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Review article

Cardio-oncology in the older adult

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ABSTRACT

Heart disease and cancer are the leading causes of death in older adults. Many first-line cancer treatments have the potential for cardiotoxicity. Age-related risk factors, pre-existing cardiac disease, and a high prevalence of co-morbidities are reasons for increased cardiotoxicity in older adults. Concerns regarding cardiotoxicity may lead to frailty bias and undertreatment, resulting in suboptimal outcomes. There is an urgent need for geriatric-specific evidence and guidelines to help tailor care for this vulnerable group. A multi-disciplinary approach based on close collaboration between oncologists, cardiologists, and geriatricians, among other specialist clinicians is essential.

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Introduction

Cardio-oncology is an area of growing interest in recent years. Data are lacking on cardio-oncology specific to older adults. This is increasingly

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becoming important as advances in cancer treatments result in longer patient survival [1]. The 5-year survival of patients diagnosed with cancer has steadily increased from 49% to 69% over the past three decades [1]. The proportion of cancer survivors that are 65 years or older has increased exponentially. By 2020, it is estimated that the number of cancer survivors will increase by 31% to 18 million, and that two-thirds of all cancer survivors will be 65 years or older [2–4]. As the incidence of cancer rises with increasing age, so does the prevalence of cardiovascular disease (CVD). Those older than 65 years account for more than half of CVD hospitalizations and approximately 80% of deaths [5]. Even more striking, those 75 years of age or older account for 50% of cardiovascular deaths despite accounting for only 6% of the population [5].

Despite the increased prevalence of older adults living with cancer and associated treatment toxicities, patients 65 years or older are underrepresented in clinical trials [5–7]. Older patients are frequently offered lower doses of chemotherapy due to concerns of toxicity, presumed frailty, and the high likelihood of coexisting comorbidities. Several observational studies have noted poorer outcomes in this group possibly due to undertreatment and age-related factors [8,9]. As a result, optimal care of older adults with cancer necessitates evidence-based and guideline-directed care specific to this vulnerable group. Such care is especially critical for elderly patients at risk for cardiotoxicity.

Risk Factors of Cardiotoxicity

The 2016 American Society of Clinical Oncology (ASCO) Clinical Practice Guideline for the prevention and monitoring of cardiac dysfunction in survivors of adult cancers identifies the following risk factors for cardiac dysfunction: older age (age greater than 60 years), high-dose anthracycline therapy, high-dose radiotherapy, cardiovascular risk factors including smoking, diabetes, dyslipidemia, and obesity, borderline low cardiac function, valvular disease, and history of myocardial infarction [10]. An estimated 80% of patients 60 years of age or older have at least one comorbid condition and 50% have two or more [11]. In patients older than 80 years, as many as 70% have multiple comorbid conditions [11]. In a retrospective analysis of patients receiving treatment for acute myeloid leukemia, a larger proportion of patients older than 60 years had significant comorbidities compared with those younger than 60 years (58.3% vs. 26.3%) [12]. Not surprisingly, these comorbidities include diabetes mellitus, chronic obstructive lung disease, chronic kidney disease, and pre-existing heart disease [12]. The cumulative effect of these factors, as illustrated in Fig. 1 and previously described by Shenoy et al. [13], can be described as a "snowball effect." The "snowball," formed of baseline age-related factors is "set in motion" by the cancer diagnosis and is further exacerbated by cancer treatments which cause direct injury to tissues and organs.

Polypharmacy and use of potentially inappropriate medications are prevalent in older adults and can exacerbate the toxicity associated with cancer treatments [14–16]. A multidisciplinary approach, including pharmacist involvement, is vital to preventing polypharmacy and inappropriate medication-related toxicities. Medication therapy management (MTM), consisting a thorough review of medications by a pharmacist, is increasingly being adopted in older patients and those with multiple comorbidities, including those with cancer [17]. A growing number of retrospective studies indicate that MTM significantly reduces drug–drug interactions, adverse drug events, and non-adherence in older patients with cancer [17,18].

Cancer Treatment-specific Considerations

Comprehensive reviews exist on the cardiac toxicity of chemotherapy agents [10,19,20]; in this article, cancer therapies with the highest risk for cardiotoxicity in the elderly population are discussed below including anthracyclines, trastuzumab, tyrosine kinase inhibitors, fluoropyrimidines, and radiation therapy.

Anthracyclines

Anthracyclines remain the first-line therapy for many cancers including breast cancer, hematological cancers, and sarcoma. They are

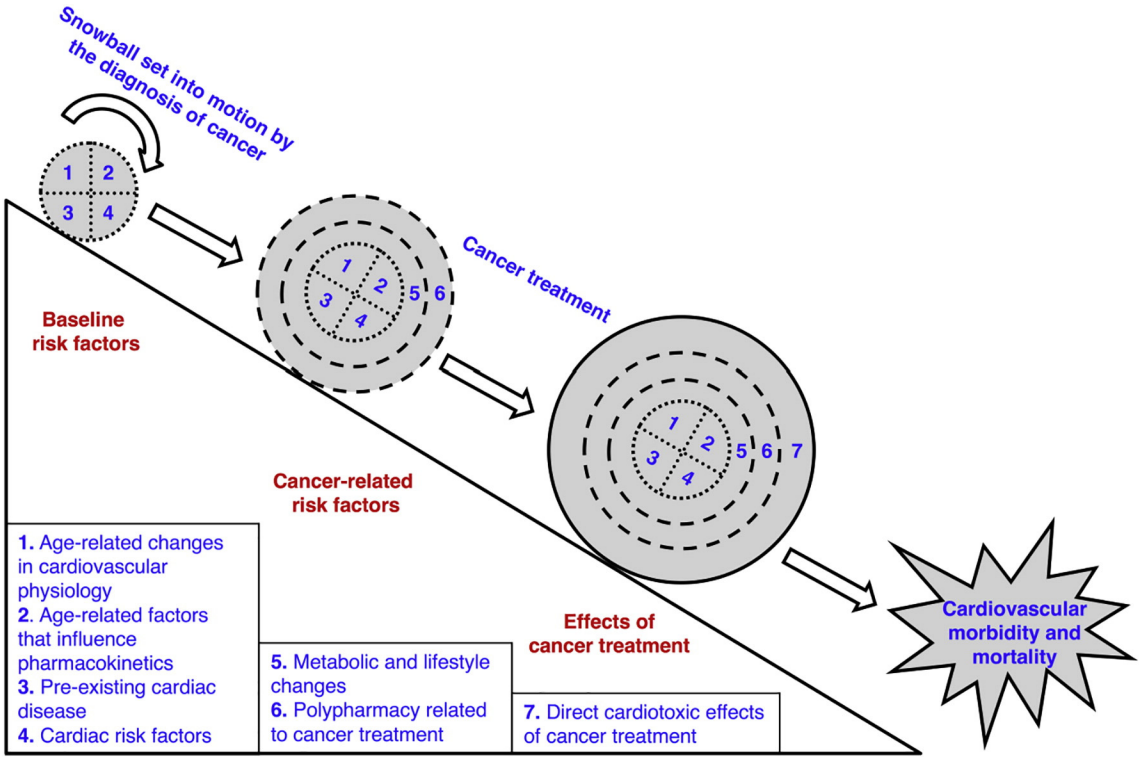

Fig. 1. The "snowball effect" resulting in cardiovascular complications of cancer therapy in older adults. See text for details. Adapted with permission from Shenoy et al. [13].

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