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## Symptomatology, assessment, and treatment of anxiety in older adults with cancer

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Anxiety is a normal response to a perceived threat and is characterized by worry that is difficult to control, restlessness, difficulty concentrating and sleeping, fatigue, and muscle tension.<sup>1</sup> The objective threat posed by cancer likely accounts for the high rates of anxiety in cancer patients and survivors.<sup>2</sup> In fact, many studies indicate that rates of anxiety are higher than rates of depression in cancer patients across age groups.<sup>3,4</sup> For older adults, the threat of cancer occurs in the context of other threats posed by aging.<sup>5,6</sup> Many older adults experience age-related physical changes such as frailty, medical co-morbidities, and mobility limitations;<sup>7–9</sup> cognitive changes ranging from normative declines in memory and processing speed to severe changes due to diseases like dementia;<sup>10,11</sup> and shrinking social networks due to the disability and death of loved ones, all of which can contribute to increasing anxiety. Cancer and treatment effects such as fatigue and nausea can add to and exacerbate these age-related changes.<sup>12–16</sup>

In the context of cancer and aging, it is perhaps unsurprising that many older adults with cancer suffer from elevated anxiety. Estimates of the prevalence of anxiety vary widely due, in part, to variation in assessment methods. However, across studies, over 40% of older adults with cancer report clinically significant anxiety.<sup>17–19</sup> While anxiety tends to reduce over time,<sup>20</sup> approximately half of older adults with cancer who are five or more years post-diagnosis endorse cancer-related worries.<sup>21</sup> This finding suggests that anxiety may be chronic, existing even after older adults complete cancer treatment.

Further, anxiety increases in the context of additional threats such as surgery and disease progression.<sup>2</sup> The role of additional threats is particularly important to consider in the context of the COVID-19 pandemic. COVID-19 has unique negative implications for patients with cancer due to delays in diagnosis and initiation of cancer treatment, disruption of ongoing treatment and supportive care, and reduced patient access to support networks

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and coping strategies, resulting in high rates of COVID-19 distress.<sup>22</sup> For older adults, the higher rates of infection and mortality from COVID-19 are additional and significant stressors that further increase the importance of addressing the mental health needs of older adults with cancer.<sup>23</sup>

Anxiety is clearly prevalent in older adults with cancer, influenced by the aging process, and exacerbated by external stressors such as COVID-19. Oncologists are often tasked with treating this anxiety, including in settings with no or limited mental health resources. Up to half of distressed older adults with cancer do not receive psychosocial services.<sup>24,25</sup> One reason for this undertreatment may be a lack of provider knowledge of the prevalence and importance of anxiety and strategies for anxiety assessment and treatment tailored for older adults with cancer.<sup>26</sup> Therefore, the purpose of this paper is to provide a brief overview of anxiety in older adults with cancer with recommendations that can be integrated into oncology care in order to reduce rates of untreated anxiety and improve the psychological well-being of older adults with cancer. The topics to be addressed are: (1) problems associated with anxiety; (2) considerations for anxiety screening; and (3) considerations for anxiety treatment.

### **Problems associated with anxiety**

Anxiety warrants treatment not only because of its inherent distress but also because of its association with other problems in older patients. Patients with elevated anxiety report worse physical symptoms, including greater fatigue, nausea, pain, shortness of breath, worse social and cognitive function<sup>27-35</sup> and poor quality of life.<sup>32,33</sup> High anxiety can also interfere with treatment and decision-making. Patients with elevated anxiety have greater difficulty communicating with the healthcare team,<sup>36</sup> worse treatment adherence and response,<sup>27,37,38</sup> more treatment interruptions,<sup>38</sup> longer hospitalizations,<sup>39</sup> and higher mortality.<sup>40</sup> Anxiety is also associated with patients' understanding of their prognosis and treatment decisions. For example, older men with prostate cancer who report high anxiety start treatment earlier, despite evidence that early initiation does not improve survival but does impair quality of life.<sup>41,42</sup>

### **Anxiety screening: Considerations for older adults with cancer**

The American Society of Clinical Oncology (ASCO) recommends screening for anxiety at the initial visit, with changes in disease status, at transition to end-of-life care, and when otherwise clinically indicated using the Generalized Anxiety Disorder-7 (GAD-7) scale.<sup>43,44</sup> Validated cut-off scores have been developed for mild (score: 5–9), moderate (score: 10–14), and severe anxiety (score: 15–21). Other anxiety screening measures have been developed for older adults (e.g., Geriatric Anxiety Inventory,<sup>45</sup> Geriatric Anxiety Scale,<sup>46</sup> Memorial Anxiety Scale for Prostate Cancer<sup>47,48</sup>) and in younger adults with validation in older adults (e.g., State-Trait Anxiety Inventory,<sup>49</sup> Beck Anxiety Inventory<sup>50,51</sup>). Important factors to consider when selecting a screening measure include the overlap of symptoms of anxiety and disease and treatment effects (e.g., fatigue, sleep disruption) and the similarity in cognitive symptoms (e.g., difficulty concentrating) of anxiety and aging.<sup>52</sup> Screening measures with less emphasis on the somatic and cognitive symptoms of anxiety may more

accurately differentiate anxiety from cancer and aging-related processes and minimize erroneous referrals to mental health treatment.

