with cancers of the pancreas, oropharynx, and breast.[36] Past history of depression is probably the single greatest risk factor for current major depression in patients with advanced cancer[12]; others include younger age, poor social support network, poor functional status, and pain.[32] Corticosteroids, hypothyroidism or hyperthyroidism, tamoxifen, interferon, anemia, brain tumors or metastases, antiandrogen treatments, and certain chemotherapeutic agents (vincristine, vinblastine, procarbazine, and L-asparaginase) can also predispose cancer patients to depression.[32,37–39] Major depression may be associated with shorter survival time in some cancer patients,[40] especially hematological cancers after stem cell transplantation and low-grade gliomas[41,42]; data on survival in lung cancers are mixed.[43,44] Depression is associated with decreased adherence to treatment, prolonged hospital stays, and reduced quality of life.[45,46] It is a major risk factor for desire to hasten death,[9,47,48] and as many as 59% of terminally ill patients who request assisted suicide are depressed.[49]

Assessment

Oncologists should begin by asking the patient if he or she feels depressed, which in itself has utility as a screening tool,[50,51] and then inquire about the cardinal signs and symptoms of major depression listed above as well as any personal or family history of depression, which is a key risk factor. The patient should be observed for evidence of depressed affect, or slowed thinking or movements (psychomotor retardation), as some patients are more depressed than they verbally report. For the same reason, it is helpful to obtain collateral information from the patient's family and/or caregivers about their behavior and mood at home. Other common signs and symptoms of depression include irritability, social withdrawal, body aches or lowered pain threshold, tearfulness, and feelings of hopelessness or helplessness. Questions about how patients see the future and how much they believe they can influence their care probe for hopelessness and helplessness, whereas questions about concerns of burdening others probe for worthlessness and guilt. Normalizing the occurrence of suicidal thoughts in advanced disease gives patients permission to be frank about suicidal thoughts or plans.[32] Also, clinicians need to assess for substance abuse and rule out a past history of mania or hypomania (defined below).

In patients with advanced disease, clinicians often need to differentiate major depression from anticipatory grieving. Both depression and grief are associated with somatic distress, sleep and appetite disturbance, poor concentration, and social withdrawal. However, patients who are grieving experience waves of sadness that is clearly linked to the loss, retain the capacity for pleasure, and may have passive wishes for death but are able to look forward to the future, whereas depressed patients present with pervasive anhedonia, are unable to look forward to anything, and may have active suicidal thoughts.[52] The treatment for anticipatory grief is supportive-expressive therapy.

Treatment

Contrary to common misconceptions, depression is a treatable condition, even in patients who are terminally ill. However, to treat depression in this setting, physical symptoms (pain, nausea, constipation, dyspnea, etc) need to be controlled, and physicians may need to address patients' concerns about being labeled "depressed" before these patients become willing to accept treatment. Because of the low rate of complications from treatment of depression, experts recommend a strategy of "if in doubt, treat." A combination of antidepressant medication, supportive psychotherapy, and patient and family education are the gold standard of treatment for depression in advanced disease.[32,52] Several randomized, controlled trials that compared antidepressants with a placebo for depression in cancer patients suggested a benefit from treatment.[53–56]

Pharmacotherapy. Antidepressants for use in patients with advanced cancer are summarized in Table 2. Because antidepressants generally have equal efficacy, they are selected based on cost, side-effect profile, potential for P450 enzyme interactions, past history of response, and the patient's life expectancy (eg, stimulants are used when life expectancy is less than 2–3 weeks).

Psychostimulants. Methylphenidate and related stimulants are widely used in cancer and palliative care, and these stimulants improve mood, appetite, energy, and cognition.[57–59] Stimulants act rapidly (24–48 hours), counter opioid-related sedation, and have adjuvant analgesic activity. They are the treatment of choice when time is short, and they are often combined with a selective serotonin reuptake inhibitor (SSRI) in severe depression. The Food and Drug Administration (FDA) recently added a black-box warning for risk of cardiac death to methylphenidate and related stimulants. This warrants informed consent but, again, should not stop oncologists from using these valuable agents when appropriate.

