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Identification and treatment of depressive disorders in older adults with cancer

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Abstract

The increasing number of older adults living with cancer will inevitably include vulnerable subgroups who experience a range of depressive symptoms throughout the care continuum. It is well established that depression can lead to decreased quality of life, poor treatment adherence, increased length of hospital stay and health service utilization, and in severe cases, suicide. Thus, clinicians working in oncology must be able to identify, conceptualize, and treat (or connect to services) the mental health concerns of their older patients. This brief review describes the unique etiologies, features, and treatments for depressive syndromes among in older adults in the oncology setting, drawing on the literature and prevailing depression management guidelines from both psycho-oncology and geriatric depression research.

Keywords

Depression; Oncology; Assessment; Older; Geriatric; Treatment

Introduction

Depressive symptoms, whether isolated or severe, are associated with decreased quality of life, significant deterioration in physical activities, relationship difficulties, and greater pain among patients with cancer¹. For the older adult, the combined impact of aging and cancer can be devastating. Comorbid medical illness is often a key feature of mood disorders in older adults, such that global medical burden is powerfully associated with depression and anxiety, independent of functional status. Moreover, older adults with cancer have some of the highest rates of completed suicide². In the healthcare setting, comorbid depression is also of great concern given its negative impact on treatment engagement and adherence³. Despite

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Author Contributions

All authors: Conceptualization of content and preparation of manuscript.

Conflict of Interest

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the high prevalence and deleterious effects of depression, older adults are far less likely to be accurately diagnosed or treated for depression compared to other age groups⁴. The consequences of missing a depression diagnosis include decreased quality of life, poor treatment adherence, increased length of hospital stay and health service utilization, and in severe cases, suicide⁵. Despite its importance, the area of mental health for older adults within oncology is underdeveloped. Thus, the following sections explore the features of depression and its treatment among older adults in the oncology setting, drawing on the separate literatures and prevailing depression management guidelines from both psycho-oncology and geriatric depression research.

Depression can emerge in late life due to a confluence of factors including bereavement, cognitive decline, illness, and changing neurobiology⁶. However, depression is not considered a normal part of aging^{7,8}. In fact, most adults report overall increases in wellbeing as they age^{9,10}. The prevalence of Major Depressive Disorder (MDD) ranges between 1 and 5 percent among community-dwelling older adults and up to 42 percent of older adults residing in long term care facilities^{6,11}. Although depression tends to be more prevalent in younger adults, its prevalence in older adults varies significantly by setting, and increases significantly among patients 80 years and older^{11,12}. Additionally, although depression does not necessarily have a more chronic course in older adults, several studies have found that it is associated with a worse trajectory for older adults^{13,14}, and that older patients are significantly more likely to have relapses and recurrences in depressive episodes¹⁵.

The spectrum of depressive disorders is important to consider when assessing for depression in older adults: between 15 and 36 percent of community-dwelling older adults endorse subthreshold (i.e., not meeting the threshold for MDD), though clinically significant, depressive symptoms^{11,16}. For many older adults, even forms of depression that are less severe than MDD (e.g., minor, subsyndromal, or subthreshold depression, dysthymia, or adjustment disorder with depressed mood) can create significant impairment and decreased quality of life¹⁶. Both major and minor forms of depression are associated with increased disability, morbidity, and mortality among older adults¹⁷⁻¹⁹. Additionally, older adults with subthreshold depressive disorders report impairments in physical, social, and role functioning that are similar to MDD, which suggests that these cases should also be carefully managed²⁰.

Barriers to Symptom Recognition

Despite its prevalence, almost half of all cancer patients who have serious depressive symptoms are not treated for these symptoms. Similarly, depressed older adults often go undiagnosed and untreated even though successful treatment options are available^{6,21,22}. There are several barriers to the identification and diagnosis of depression among older adults in the medical setting. First, inappropriate normalization of depressive symptoms occurs for both the medically ill and older adults. Many patients and clinicians feel that depression is expected in people with cancer, and that it therefore may not warrant mentioning, discussing, or treating^{22,23}. Similarly, there is often pressure on all those involved in the patient's care to "think positively."