Anxiety in response to a threat can be adaptive by motivating patients to take action to address problems and meet their needs. However, if the severity of the anxiety is disproportionate to the threat, it can be maladaptive and problematic. Determining whether anxiety in older adults with cancer is disproportionate to the threat is difficult due to the challenge of quantifying the threat posed by cancer and aging, change in that threat over time, and lack of clarity regarding the normal course of anxiety during cancer.<sup>2,53</sup> One benchmark for identifying maladaptive anxiety is the degree to which anxiety symptoms impair function. For example, anxiety-driven behaviors such as avoidance and frequent reassurance seeking can interfere with relationships and patients' ability to engage in daily tasks.<sup>2</sup> Strategies for screening for functional impairment due to anxiety are available. For example, the GAD-7 includes a final item that assesses the impact of anxiety symptoms on the patient's ability to "do your work, take care of things at home, or get along with other people."<sup>44</sup> Defining maladaptive anxiety based on this type of functional impairment allows for a patient-centered approach that considers the threat posed by both cancer and aging and the unique characteristics and situation of each older adult.

Older adults have higher rates of medical comorbidities and frailty than younger patients.<sup>54</sup> Therefore, consideration of underlying physiological conditions that may present as anxiety (e.g., pain, dyspnea, delirium) is particularly important in this population.<sup>54,55</sup> Further, central nervous system metastases, pheochromocytomas and pituitary microadenomas, non-hormone secreting pancreatic cancers, and dyspnea associated with lung cancer have symptoms that mimic anxiety disorders.<sup>56</sup> Metabolic and endocrine abnormalities, as well as some medications used in the cancer setting, such as steroids, antiemetics and some chemotherapy agents, can also cause anxiety.<sup>57</sup> Identifying and treating these underlying causes reduces the likelihood of misdiagnosis and long-term impact of a condition mistaken for anxiety.

### **Anxiety treatment: Considerations for older adults with cancer**

ASCO recommends cognitive-behavioral therapy (CBT) and/or pharmacologic treatment for anxiety in patients with cancer using a stepped-care approach based on anxiety severity.<sup>43</sup> CBT is a time-limited (2–10 sessions) problem-focused<sup>58,59</sup> psychological treatment that targets thoughts and behaviors that increase distress.<sup>58,60</sup> CBT is among the most researched psychotherapies across age groups with enough studies to warrant reviews of meta-analyses over the past 10–15 years.<sup>61,62</sup> Effect sizes for CBT relative to wait list, no-treatment, and psychological placebo control conditions are medium to large with some studies showing a sustained effect of CBT 8–10 years post-treatment.<sup>62,63</sup> A review of 17 studies of evidence-based treatments (as defined by the American Psychological Association<sup>64</sup>) in older adults identified CBT as an efficacious treatment for late-life distress.<sup>65,66</sup>

CBT has also been extensively evaluated in cancer patients.<sup>67</sup> CBT has been shown to be efficacious for depression and anxiety in cancer patients,<sup>59,67,68</sup> including when telephone delivered<sup>69,70</sup> and is a cost-effective treatment for psychological distress in cancer care.<sup>71–74</sup>

CBT is particularly appropriate for older adults with cancer due to the high adverse effect rates of and limited research on psychotropic medications in this population.<sup>75,76</sup> Further, polypharmacy is prevalent in older adults with cancer<sup>77,78</sup> and is associated with adverse outcomes.<sup>78–80</sup> CBT is beneficial in that it can reduce distress without contributing to polypharmacy.

Pharmacologic management of anxiety in older adults with cancer involves the judicious use of antidepressants, benzodiazepines, and antipsychotics.<sup>81</sup> Clinical evidence supports the use of the medications in the treatment of anxiety in older adults with cancer. However, randomized controlled trials are required to establish the risks and benefits of medication use for this patient population. Benzodiazepines are often first line of treatment for anxiety in younger adults due to their positive impact on ongoing and high intensity anxiety and panic attacks. Additional benefits include decreased restlessness, improvements in sleep initiation and insomnia, reduced irritability and chemotherapy-induced nausea, and enhanced muscle relaxation. However, the calming effects of benzodiazepines can overextend to cause sedation, problems concentrating, forgetfulness, dizziness and muscle relaxation, which can lead to problems with ambulation, driving, focusing and working. Individually or combined, these side effects make falls and other accidents more likely in vulnerable populations. Further, benzodiazepines are prescribed as controlled substances due to the potential for misuse and subsequent harm. It is important to discuss the distinctions between dependence, tolerance, and addiction with patients and be aware of concomitant substance use or abuse.

Antidepressants can be alternative medications for anxiety and may be a more appropriate initial preventive treatment for generalized anxiety or panic attacks in older people with cancer.<sup>82</sup> If a benzodiazepine is prescribed, consider using lower doses depending on patient frailty. As always, evaluate drug–drug interactions and liver, kidney and cardiac function; gradually increase the dose; and closely monitor for side effects. For older adults, it is particularly important to check liver function tests and conduct a baseline cognitive screen to allow for evaluation of the impact of the medication on cognitive function.

The use of low-dose antipsychotics is common clinical practice for short-term treatment of severe anxiety when benzodiazepines cannot be used because of frailty or respiratory compromise. However, in older adults, clinicians should consider the risks and benefits of antipsychotics carefully, especially in patients with underlying dementia, due to reports of increased mortality and risk of cardiovascular and cerebrovascular events in this population.

### **Take home messages on anxiety in older adults with cancer**

Older adults with cancer face the dual threat of aging and cancer. Anxiety is prevalent in older adults with cancer and associated with poor quality of life and cancer treatment response. External stressors such as COVID-19 further exacerbate this anxiety and heighten the importance of identifying and treating anxiety in older adults with cancer. The evaluation and treatment of anxiety in older adults must consider the overlap of symptoms of anxiety, disease and treatment effects, and aging processes. Screening for anxiety using measures validated in older adults promotes referral to evidence-based psychotherapy and pharmacologic interventions effective for anxiety. Reducing anxiety symptoms with these

treatments has the potential to improve the quality of life, physical symptoms, and engagement in cancer care of older adults with cancer.

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