SSRIs. Serotonin-specific reuptake inhibitors are the first-line agents when life expectancy is 2–3 weeks or more, and they are safe and well tolerated in cancer patients.[60–62] They are especially useful for depression with irritability and/or comorbid anxiety. To avoid initial side effects, oncologists should prescribe a starting dose for 4–7 days, then increase to the normal dose (see Table 2). Educate the patient that antidepressants take about 2 weeks for initial response and 4–6 weeks to reach peak effect at a given dose. If the patient obtains a partial response after 1 month on a normal dose, increase to a higher dose to get a complete response. If the patient shows little or no response, switch to another agent. Patients who fail 2 different SSRIs, or obtain only a partial response, should be referred to a psychiatrist for further evaluation and treatment.

SNRIs. Serotonin-norepinephrine reuptake inhibitors (SNRIs) may be efficient choices for depression with comorbid neuropathic pain, as they can have antipain properties similar to those of tricyclics. Note that both SSRIs and SNRIs can prolong bleeding time, thus informed consent is advised in patients who are at high risk of serious gastrointestinal or cerebral bleeding; however, this side effect is rare and should not deter oncologists from using these agents in all but a few patients.[63]

Other antidepressants. Mirtazepine is especially useful as it can improve multiple symptoms, including depression, appetite loss, pain, nausea, anxiety, and insomnia.[64] Bupropion has reduced fatigue in cancer patients and may lower tumor necrosis factor alpha but is a second-line agent in advanced disease because of seizure risk.[65,66] Tricyclics are effective for depression in cancer patients but are also second-line agents because of their frequent side effects (Table 2).

Psychotherapy

The most recent systematic review found insufficient trial data to judge the efficacy of either antidepressants or psychotherapy for treating major depression in cancer patients. However, several small-scale trials of psychotherapy (especially CBT) were noted to improve depressive symptoms in cancer patients.[67] Current evidence indicates that a variety of treatment models are helpful for depression, such as training oncology nurses to diagnose and treat depression in cancer patients,[68] exercise (even in patients with advanced disease),[69,70] and cognitive therapy delivered by videophone to terminally ill patients.[71]

Anxiety and Post-traumatic Stress

Definition

Anxiety disorders include generalized anxiety disorder, panic disorder, obsessive-compulsive disorder, social anxiety disorder, specific phobias (such as of needles or blood), and post-traumatic stress disorder (PTSD). This section emphasizes PTSD, which in cancer patients can result from the psychological trauma of diagnosis and/or treatment, especially if the patient experiences unexpected and highly debilitating complications of treatment. The cardinal signs and symptoms of PTSD include persistently re-experiencing the traumatic event(s) through intrusive recollections, distress-

ing dreams, or flashbacks; high emotional distress when exposed to reminders of the event(s); persistent avoidance of stimuli associated with the trauma; general numbing of emotion; and increased physiological arousal or hypervigilance.[16,72,73]

Epidemiology

Significant anxiety symptoms occur in about 25% to 48% of cancer patients,[74,75] whereas 2% to 14% of patients with advanced disease meet diagnostic criteria for an anxiety disorder (Table 1). Subsyndromal PTSD occurs in 20% to 80% of cancer patients,[72] depending on methodological factors involved in assessment. Anxiety symptoms may also result from substance abuse, medication side effects, delirium, or undertreated physical symptoms, especially pain. Medications that can contribute to anxiety include antipsychotics, such as phenothiazines and butyrophenones used to control delirium, and antiemetics, such as prochlorperazine and metoclopramide. These agents block dopamine centrally and can cause akathesia. Rapid withdrawal of opioids, corticosteroids, anticonvulsants, benzodiazepines, nicotine, and clonidine can also precipitate anxiety.[76]

Assessment

Patients with high situational anxiety often repeat questions, cannot hold onto information provided, and may either over-react to side effects of treatment or demonstrate stoic, restricted affect. They may be suspicious of the physician's recommendations or not ask questions at all due to paralyzing fear.[10] Patients with anxiety due to substance abuse or medication side effects and/or withdrawal are often physically restless or agitated, and they may have diarrhea, tachycardia, diaphoresis, hyperreflexia, and hypertension. Patients with PTSD often present with high levels of anxiety, pronounced insomnia, frequent panic attacks, comorbid depression, excessive fear of medical recommendations, and avoidance of medical settings or procedures that trigger traumatic memories. They may also engage in substance abuse in an attempt to self-medicate their symptoms. Risk factors for PTSD include prior history of traumatic exposure (such as physical or sexual abuse), negative interactions with physicians and nurses, and poor social or interpersonal support.[72] There is some evidence that cancer recurrence leads to increased symptoms of PTSD in patients with advanced disease[77] and that pain can be a traumatizing stimulus that reawakens or heightens PTSD symptoms at the end of life.[78]