Similarly, in older adults, somatic symptoms and depressive cognitions are often viewed as a normal part of the aging process, and cognitive dysfunction can also obscure depressive symptoms⁶. The presence of cancer also complicates the ability of clinicians to accurately identify depressive symptoms^{24–26}. The primary source of this difficulty lies in the overlap between the diagnostic criteria for depression, as detailed in the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders – Fifth Edition (DSM-5²⁷), and the symptoms often attributable to cancer and/or the side effects of treatment^{28–30}. Specifically, DSM-5 criteria for depression include several somatic items, which include poor appetite or weight loss, sleep disturbance, loss of energy/fatigue, and diminished concentration. (Table 1). The same symptoms may arise from depression, from the cancer itself, from treatment side effects, or from some combination of these three. Identifying depression in older cancer patients presents an even greater challenge, as it combines both the difficulty diagnosing depression in patients with cancer generally and with the complexities rooted in the aging process^{23,24}.

Finally, practical limitations such as time and resources on the part of both the clinician and the patient create a systemic barrier to depression recognition and treatment in older adult patients with cancer. For example, Rhondali and colleagues²² found that although oncologists tended to have a good understanding of depression screening, they believed that screening would be difficult to implement and need to be adapted in order to integrate it into routine care without disrupting current practice. The current focus in oncology on distress screening and implementation should shed some light on best practices for embedding depression assessment into routine clinical care.

Diagnostic Considerations for Older Adults

The relationship between depression and cancer is complicated, with mixed evidence suggesting that depression can actually predict cancer incidence³¹. Although still mixed, there is stronger evidence that the presence of comorbid depression predicts cancer progression and mortality^{31,32}. Regardless of the underlying mechanism(s), our research indicates that a history of depression treatment prior to cancer diagnosis is significantly associated with the presence of elevated depressive symptoms among older adults with cancer³³. Therefore, clinicians should obtain a careful psychiatric history of their older patients when evaluating their risk for current depressive syndromes. Similarly, there is currently insufficient research to describe the typical course of depression in cancer based on cancer type and prognosis. Across age groups, however, several studies of mixed cancer samples have found depression to be more prevalent among patients with lung, gynecological, pancreatic, head and neck, and lung cancers relative to other types^{34–36}. Inconsistent differences in prevalence have been identified when comparing patients in palliative and non-palliative care settings^{36,37}. It is difficult to draw reliable conclusions from these literatures, as studies vary significantly in inclusion criteria and depression assessment method.

Several authors have contended that DSM-5 criteria (Table 1) may underestimate depression in older adults based on its emphasis on depressed mood as a gateway symptom^{38–40}. Gallo and colleagues³⁸ found that community-dwelling older adults were significantly less likely

to endorse dysphoria compared to other depressive symptoms. They characterized depression in older adults as “depression without sadness”, noting that depressed older adults manifest irritability or withdrawal more often than dysphoric mood³⁹. These authors described non-dysphoric depression as a syndrome that includes apathy, anhedonia, fatigue, sleep disturbance, and other somatic symptoms. Over a 13-year follow-up period, non-dysphoric depression was associated with increased mortality (relative risk (RR)=1.70; 95% CI (1.09, 2.67))), impairment in activities of daily living (RR=3.76; 95% CI (1.73, 8.14)), and psychological distress (RR=3.68; 95% CI (1.47, 9.21)). Therefore, despite a lower prevalence of affective and cognitive symptoms in depressed older adults, Gallo et al.³⁹ concluded that non-dysphoric depression is as likely as classic MDD to generate significant distress and impairment in older adults.

Consistent with “depression without sadness,” variants of traditional MDD have been postulated to occur in older adults. These variants describe late life depression (LLD), which is MDD with first onset in individuals 60 years and older. Most notable is Alexopoulos and colleagues’ research on “vascular depression” and “depression-executive dysfunction syndrome”, thought to reflect unique manifestations of geriatric depression^{41–43}. Both of these labels have been used to describe older adults who exhibit a marked reduction in their interest in pleasurable activities, increased suspiciousness, worsening psychomotor retardation, and impaired insight, but report few feelings of guilt or worthlessness. Because these syndromes often arise in the absence of a personal or family history of depression, they have been conceptualized as having a distinct vascular etiology related to aging (i.e., structural changes in the brain) and executive functioning. The distinct pathology associated with this variant of late life depression has important implications for how it is treated, which is discussed below.

