Cancer and Aging

General Principles, Biology, and Geriatric Assessment

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KEYWORDS

• Cancer • Aging • Biology • Biomarker • Geriatric assessment

KEY POINTS

- The biology of cancer and aging remains complex and is likely intertwined through multiple molecular, cellular, and physiologic interactions.
- Geriatric assessment can identify areas of vulnerability in older adults and be used to predict potential treatment toxicity and overall survival among elderly patients with cancer.
- Biomarkers of functional aging along with geriatric assessment may help facilitate personalized treatment decisions among older adults with cancer, through weighing the risks and benefits of cancer treatment in the setting of overall life expectancy and health status.

INTRODUCTION

Cancer is a disease of aging as older adults are much more likely to develop cancer compared with their younger counterparts. In the United States, approximately 60% of all cancer diagnoses and 70% of cancer-related mortalities occur in patients 65 years or older.[1] As the population continues to age, an estimated 70% of all cancer diagnoses will occur in patients over the age of 65 by the year 2030.[2] Understanding the biology of cancer and aging remains complex, and numerous theories regarding the relationship between the 2 have been proposed. Furthermore, treatment decisions regarding older adults with cancer are often difficult due to limited evidence on which to base treatment decisions given the poor representation of this patient population in cancer clinical trials.[3] In this article, the topic of cancer and aging in terms of general principles, biology, and the role of geriatric assessment in older adults with cancer is discussed.

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GENERAL PRINCIPLES

Chronologic age has been identified as a risk factor for numerous malignancies.[4] However, chronologic age alone is not reliable in predicting overall life expectancy, physical function, or the ability to tolerate treatment in older adults with cancer.[5] Rather, aging is a heterogeneous process in regards to individual changes in physiologic status, comorbidities, and cancer biology. In fact, for certain malignancies, the tumor biology and its response to treatment are integrally related to age.[6]

In treating older adults with cancer, chronologic age alone should not exclude patients from the use of therapies that could prolong survival.[7,8] However, the benefit of treatment in terms of prolonging survival must be weighed against potential treatment toxicities and the overall impact on quality of life. Although large randomized clinical trial data for the treatment of older adults with various malignancies are limited, some studies have shown that older patients with good performance status are often able to tolerate and benefit from the same therapies compared with younger patients.[9–11] Nevertheless, individualization of treatments for older adults with cancer requires more data beyond just chronologic age.[12] Use of tools to predict life expectancy,[13,14] establishment of objective biomarkers to predict functional age,[12] and incorporation of geriatric assessment to identify older adults at risk for adverse outcomes and pinpoint interventions to decrease this risk are needed.[15] These tools may ultimately help guide physicians in the shared decision-making process with older adults contemplating cancer treatment, thus facilitating and personalizing care for the older adult.

BIOLOGY OF CANCER AND AGING

A better understanding of the biology of aging may provide valuable clues to understanding cancer development. The term senescence is often synonymous with biologic aging and is characterized by a decrease in stress response, disruptions in homeostatic balance, and an increased risk of chronic illnesses such as cancer. At the cellular level, senescence is characterized by the cessation of replicative division within normal cells of the human body. The relationship between aging, cellular senescence, and cancer is complex, and numerous theories have been proposed to elucidate the relationship (**Table 1**).

Theories on Aging and Potential Impact on Cancer

Mutation accumulation

One of the early theories of aging focused on the accumulation of mutations throughout a lifetime. In this theory, mutations that are not affected by natural selection early in life tend to accumulate and ultimately result in aging.[16] Building on this concept, Denham Harman[17] proposed the free radical theory initially in 1954. Through various oxidative stress reactions occurring within organisms, free radicals are generated that lead to damaging effects in DNA and proteins, thereby contributing to aging and potential carcinogenesis. Furthermore, scientists have also reported that changes in the composition of chromatin such as general hypomethylation,[18] hypermethylation of CpG islands, and accumulation of heterochromatin are associated with an aging phenotype as well. The DNA damage response is essential to the maintenance of the human genome and epigenome. For severe damage, programmed cell death or cell-cycle arrest occurs, allowing for potential anti-cancer protection. However, the cost of this response could be a further depletion of stem-cell reserves, which may promote an aging phenotype. Furthermore, DNA and chromatin repair in itself can be error prone, leading to the accumulation of additional mutations. Interestingly,