Treatment

Oncologists can help anxious patients by exploring their fears and concerns in a nonjudgmental fashion and by prescribing SSRIs or benzodiazepines for especially anxious patients (Table 2). Providing reassurance generally does not lower anxiety and can make highly anxious patients even more anxious.[79] A more effective strategy is to listen, acknowledge the patient's concerns, agree that dealing with advanced disease is difficult, and remind them that you will remain available to help, seeking psychiatric consultation if these interventions do not work. Supportive-expressive therapy is generally the best approach for treating anxiety disorders in patients with advanced cancer, the aim being to reduce symptoms and maintain coping, rather than to provide curative treatment. Supportive-expressive therapy has been shown to reduce distress and subsyndromal symptoms of PTSD in women with advanced breast cancer.[30]

Personality Disorders

Definition

Personality disorders are chronic character styles that lead to clinically significant interpersonal and behavioral problems. Narcissistic, histrionic, and borderline personality disorders are the ones that most commonly cause problems in medical settings. These are characterized by demanding, seductive, manipulative, and/or aggressive behaviors.

Epidemiology

The prevalence of borderline and histrionic personality disorders is about 2% to 3% each in the general population, whereas narcissistic personality disorder occurs in $<1\%$ of the general population.[16] Prevalence rates in cancer patients are about the same.[74]

Assessment

Patients with narcissistic personality disorder are demanding, exploitative, entitled, and often expect "royal" treatment from physicians; those with histrionic personality disorder are overly dramatic, "hysterical," and/or seductive; and those with borderline personality disorder have a turbulent and provocative interpersonal style characterized by impulsivity, excessive anger, marked mood swings, recurrent suicidal behavior or threats, and alternating between extremes of idealizing and devaluing others.[16] They also tend to present different information and feelings to different healthcare providers (splitting), which can lead to conflicts with staff and among members of the medical team.[80] Most patients with personality disorders show a mixture of these traits, and their behavior elicits difficult reactions in clinicians (such as feeling overwhelmed, inadequate, disengaged, parental or overprotective, mistreated, sexually aroused, and/or guilty).[81] Oncologists who are struggling with these

sorts of feelings about a patient should consider the diagnosis of a personality disorder in the patient.

Treatment

In the oncology setting, the main treatment for patients with personality disorders is close liaison with mental health consultants, who can help set limits with the patient, guide team meetings to reduce conflict among staff members, and provide education and emotional support to medical providers.[80] Psychotherapies can be effective for treating personality disorders, but often take years and are generally not feasible for patients with advanced disease. Pharmacotherapy for personality disorders has limited utility, but comorbid anxiety, mood, and substance abuse disorders should be treated.

Substance Abuse

Definition

Substance abuse is defined as a maladaptive pattern of substance use that is associated with failure to fulfill major role obligations at home or work, driving or operating machinery while intoxicated, and legal or interpersonal problems related to the substance. Substance dependence involves substance abuse plus physiological tolerance and withdrawal, failed efforts to control substance abuse, or continued abuse despite significant medical consequences.[16]

Epidemiology

The prevalence of alcoholism ranges from 7% to 27% in different palliative care settings.[82,83] In patients with head and neck cancer, 33.6% meet criteria for alcohol dependence, whereas 6.5% meet criteria for abuse.[5] In patients with lung cancer, 13% meet criteria for alcohol dependence.[15] Point prevalence for other substance-use disorders varies widely in the general population, but in the United States, it is about 0.1% to 1.5% (each) for benzodiazepines, opioids, amphetamines, cocaine, hallucinogens, and marijuana.[16]