Although debate continues regarding the distinct phenomenology of depressive symptoms in younger and older adults¹⁵, several studies have suggested key differences. For example, guilt and thoughts that life is not worth living were significantly less common among participants with MDD whose depression began after age 60 compared to those with who had an earlier onset of depression⁴⁴. Additionally, a recent meta-analysis found that, compared to younger adults with depression, older adults with depression tended to experience more psychomotor agitation (Odds Ratio [OR]=1.84), hypochondriasis (OR=3.13), gastrointestinal somatic symptoms (OR=1.58) and general somatic symptoms (OR=2.01)⁴⁵. Another closely related construct is social connectedness, including both social withdrawal and loneliness. Older adults who experience social isolation are at greater risk for increased morbidity, diminished immune function, depression, and cognitive decline⁴⁶. Loneliness specifically has been linked closely to depressed mood, decreased well-being, and even higher mortality⁴⁷. Importantly, patients may not immediately recognize any of these symptoms as being related to depression. Thus, clinicians must carefully consider these symptom relationships when evaluating their older patients^{27,48}.

Treatment Options for Depression

Clinicians are encouraged to select screening and assessment measures for use with older adults with cancer that have demonstrated adequate reliability and validity and can be

repeatedly implemented throughout the care trajectory. Despite a dearth of depression screening instruments specifically developed for this population, our past research suggests that among existing instruments, the Beck Depression Inventory (BDI-II⁴⁹), Center for Epidemiologic Studies Depression Scale Revised (CESDR⁵⁰), or the Hospital Anxiety and Depression Scale (HADS-D⁵¹) appear to have the most promise for use with this population^{52–54}. Utilizing lower cut-off scores as an indication of clinically significant depressive symptoms may be warranted when screening among older adults with cancer. For example, we identified a cut-off score of 14 as an appropriate threshold that maximizes sensitivity and specificity on the CESDR for specifically identifying MDD compared to the traditional cutoff of 15; we also found a cutoff score of 4 on the HADS-D as a better option than the previously recommended score of 6. These scores are suggested for MDD, while subthreshold depressive disorders can be identified using even lower scores⁵². The Patient Health Questionnaire – 9 item (PHQ-9⁵⁵) has been widely utilized with older adults in other medical settings. It can be used with older adults in oncology, but may produce an inflated number of false positives because of its reliance on traditional DSM-5 symptoms, several of which are somatic³⁰. Finally, when evaluating for a mood disorder in an older adult with cancer, soliciting input from caregivers with the patient's consent can provide invaluable information about whether or not the patient has exhibited worsening depressive symptoms.

Unfortunately, empirically validated guidelines that combine together best practices for depression management in both oncology and geriatrics do not yet exist. However, guidelines are available from the American Society of Clinical Oncology regarding the screening, assessment, and management of both depression and anxiety among patients with cancer, including detailed descriptions of the recommended stepped-care model^{56,57}. Separate but overlapping guidelines for the management of depression among older adults are also widely available, stemming from a large body of work developed for primary care for older adults⁴⁸. A combination of these guidelines can be utilized when deciding on optimal systems and treatment-related decision making for older patients across diverse care settings. Moreover, the implementation of comprehensive geriatric assessment (CGA⁵⁸), which includes screening measures of depression, is the current gold standard in the management of older adults with cancer, and it is an important opportunity to identify those patients experiencing concerning mood symptoms. After careful screening and assessment, older patients with cancer can be triaged to appropriate mental health services. Older adults can benefit from many existing treatment modalities, including psychotherapeutic and psychopharmacological interventions, or a combination of both.

