Assessing and treating depression in palliative care patients

Antidepressants, psychotherapy can improve dying patients' quality of life

Depression is highly prevalent in hospice and palliative care settings—especially among cancer patients, in whom the prevalence of depression may be 4 times that of the general population.[1] Furthermore, suicide is a relatively common, unwanted consequence of depression among cancer patients.[2] Whereas the risk of suicide among advanced cancer patients may be twice that of the general population,[3] in specific cancer populations (male patients with pancreatic adenocarcinoma) the risk of suicide may be 11 times that of the general population.[4]

Mental health professionals often are consulted when treating depressed patients with advanced illness, especially when suicidal thoughts or wishes for a hastened death are expressed to oncologists or primary care physicians. To mitigate the effects of depression among seriously ill patients (***Box, page 36***),[5,6] mental health professionals must be able to assess and manage depression in patients with progressive, incurable illnesses such as advanced malignancy.

Diagnostic challenges

Assessing depression in seriously ill patients can be a challenge for mental health professionals. Cardinal neurovegetative symptoms of depression, such as anergia, anorexia, impaired concentration, and sleep disturbances, also are common manifestations of advanced medical illness.[7] Furthermore, it can be difficult to gauge the significance of psychological distress among cancer patients. Although depressive thoughts and symptoms may be present in 15% to 50% of cancer patients, only 5% to 20% will meet diagnostic criteria for major depressive disorder (MDD).[8,9] You may find it challenging to deter-

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Palliative care

Clinical Point

Side effects from commonly used therapeutics for cancer patients can mimic depressive symptoms

Box

Don't underestimate the impact of depression in this setting

Left untreated, depression in seriously ill patients can be associated with increased physical symptoms, suicidal thoughts, worsened quality of life, and emotional distress.[5] Moreover, depression can impair the patient's interaction with family during a pivotal time in which patients may be saying goodbye, thank you, or planning for their death. Depressive symptoms even can erode the construct of patient autonomy by interfering with one's ability to engage in medical decisions and attain a sense of meaning from their illness.[6]

Table 1

Questions included in Robinson's 4-point algorithm

1. In the past 2 weeks, have you been worn out or had too little energy, even when you haven't been doing a lot?
2. During the past 2 weeks, have you often been bothered by a lack of interest or pleasure in doing things?
3. In the past 2 weeks, have you been feeling depressed or sad at all?
4. In the past 2 weeks, have you talked or moved more slowly than is normal for you? Were you so restless that you couldn't sit still?

Source: Reference 15

mine whether to use pharmacotherapy for depressive symptoms or whether engaging in reflective listening and exploring the patient's concerns is the appropriate therapeutic intervention.

Side effects from commonly used therapeutics for cancer patients—chemotherapeutic agents, opioids, benzodiazepines, glucocorticoids—can mimic depressive symptoms. Clinicians should include hypoactive delirium in the differential diagnosis of depressive symptoms in cancer patients. Delirium is an important consideration in the final days of life because the condition has been shown to occur in as many as 90% of these patients.[10] A mistaken diagnosis of depression in a patient who has hypoactive delirium (see "Hospitalized, elderly, and delirious: What should you do for these patients?" page 10) might lead to a prescription for an antidepressant or a psychostimulant, which can exacerbate delirium rather than alleviate depressive symptoms.

Significant attitudinal barriers from both clinicians and patients can lead to underrecognition and undertreatment of depression. Clinicians may believe the patient's depression is an appropriate response to the dying process; indeed, feeling sad or depressed may be an appropriate response to bad news or a medical setback, but meeting MDD criteria should be viewed as a pathologic process that has adverse medical, psychological, and social consequences. Time constraints or personal discomfort with existential concerns may prevent a clinician from exploring a patient's distress out of fear that such discussions may cause the patient to become more depressed.[11] Patients may underreport or consciously disguise depressive symptoms in their final weeks of life.[12]

Responding to these challenges

The Science Committee of the Association of Palliative Medicine performed a thorough assessment of available screening tools and rating scales for depressive symptoms in palliative care. Although the committee found that commonly used tools such as the Edinburgh Depression Scale and the Hospital Anxiety and Depression Scale have validated cutoff thresholds for palliative care patients, the depression screening tool with the highest sensitivity, specificity, and positive predictive value was the question: "*Are you feeling down, depressed, or hopeless most of the time over the last 2 weeks*?"[13,14]

Other short screening algorithms have been validated among palliative care patients (***Table 1***).[15] Endicott proposed a structured approach to help clinicians differentiate MDD from common physical ailments of progressive cancer in which physical criteria for an MDD diagnosis are substituted by affective symptoms (***Table 2***).[16] The improved risk-benefit ratio of selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs), coupled with the potential significant morbidity associated with MDD and subsyndromal depressive symptoms, makes it necessary to recognize and treat those symp-

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toms even when the cause of the depressive symptoms is unclear.

