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Cancer in the Older Adult: Implications for Therapy and Future Research

Mina S. Sedrak, MD, MS¹ and Arti Hurria, MD¹

¹Department of Medical Oncology, Cancer and Aging Research Program, City of Hope Comprehensive Cancer Center, Duarte, CA

Editorial

Over the next two decades there will be an unprecedented increase in the number of older adults diagnosed or living with cancer. In 2016, sixty-two percent of the nearly 16 million cancer survivors in the United States were 65 years of age or older.¹ By 2040, it is expected that older adults will account for two-third of the projected 26 million cancer survivors. The growth in the number of older adult cancer survivors is a consequence of the aging of the US population, the association of cancer and aging, and the steadily increasing length of survival from cancer.^{1–6} However, several gaps in knowledge remain regarding the unique needs of this growing population of older adult cancer survivors. Clinical trials to date primarily report on overall survival and disease-free survival; however, additional focus is needed on health outcomes salient to this population including the impact of treatment on function, autonomy, and cognition.⁷ A deeper understanding of the impact of cancer and its treatment on the aging process, as well as interventions to reduce the risk of accelerated aging among older cancer survivors are needed. These represent key priorities for geriatric oncology research and practice.

The study by Gresham et al in this issue of *Cancer* is an example of the type of research that is needed to bridge these knowledge gaps in the field of geriatric oncology.⁸ In this study of healthy middle- and older-aged adults in Baltimore, Gresham et al prospectively evaluated fatigability (using a validated Borg rating of perceived exertion after a 5-minute, slow treadmill walk) and endurance performance (defined as the ability and time to complete a fast 400-meter walk) over time, and compared these observations to those with and without a history of cancer. The authors found that the combination of older age (>65 years) and cancer history was associated with a 3.8-fold greater odds of high perceived fatigability and 8.6-fold greater odds of poor endurance, when compared with younger (<65 years) cancer-free adults. The authors concluded that the additive effect of cancer and aging appears to accelerate the onset and progression of fatigability as well as poor endurance.

We applaud the authors of this study for tackling a key research priority identified by the Institute of Medicine, the American Society of Clinical Oncology, and the Cancer and Aging

Corresponding Author: Mina S. Sedrak, MD, MS, City of Hope Comprehensive Cancer Center, 1500 E. Duarte Road, Duarte CA, 91010.

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Research Group: To expand studies focusing on the survivorship issues facing older adults with cancer and the impact of cancer on the aging process.^{9,10,11,12} Emerging evidence is demonstrating that older adults are at an increased risk of developing latent and long-term effects related to cancer and/or its treatment compared with younger individuals.^{3,12,13} Prior studies have demonstrated that older adult cancer survivors, compared with older adults without a history of cancer, report poorer physical function,^{14,15,16} an increase in the number of comorbidities,^{17,18,19} poorer quality of life,²⁰ and decrements in cognitive function.^{21,22} Combining aging and cancer survivorship research can clarify the extent to which cancer and its treatment influences the aging processes.

The research by Gresham et al highlights an interaction between cancer, aging, and physical function among older adults, supporting the hypothesis that cancer and/or its treatment may contribute to an accelerated aging phenotype.^{23,24} This risk for an accelerated aging phenotype is relevant to the field of geriatric oncology; however, it is informed by research in pediatric cancer survivors which demonstrates that pediatric cancer survivors are more likely to develop frailty as well as chronic conditions, such as myocardial infarction, congestive heart failure, and second cancers.^{25,26,27}

The characteristics of those cancer survivors who are most at risk for accelerated aging with cancer treatment is unknown. Melding geriatrics and oncology research could help to bridge this knowledge gap. Incorporation of clinical and biological measures of aging before, during, and after cancer treatments is a first step towards understanding the risk factors and clinical manifestations of accelerated aging in cancer survivors as well as elucidating the underlying mechanism of this risk. A clinical assessment of aging can be captured through a geriatric assessment (GA) which evaluates factors other than chronological age that predict the risk of morbidity and mortality in older adults including functional status, co-morbid medical conditions, cognitive function, nutritional status, social support, psychological state, and a review of medications for evaluation of polypharmacy and drug interactions.^{10,22} Inclusion of biological markers of aging could identify the potential mechanism underlying the accelerated aging phenotype. Examples of biological markers of aging include markers of chronic inflammation and coagulation (CRP, IL-6, D-dimer), cellular senescence (telomere length and p16^{INK4a}), and sarcopenia.²⁸

Studies are needed to identify the clinical and biological characteristics of those individuals who are most vulnerable to accelerated aging from cancer treatment. This will set the platform to test interventions to prevent or minimize the short- and long-term treatment-related toxicity. Studies in younger patients with cancer have demonstrated the benefits of exercise interventions and shown that supervised aerobic training is safe, tolerable, and efficacious in potentially offsetting as well as recovering impaired exercise capacity in a patient with cancer.^{29,30} However, studies are needed which specifically focus on older adults in order to determine the optimal timing and “dose” (type and schedule of exercise training) which is feasible, effective and safe. Prior intervention trials in the general cancer population have shown positive effects of aerobic and resistance exercises among cancer patients receiving neoadjuvant^{31,32} and adjuvant chemotherapy,^{33,34} as well as radiation therapy.³⁵ Among older adults, the Reach Out to Enhance Wellness international trial found that a home-based diet-exercise 12-month intervention, delivered via tailored mailed-print

materials and telephone counseling led to improved diet quality, physical activity, and resulted in significant weight loss and higher levels of quality of life and physical functioning among sedentary and obese/overweight cancer survivors age 65 and older.^{36,37} Additionally, the Walk With Ease feasibility study was performed testing whether minimum of 30 minutes of walking five days a week (150 minutes per week) improved physical activity and reduced joint symptoms among older breast cancer survivors on aromatase inhibitors.³⁸ Identifying and testing which single intervention or combination of interventions prove the most effective is a priority in treating late and chronic treatment-related toxicity among older cancer survivors.^{4,12,39}

In conclusion, based on the aging of the cancer population and growth in the number of cancer survivors, this is an opportune time to invest in and accelerate research to mitigate the risk of accelerated aging. Melding the principles of geriatrics and oncology research will be needed to fill this knowledge gap. The discoveries which emerge from this research will be far reaching as they will ultimately improve the well-being and quality of life of the growing population of older cancer survivors.

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