

Depression Screening and Treatment: A Missed Opportunity in Lung Cancer Care

Donald R. Sullivan, MD, MA; and Alan R. Teo, MD, MS

The integrated VA system is well positioned to be a leader in depression screening and treatment, and VA clinicians who care for patients with lung cancer are encouraged to take advantage of available mental health resources.

Dr. Sullivan is an investigator, and **Dr. Teo** is a core investigator, both in the HSR&D Center to Improve Veteran Involvement in Care at VA Portland Health Care System in Oregon. Dr. Sullivan is an assistant professor in the Department of Medicine, in the Division of Pulmonary and Critical Care Medicine, and Dr. Teo is an assistant professor in the Department of Psychiatry and School of Public Health, both at Oregon Health & Science University in Portland.

ABOUT RESEARCH IN CONTEXT

In this article, the authors of recent scholarship have been asked to discuss the implications of their research on federal health care providers and specifically the veteran and active-duty service member patient populations. Because the article does not include new research and cannot be blinded, it has undergone an abbreviated peer review process. The original article can be found at Sullivan DR, Forsberg CW, Ganzini L, et al. Longitudinal changes in depression symptoms and survival among patients with lung cancer: a national cohort assessment. J Clin Oncol. 2016;34(33):3984-3991.

Although depression is common among patients with cancer, patients with lung cancer are at particularly high risk. The prevalence of major depressive disorder (MDD) among patients with cancer can be as high as 13%, whereas up to 44% of patients with lung cancer experience depression symptoms at some point following their cancer diagnosis.¹⁻³ These estimates are consistently higher than those of other types of cancer, possibly related to the stigma of the disease and the associated morbidity and mortality that are its hallmarks.⁴⁻⁸ This potentially life-threatening cancer diagnosis often evokes psychological distress; however, additional stressors contribute to the development of depression, including the effects of chemotherapeutic agents, surgical procedures, radiotherapy, and the consequences of physical symptoms and paraneoplastic syndromes.

In addition to the crippling effects of comorbid depression on patients' quality of life (QOL), severe and persistent depression among patients with cancer is associated with prolonged hospital stays, worse treatment adherence, physical distress and pain, and increased desire for

hastened death.⁹⁻¹¹ During treatment, depression can amplify physical symptoms and interfere with effective coping.^{12,13}

Depression also is likely a significant factor for the risk of suicide, which is 4 times higher in patients with lung cancer than that of the general population.¹⁴ Most important, as our recent study demonstrated, depression that develops at cancer diagnosis or during cancer treatment may contribute to worse survival. This effect was strongest among patients with early stage disease, in other words, the patients who are most likely to achieve cure.³ This association with early stage disease also has been observed in a strictly veteran population from the northwest U.S.¹⁵

Another key finding of our study was the similar survival among patients who experienced a remission of their depression and those who were never depressed. This finding reinforces the importance of effective depression treatment, which has the potential to reduce depression-related mortality; however, depression treatment was not fully captured and could not be directly compared in our study. Unfortunately, comorbid depression often goes undiagnosed and untreated in cancer patients as they report unmet emotional needs and a desire for psychological support during and after completion of cancer treatment.^{16,17}

Given the general lack of depression treatment that occurs in patients with cancer, the negative consequences of depression can be sustained well into survivorship—defined clinically as someone who is free of any sign of cancer for 5 years. Cancer survivors frequently report fatigue, mood disturbance, sleep disruption, pain, and cognitive limitations that significantly impact QOL and are associated with disability and increased health care use.¹⁸ These

symptoms likely are intertwined with and contribute to the development and persistence of depression. The ramifications of untreated depression on long-term cancer survivor outcomes are not completely understood, as few high-quality studies of depression in cancer survivors exist. However, in a mixed group of patients with cancer, there was a 2-fold risk of mortality in survivors with depression symptoms when these patients were assessed from 1 to 10 years into survivorship.¹⁹ The impact of depression on cancer survivorship is an important aspect of cancer care that deserves significantly more attention from both a research and clinical perspective.