Psychotherapy in palliative care

Psychotherapeutic interventions such as dignity therapy, which invites patients to utilize a meaning-centered life review to address his (her) existential concerns, may help depressed palliative care patients.[17] Evidence suggests a strong association between diminished dignity and depression in patients with advanced illness.[18] Individualized psychotherapeutic interventions that provide a framework for addressing dignity-related issues and existential distress among terminally ill patients could help preserve a sense of purpose throughout the dying process. Surveys of dignity therapy have been encouraging: 91% of participants reported being satisfied with dignity therapy and more than two-thirds reported an improved sense of meaning.[18]

Other promising psychotherapeutic interventions include supportive-expressed group therapy, in which a group of advanced cancer patients meets with a mental health professional and discusses goals of building bonds, refining life's priorities, and "detoxifying" the experience of death and dying.[19] A primary purpose of this therapy is not just to foster improved relationships within a group of cancer patients, but also within their family and oncology team, with the aim of improving compliance with anticancer therapies. Nurse-delivered, one-on-one sessions focusing on depression education, problem-solving, coping techniques, and telecare management of pain and depression also improves outcomes among depressed cancer patients.[20]

Hospital-based inpatient and outpatient palliative care consultation teams are becoming more common. A randomized controlled trial of early palliative care outpatient consultation for patients with incurable lung cancer showed improved depression outcomes, better quality of life, and a modest improvement in survival.[21] Although the most effective elements of a palliative care consult remain unspecified and require further research, improvement in outcomes may result from more effective symptom management, better acknowledgement of the burden of illness on the patient or family, or reduced need for hospitalization. Therefore, mental health professionals should consider palliative care consultation for advanced cancer patients with signs of psychological distress.

Table 2

Physical depressive symptoms vs replacement psychological symptoms

Physical symptoms…
Change in appetite
Sleep disturbance
Fatigue
Diminished ability to think or concentrate
…are replaced by psychological symptoms
Tearfulness, depressed appearance
Social withdrawal, decreased talkativeness
Brooding, self-pity, pessimism
Lack of reactivity, blunting

Source: Reference 16

Pharmacotherapy options

Antidepressants. Patients with excessive guilt, anhedonia, hopelessness, or ruminative thinking along with a related impairment in quality of life may benefit from pharmacotherapy regardless of whether they meet diagnostic criteria for MDD. Although SSRIs and SNRIs have become a mainstay in managing depression, placebo-controlled trials have yielded mixed results in depressed cancer patients. Furthermore, differences in efficacy among these antidepressants may not be significant, according to a recent meta-analysis.[22]

Select an antidepressant based on the patient's past treatment response, target symptoms, and potential for adverse events. Mirtazapine has relatively few drug interactions; the side effects of sedation and weight gain may be welcome among patients with insomnia and impaired appetite.[23] Furthermore, mirtazapine is a 5-HT3 receptor antagonist,[24] which suggests it might act as an effective antiemetic.[25] Other SNRIs, such as venlafaxine and duloxetine, have demonstrated benefits in managing neuropathic pain in patients who do not have cancer.[26]

continued

Clinical Point

Placebo-controlled trials of SSRIs and SNRIs have yielded mixed results in cancer patients; differences in efficacy may not be significant

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Table 3

Dosing recommendations for possible pharmacotherapy options

Drug	Onset of action	Starting dose	Usual daily dose	Maximum daily dose	Schedule
Methylphenidate	<24 hours	2.5 to 5 mg	5 to 10 mg	60 to 90 mg	8 AM and 12 PM
Modafinil	<24 hours	100 to 200 mg	200 to 300 mg	400 mg	Single early morning dose
Transdermal selegiline	Weeks	6 mg/d	6 to 12 mg/d	12 mg/d	Daily

Source: Reference 32

Clinical Point

Psychostimulants can improve cancer-related fatigue and quality of life while augmenting the action of antidepressants

Psychostimulants. Patients with a prognosis of days or weeks might not have enough time for an antidepressant to achieve full effect. Open prospective trials and pilot studies have shown that psychostimulants can improve cancer-related fatigue and quality of life while also augmenting the action of antidepressants.[27] Psychostimulants, such as methylphenidate, have been used for treating cancer-related fatigue and depressive symptoms in medically ill patients. Their rapid onset of action, coupled with minimal side effect profile, make them a good choice for seriously ill patients with significant neurovegetative symptoms of a depressive disorder. Note: Avoid psychostimulants in patients with delirium and use with caution in patients with heart disease.[28]

Novel agents. A growing body of preclinical research suggests that glutamate may be involved in the pathophysiology of MDD. Ketamine modulates glutamate neurotransmission as an *N*-methyl-D-aspartate receptor antagonist. A recent evaluation of a single dose IV of ketamine in a placebo-controlled, double-blind trial found that depressed patients receiving ketamine experienced significant improvement their depressive symptoms.[29] Irwin and Iglewicz[30] describe 2 hospice patients administered a single oral dose of ketamine, which provided rapid relief of depressive symptoms and was well tolerated.