Assessment

In the setting of advanced cancer, substance abuse often presents as use of benzodiazepines and/or opioids in excess of amounts typically needed to control symptoms. However, before jumping to conclusions, clinicians should try to differentiate substance abuse (“chemical coping”) from drug-seeking behavior due to unrelieved pain, anxiety, or insomnia. Begin with a nonjudgmental approach, ie, review the quantity and frequency of both prescription and nonprescription substance use, ask how the patient feels the substance(s) help, whether they have any concerns about addiction, and what other treatments they have tried for their distressing symptoms. Also inquire about any past history of substance abuse, treatments sought and how well they worked, longest period of sobriety or abstinence, and level of interest in seeking help for any current substance abuse problem. While taking this history, observe the patient for any signs of lying, and consider how believable their explanations about lost prescriptions or requests for early refills seem. Using the CAGE assessment or the Alcohol Use Disorders Identification Test (AUDIT) questionnaire can help screen for alcohol abuse among medical patients, but there are no validated instruments for assessing other abused substances.[84,85]

Treatment

Managing substance abuse is important in advanced disease because uncontrolled substance abuse tends to worsen psychiatric conditions and decrease the effectiveness of palliative-care interventions. However, the goal of treatment shifts from abstinence to decreasing illicit drug or alcohol intake sufficiently to improve symptom control and quality of life.[86] Patients with a history of addiction may require higher doses of analgesics to achieve adequate pain relief, as they may have developed tolerance to opioids and have low tolerance for distress. Clinical recommendations include repeated assessments of pain and analgesic use, medication contracts, dispensing limited supplies of controlled substances, encouraging participation in recovery programs such as Alcoholics Anonymous (AA) and Narcotics Anonymous (NA), and using pill counts and urine toxicology screens as necessary.[87] Liaison with psychiatrists and substance abuse counselors and/or programs can help the oncologist achieve these goals. Benzodiazepines are used to treat alcohol or sedative/hypnotic withdrawal, but there are no reliable medications for treating addiction.

Major Mental Illness

Schizophrenia

Definition. Schizophrenia is a chronic psychotic illness characterized by delusions, hallucinations, disorganized speech or behavior, flattened affect, and apathy.[16]

Epidemiology. Prevalence rates of schizophrenia are 0.5% to 1.5% worldwide.[16] Rates should be the same for cancer patients.

Assessment. Disheveled appearance, disorganized speech or behavior, odd beliefs or mannerisms, poor eye contact, blunted affect, reported delusions or hallucina-

tions, paranoia, homelessness, being on antipsychotic medication(s), and/or living in a group home are all possible clues to the diagnosis of schizophrenia. Many of these factors may frighten medical staff or make it difficult to form an alliance with the patient.

Treatment. Taking care of schizophrenic patients with cancer can be challenging, as they frequently have poor insight and recall of medical recommendations, are often socially isolated and economically disadvantaged, may have problems with substance abuse, and are often diagnosed with late-stage disease because of lack of access to or poor compliance with primary care.[88–90] Therefore, close collaboration with mental health providers is advisable to ensure appropriate use of medications and community resources. Although some mentally ill patients may lack decision-making capacity around cancer treatment(s) or end-of-life care, data show that typical patients with serious mental illness are interested in advance care planning but often have not discussed it, are able to consider and communicate their preferences, and share the same end-of-life concerns as patients without mental illness, ie, pain and suffering, financial and emotional burden on family, saying "goodbye," spiritual issues, and final arrangements.[91,92]

Bipolar Disorder

Definition. Bipolar disorder is a chronic mood disorder characterized by recurrent episodes of mania (described below) with or without interspersed spells of depression.[16]

Epidemiology. Lifetime prevalence of bipolar disorder is 0.4% to 1.6% in the general population.[16] Rates should be the same for cancer patients. Corticosteroids, stimulants, antidepressants, and interferon[93] can all induce or exacerbate mania in patients with bipolar disorder.

Assessment. Signs and symptoms of mania include elevated or expansive mood, pronounced irritability, pressured speech, decreased need for sleep, grandiosity (sometimes with religious preoccupation or delusions), racing thoughts, distractibility, increased goal-directed activity (either socially or vocationally), and excessive involvement in pleasurable activities, such as shopping, gambling, or sexual activity. Severe mania can present as agitation or even frank psychosis.

Treatment. Patients with bipolar disorder should be followed by a psychiatrist while undergoing cancer treatment to maintain mood stabilization and ensure proper use of psychiatric medications. Standard treatments are mood-stabilizing agents, such as lithium, anticonvulsants, and antipsychotics. Manic patients often lack decision-making capacity but generally regain it when psychiatrically stabilized. Oncologists should review the potential for inducing mania of all chemotherapeutic agents being considered in patients with bipolar disorder.