SPECIAL CONSIDERATIONS FOR VETERANS

There is a higher prevalence of mental health diagnoses in veterans than that in the general population, and depressive disorders are the most common.²⁰⁻²² According to the VA National Registry for Depression, 11% of veterans aged ≥ 65 years have a diagnosis of MDD, a rate more than twice that in the general population of a similar age.²³ However, the actual rate of depression among veterans may be even higher, as studies suggest depression is underdiagnosed in the veteran population.²⁴ In addition to depression, veterans experience other disabling psychological illnesses, such as posttraumatic stress disorder (PTSD) related to deployment and combat duty or combat-related injuries, such as traumatic brain injuries. The negative consequences of PTSD on cancer outcomes are largely unexplored, but PTSD can contribute to increased health care utilization and costs.^{25,26} A similar psychological construct, cancer-related posttraumatic stress (PTS), which develops as a result of a cancer diagnosis or treatment, is associated with missed medical appointments and procedures, which could impact survival.²⁷

DEPRESSION SCREENING AND TREATMENT

Given the negative consequences of comorbid mental illness, professional oncology societies have started developing guidelines regarding the assessments and care of patients with cancer who are experiencing symptoms of depression and/or anxiety.^{11,28,29} Among these, the American Society of Clinical Oncology (ASCO) has adapted the Pan-Canadian Practice Guideline on Screening, Assessment, and Care of

Psychosocial Distress (Depression, Anxiety) in Adults With Cancer.²⁸ Per ASCO, the target audience for these guidelines is health care providers (eg, medical, surgical, and radiation oncologists; psychiatrists; psychologists; primary care providers; nurses; and others involved in the delivery of care for adults with cancer) as well as patients with cancer and their family members and caregivers.²⁸ These guidelines address the optimum screening, assessment, and psychosocial-supportive care interventions for adults with cancer who are identified as experiencing symptoms of depression. Among the most imperative recommendations are periodic assessments across the trajectory of cancer care, including after cure, as well as employing institutional and community resources for depression treatment.

In clinical practice in a VA setting, implementing these guidelines might involve various interventions. First, it is vital for providers to conduct depression screening during periodic health care encounters. Given the high prevalence of depression in patients with lung cancer, we suggest using the 9-item Patient Health Questionnaire (PHQ-9) as an initial screening tool.³⁰ Unlike the abridged 2-item PHQ-2 commonly used in the VA, the PHQ-9 provides an assessment of the full range of depressive symptoms. An elevated PHQ-9 score (≥ 10) is consistent with a major depressive episode and should trigger next steps.³⁰

Once clinically significant depression is identified, initiation of treatment should occur next. The VA is well suited to assist and support nonmental health clinicians—particularly primary care—in treatment initiation and monitoring. This model of partnership is frequently called collaborative care, or integrated care, and it is well positioned to help patients with lung cancer with concomitant depression. In the VA, this model of care is called primary care-mental health integration (PC-MHI). One PC-MHI resource is called TIDES (Translating Initiatives for Depression into Effective Solutions), and when a patient is referred, a mental health nurse care manager helps to track the patients' antidepressant adherence and treatment response while reporting results to primary care clinicians, who are generally responsible for initiating and continuing the antidepressant prescription. For patients preferring nonpharmacologic approaches or for whom an antidepressant may be contraindicated,

PC-MHI can provide other assistance. For example, psychologists working in PC-MHI are equipped to provide a brief course of cognitive behavioral therapy sessions, another first-line, evidence-based treatment for clinical depression.

Clinician follow-up to ensure patient adherence, response, and satisfaction, and to adjust treatment as needed is essential. Besides ongoing coordination with PC-MHI services, including mental health clinicians as part of multidisciplinary cancer clinics could offer substantial added value to patients' comprehensive cancer care. Indeed, the initiation of multicomponent depression care has been shown to improve QOL and role functioning in patients with cancer.³¹ Besides the established benefits on QOL, patients with lung cancer who achieve depression symptom remission also may enjoy a significant survival benefit over patients whose depression symptoms remain untreated during lung cancer treatment as our study suggests.³

CONCLUSION

Depression is a common comorbid disease among patients with lung cancer with important negative implications for QOL and survival. When it occurs after a cancer diagnosis, depression is expected to impact all phases of a patient's life through treatment and survivorship—ultimately affecting long-term survival. Veterans may be at particularly high risk given the increased prevalence of mental illness, including depression and PTSD in this group compared with that of the general population. Early detection and prompt treatment can promote depression remission, prevent relapse, and reduce the eventual emotional and financial burden of the disease. This approach may ultimately diminish the prevalence and persistence of depression symptoms and decrease the associated negative effects of this disease on patients with lung cancer.