Transdermal selegiline may help patients who have trouble taking oral medications, including antidepressants. Inability to tolerate or absorb medications may be related to several conditions such as head and neck cancer, severe mucositis, and dysphagia. The dose-related dietary requirements—tyramine restriction—and careful monitoring for drug interactions may limit the use of selegiline in medically ill patients.[31] See ***Table 3*** for a list of dosing recommendations for pharmacotherapeutic options.[32]

Use the strategy of "start low, go slow" when initiating and adjusting antidepressants because patients with cancer and other advanced illnesses often have concomitant organ failure and are at risk of drug interactions. Carefully review your patient's medication list for agents that are no longer beneficial or possibly contributing to depressive symptoms to help reduce the risk of adverse pharmacokinetic and pharmacodynamic interactions.

Requests for a hastened death

As many as 8.5% of terminally ill patients have a sustained and pervasive wish for an early death.[33] Although requests for a hastened death may evoke strong emotional reactions and compel many clinicians to recoil or harshly reject such requests, consider such requests as an opportunity to gain insight into the patient's narrative of his (her) suffering. The clinician's role in such cases is to identify suicidality and perform a thorough suicide risk assessment. Interventions to prevent suicide should attempt to balance the seriousness of self-harm threats with restrictions on the patient's liberty.[34]

Clinicians also need to consider the patient's prognosis in their decision-making. For example, an extremely depressed or suicidal patient may not benefit from psychiat-

Table 4

The legality of physician-assisted suicide, euthanasia, and palliative sedation

Term	Definition	Legality in the United States
Physician-assisted suicide	A doctor intentionally helps a person commit suicide by providing drugs for self-administration at that person's voluntary and competent request	Legal in Oregon, Washington, and Vermont by legislation and Montana by court ruling
Euthanasia	A doctor intentionally kills a person by administering drugs at the person's voluntary and competent request	Illegal
Palliative sedation	Controlled administration of sedative medications to reduce patient consciousness to the minimum extent necessary to render intolerable and refractory suffering tolerable	Legal

Source: References 35,36

ric hospitalization if she (he) has progressive neurovegetative symptoms and a prognosis of only a few weeks to live. These situations often are challenging and require a careful, informed discussion of the risks and benefits of all proposed interventions.

Clinicians also should be familiar with distinctions among ethical issues in end-of-life care, including physician-assisted suicide, euthanasia, and palliative sedation (***Table 4***).[35,36]

In Oregon, requests for physician-assisted suicide and hastened death through the state's Death with Dignity Act often are short lived, and may not persist when clinicians offer patients good symptom management and psychological support.[37] Requests for a hastened death often are motivated by loss of control, inability to find meaning in death, indignity from being dependent, and concern for future suffering and burden on loved ones.[37]

Carefully evaluate requests for hastened death in a manner that balances your personal and professional integrity. To preserve personal integrity, clearly communicate therapeutic interventions that you can and cannot provide. To ensure the patient does not feel abandoned, identify factors that contribute to the patient's suffering and express a desire to search for alternative care approaches that will be mutually acceptable to the patient and to you.

Advance care planning and palliative care consultations may help in these circumstances. A randomized trial comparing advance care planning vs standard care in hospitalized geriatric patients found that advance care planning was more likely to lead to end-of-life wishes that were recognized by clinicians, and was associated with less distress, anxiety, and depression as reported by bereaved family members.[38]

Clinicians can assist patients with advanced care planning by helping them fill out advance directives, such as durable health care power of attorney documents and a living will. Palliative care clinicians can offer specialty-level assistance in advance care planning, provide focused assessments of physical and psychosocial symptoms, develop appropriate clinical goals, and assist in coordinating individualized care plans for seriously ill patients.[2]

Clinical Point

When a patient requests a hastened death, a clinician's role is to identify suicidality and perform a suicide risk assessment

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Clinicians can assist patients with advance planning by helping them fill out advance directives, such as a living will

Related Resources

- American Academy of Hospice and Palliative Medicine. www.aahpm.org.
- Death with Dignity National Center. www.deathwithdignity.org.
- National Hospice and Palliative Care Organization. www.nhpco.org.
- Oregon Health Authority. Death with Dignity Act. http://public.health.oregon.gov/ProviderPartnerResources/Evaluationresearch/deathwithdignityact/Pages/index.aspx.

Drug Brand Names

Duloxetine • Cymbalta
Ketamine • Ketalar
Methylphenidate • Concerta, Ritalin
Mirtazipine • Remeron
Modafinil • Provigil
Selegiline (transdermal) • EMSAM
Venlafaxine • Effexor

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Bottom Line

Depression commonly is encountered in hospice and palliative care patients and is associated with morbidity and distress. Validated screening tools can help you distinguish major depressive disorder from depressive symptoms in this population. Several psychotherapeutic techniques have been shown to be beneficial. In addition to traditional antidepressants, psychostimulants or ketamine may help address acute depressive symptoms in patients who have days or weeks to live.