Role of the Oncologist

Communication

The most important communication skill for helping patients cope with advanced disease is empathic listening. By listening, the physician provides the patient a chance to be heard and understood, explore fears and concerns, mourn losses, articulate hopes and final wishes, and share the unique meaning that illness has for each individual. Listening reminds the patient that the physician is not too scared, too tired, or too busy to be present, and demonstrates that the patient, who may be diminished by illness, is still valued. Techniques that can facilitate active listening include using open-ended questions, following up on emotionally charged comments, exploring associations and expressed concerns, and reflecting on the patient's affect.[10] Checking understanding, encouraging question-asking, offering to delay decisions when needed, and nonverbal behaviors that convey warmth and empathy can also help.[94] Physician burnout is associated with poor communication skills;[95] training programs improve skills and physician satisfaction.[96–98]

Prognostic discussions are important, but the evidence on how best to conduct them is still incomplete, especially in advanced disease.[99] Data indicate that up to 98% of patients with advanced disease want their physicians to be realistic, to provide an opportunity to ask questions, and to acknowledge them as individuals when discussing prognosis.[100] Before embarking upon prognostic discussions, it is important to negotiate who should be present and who should deliver the information; also, clarify what patients and caregivers understand and how much information each party wants. It can be useful to have separate discussions with patients and caregivers. Dealing with desire to restrict access to information by either party is challenging.[101,102] Discussing life expectancy is helpful, as it allows patients to focus on personal goals about how to use remaining time, but it is also important to explain the uncertainties and limitations in making survival predictions.[103]

End-of-Life Issues

Supporting physical comfort, easing emotional distress, treating depression and anxiety, and helping patients achieve a degree of peace are key goals in end-of-life care. Oncologists can help foster coping

in terminally ill patients by emphasizing what can be done, such as controlling physical symptoms, providing emotional support, assisting with practical matters, supporting key family members, and setting realistic goals.[104] Validating patients' search for meaning and spiritual peace at the end of life is also important.[105] Psychotherapies focused on dignity and meaning have been developed for terminally ill patients and appear to be effective.[106,107] Psychiatric consultants can help oncologists assess suicidality in terminally ill patients, treat depression and anxiety in difficult cases, and deliver targeted psychotherapy.

Important areas for oncologists to address when discussing the end of life include treatment decisions, potential future symptoms, preferences for place of death, what needs to be done immediately after death, and existential issues. Also, it is important to discuss the patient's concerns about the process of dying, explore fears about the process, dispel misconceptions, and describe what the patient is (and is not) likely to experience in the final days.[108] Recent data show that patients who are aware of their terminal prognosis and are at peace with it have higher rates of advance care planning, better quality of death, and better mental health outcomes.[109]

Finally, as patients approach the end of life, the focus of care shifts increasingly to include the caregiver. Caregivers have similar rates of psychiatric disorders as patients with advanced disease (Table 1).[12,110] Notably, when patients with advanced disease meet criteria for any psychiatric diagnosis, their caregivers are 7.9 times more likely to meet criteria for any psychiatric diagnosis as well, and vice versa. This mutuality of risk suggests that patients and caregivers should be assessed and treated as a unit.[111] Also, hospice enrollment of 3 days or less before death is a significant risk factor for later depression in the bereaved caregiver, suggesting that early hospice referral may be a preventive mental health intervention for caregivers.[112]

Care of the bereaved is beyond the scope of this article but represents the final phase of oncologic care. In general, no mental health treatment is needed for caregivers who exhibit normal grieving, although they may find bereavement support groups to be helpful. Family members benefit from a condolence telephone call and a written note from the oncologist; many community-based resources exist, especially in hospice programs, to support the bereaved.

CONCLUSION

Psychiatric conditions are common in patients with advanced cancer and adversely affect quality of life but are generally treatable. Oncologists can help reduce psychological distress in patients with advanced cancer through communicating effectively, providing routine emotional support, screening for psychiatric disorders, appropriately prescribing anxiolytic and antidepressant medications, referring patients to support groups, collaborating with mental health professionals, and dealing with end-of-life issues.

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