The importance of integrated systems of depression treatment for patients with cancer as part of comprehensive cancer care cannot be overstated. Development and implementation of these systems should be a priority of lung cancer clinicians and treatment centers. The integrated system within the VA is well positioned to be a leader in this area, and VA clinicians who care for patients with lung cancer are encouraged to take advantage of available mental health resources. Additional research is urgently needed to explore optimal implementation of depression

screening and subsequent treatment delivery to improve cancer patient outcomes in VA and non-VA health care settings.

Overall, there is minimal evidence that depression treatment can improve lung cancer survival; however, the lack of high-quality studies is a considerable limitation. Given the significant impact of depression on survival among patients with lung cancer, additional funding and resources are urgently needed to combat this debilitating comorbid disease.

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AUTHOR DISCLOSURES

The authors report no actual or potential conflicts of interest with regard to this article.

DISCLAIMER

The VA had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication. The opinions expressed herein are those of the authors and do not necessarily reflect those of Federal Practitioner, Frontline Medical Communications Inc., the U.S. Government, or any of its agencies.

REFERENCES

- Derogatis LR, Morrow GR, Fetting J, et al. The prevalence of psychiatric disorders among cancer patients. *JAMA*. 1983;249(6):751-757.
- Walker J, Holm Hansen C, Martin P, et al. Prevalence of depression in adults with cancer: a systematic review. *Ann Oncol*. 2013;24(4):895-900.
- Sullivan DR, Forsberg CW, Ganzini L, et al. Longitudinal changes in depression symptoms and survival among patients with lung cancer: a national cohort assessment. *J Clin Oncol*. 2016;34(33):3984-3991.
- Linden W, Vodermaier A, Mackenzie R, Greig D. Anxiety and depression after cancer diagnosis: prevalence rates by cancer type, gender, and age. *J Affect Disord*. 2012;141(2-3):343-351.
- Massie MJ. Prevalence of depression in patients with cancer. *J Natl Cancer Inst Monogr*. 2004;(32):57-71.
- Brown Johnson CG, Brodsky JL, Cataldo JK. Lung cancer stigma, anxiety, depression, and quality of life. *J Psychosoc Oncol*. 2014;32(1):59-73.
- Cataldo JK, Jahan TM, Pongquan VL. Lung cancer stigma, depression, and quality of life among ever and never smokers. *Eur J Oncol Nurs*. 2012;16(3):264-269.
- Howlader N, Noone AM, Krapcho M, et al. SEER cancer statistics review, 1975-2010. https://seer.cancer.gov/archive/csr/1975_2010/. Revised February 21, 2014. Accessed July 12, 2017.
- Li M, Boquiren V, Lo C, et al. Depression and anxiety in supportive oncology. In: Davis M, Feyer P, Ortner P, Zimmermann C, eds. *Supportive Oncology*. 1st ed. Philadelphia, PA: Elsevier; 2011:528-540.
- Brown LF, Kroenke K, Theobald DE, Wu J, Tu W. The association of depression and anxiety with health-related quality of life in cancer patients with depression and/or pain.