A meta-analysis of psychotherapy for depression in older adults found a medium to high effect size with a more modest effect size after six months post-randomization (post-treatment: $g=0.64$ (95% CI: 0.47–0.80)); 6-months post randomization: $g=0.27$ (95% CI: 0.16–0.37))⁵⁹. General consensus is that directive, structured modalities such as cognitive behavior therapy (CBT) and problem solving therapy (PST) are more effective for older adults than less directive approaches^{15,49}. Both approaches are thought to be particularly well suited for late life depression given its associated executive dysfunction, which may make it more difficult to initiate and complete day to day tasks⁶⁰. CBT focuses on having patients learn to restructure maladaptive patterns of thinking while also engaging in behavioral activation and relaxation between sessions. PST seeks to help patients develop

more effective coping through improved problem solving skills. PST has been extensively studied in geriatric psychiatry and continues to be adapted for diverse medically ill groups (e.g., homebound older adults, cognitively impaired)⁶⁰. Regardless of modality, traditional psychotherapy may need to be adapted for patients' mobility, ability to get to sessions, cancer treatment schedules, diminished stamina or increased pain or discomfort that can make it difficult to sit for long periods. Of course, treatment modalities should be selected based on patient variables and available local resources. Additionally, non-mental health specialists can be trained in basic psychological interventions such as psycho-education, problem solving, and behavioral activation⁵⁷. We recommend utilizing these psychotherapies with older adults in oncology, who can benefit from many of the structured exercises, skill development, and behavioral activation that are featured in both CBT and PST.

Antidepressants are generally reserved for depressive symptoms that meet criteria for MDD or mild depression. Antidepressant medications have demonstrated modest efficacy for use with community-dwelling older adults⁴⁸. However, when compared to younger adults, and when examined in certain subgroups (e.g., long term care), they tend to have lower response rates¹⁵. Older adults may also have more difficulty adhering to antidepressant medication in the context of cognitive decline and the complexity of polypharmacy. Additionally, physicians (non-psychiatrists) tend to prescribe suboptimal doses of these medications to older patients^{15,48}. It is important to “start low and go slow” when prescribing antidepressants to older adults, but often physicians do not follow these patients closely enough to properly titrate their anti-depressant medication(s). Specific recommendations for antidepressant selection for older patients are not included here (see Kok & Reynolds for a good review on this topic⁴⁸). Regardless, prescribing clinicians should ensure that there are no contraindications with standing cancer or other medications that may be impacted by the introduction of an antidepressant (e.g., tamoxifen and certain antidepressants)⁵⁶.

Conclusion

Depression in older adults is a multiply-determined, heterogeneous disorder. Older adults with depressive symptoms, ranging from mild to more severe, are at increased risk of being overlooked and undertreated across care settings, and especially in the context of cancer and other medical comorbidities. The impact of depressive symptoms on quality of life and survival should not to be overlooked, and older adults with cancer are one of the most at-risk demographic groups for suicide. Therefore, clinicians should work closely with older patients and caregivers in order to identify and treat impairing symptoms, making appropriate referrals to psychosocial services when necessary. Although much can be learned from the separate psycho-oncology and geriatric psychiatry literatures, research and clinical efforts to incorporate best practices from both worlds is an ongoing and critical next step for advancing cancer care.

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Table 1.**DSM-5 Criteria for Major Depressive Disorder (MDD)**

Five or more of nine key symptoms including at least one of the two “gateway” symptoms (i.e., depressed mood, anhedonia) for a minimum period of two weeks, together with either distress or impaired functioning:

- Depressed mood
 - Loss of interest or pleasure (anhedonia)
 - Weight loss or appetite changes
 - Insomnia or hypersomnia
 - Psychomotor retardation or agitation
 - Loss of energy or fatigue
 - Worthlessness or guilt
 - Diminished concentration or indecisiveness
 - Thoughts of death or suicidal ideation
 - These symptoms can also be assigned a severity specifier (i.e., mild, moderate, severe) based on the number of symptoms present and qualification is made as to whether it is a single episode or recurrent.
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Note. Minor depression is not formally recognized in the DSM-5, but was described in the DSM-IV (1994) as an example of depressive disorder not otherwise specified (NOS). The DSM-IV described minor depression as the presence of at least one gateway symptom and at least one other depressive symptom that persist for at least two weeks.