- Psychooncology*. 2010;19(7):734-741.
11. Lazenby M, Ercolano E, Grant M, Holland JC, Jacobsen PB, McCorkle R. Supporting Commission on Cancer-mandated psychosocial distress screening with implementation strategies. *J Oncol Pract*. 2015;11(3):e413-e420.
 12. Mystakidou K, Tsilika E, Parpa E, Katsouda E, Galanos A, Vlahos L. Psychological distress of patients with advanced cancer: influence and contribution of pain severity and pain interference. *Cancer Nurs*. 2006;29(5):400-405.
 13. Passik SD, Dugan W, McDonald MV, Rosenfeld B, Theobald DE, Edgerton S. Oncologists' recognition of depression in their patients with cancer. *J Clin Oncol*. 1998;16(4):1594-1600.
 14. Rahuma M, Kamel M, Nasar A, et al. Lung cancer patients have the highest malignancy-associated suicide rate in USA: a population based analysis. *Am J Respir Crit Care Med*. 2017;195:A6730.
 15. Sullivan DR, Ganzini L, Duckart JP, et al. Treatment receipt and outcomes among lung cancer patients with depression. *Clin Oncol (R Coll Radiol)*. 2014;26(1):25-31.
 16. Merckaert I, Libert Y, Messin S, Milani M, Slachmuylder JL, Razavi D. Cancer patients' desire for psychological support: prevalence and implications for screening patients psychological needs. *Psychooncology*. 2010;19(2):141-149.
 17. Harrison JD, Young JM, Price MA, Butow PN, Solomon MJ. What are the unmet supportive care needs of people with cancer? A systematic review. *Support Care Cancer*. 2009;17(8):1117-1128.
 18. Wu HS, Harden JK. Symptom burden and quality of life in survivorship: a review of the literature. *Cancer Nurs*. 2015;38(1):E29-E54.
 19. Mols F, Husson O, Roukema JA, van de Poll-Franse LV. Depressive symptoms are a risk factor for all-cause mortality: results from a prospective population-based study among 3,080 cancer survivors from the PROFILES registry. *J Cancer Surviv*. 2013;7(3):484-492.
 20. Hoge CW, Castro CA, Messer SC, McGurk D, Cotting DI, Koffman RL. Combat duty in Iraq and Afghanistan, mental health problems, and barriers to care. *N Engl J Med*. 2004;351(1):13-22.
 21. Fortney JC, Curran GM, Hunt JB, et al. Prevalence of probable mental disorders and help-seeking behaviors among veteran and non-veteran community college students. *Gen Hosp Psychiatry*. 2016;38:99-104.
 22. Pickett T, Rothman D, Crawford EF, Brancu M, Fairbank JA, Kudler HS. Mental health among military personnel and veterans. *N C Med J*. 2015;76(5):299-306.
 23. U.S. Department of Veterans Affairs, Veterans Health Administration. One in ten older vets is depressed. <https://www.va.gov/health/NewsFeatures/20110624a.asp>. Updated April 17, 2015. Accessed July 12, 2017.
 24. Fontana A, Rosenheck R. Treatment-seeking veterans of Iraq and Afghanistan: comparison with veterans of previous wars. *J Nerv Ment Dis*. 2008;196(7):513-521.
 25. Kessler RC. Posttraumatic stress disorder: the burden to the individual and to society. *J Clin Psychiatry*. 2000;61(suppl 5):4-12; discussion, 13-14.
 26. Kartha A, Brower V, Saitz R, Samet JH, Keane TM, Liebschutz J. The impact of trauma exposure and post-traumatic stress disorder on healthcare utilization among primary care patients. *Med Care*. 2008;46(4):388-393.
 27. National Cancer Institute. Cancer-related post-traumatic stress (PDQ®)—Patient version. <https://www.cancer.gov/about-cancer/coping/survivorship/new-normal/ptsd-pdq>. Updated July 7, 2015. Accessed July 12, 2017.
 28. Andersen BL, DeRubeis RJ, Berman BS, et al; American Society of Clinical Oncology. Screening, assessment, and care of anxiety and depressive symptoms in adults with cancer: an American Society of Clinical Oncology guideline adaptation. *J Clin Oncol*. 2014;32(15):1605-1619.
 29. Howell D, Keller-Olaman S, Oliver TK, et al. A pan-Canadian practice guideline and algorithm: screening, assessment, and supportive care of adults with cancer-related fatigue. *Curr Oncol*. 2013;20(3):e233-e246.
 30. Kroenke K, Wu J, Bair MJ, Krebs EE, Damush TM, Tu W. Reciprocal relationship between pain and depression: a 12-month longitudinal analysis in primary care. *J Pain*. 2011;12(9):964-973.
 31. Walker J, Hansen CH, Martin P, et al; SMaRT (Symptom Management Research Trials) Oncology-3 Team. Integrated collaborative care for major depression comorbid with a poor prognosis cancer (SMaRT oncology-3): a multicentre randomised controlled trial in patients with lung cancer. *Lancet Oncol*. 2014;15(10):1168-1176.

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