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Research paper

Introduction: A cardiologist's perspective

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Cardiovascular disease (CVD) and cancer have long been the leading causes of death among Americans. Over the course of four decades from 1968 to 2010, there was a dramatic, multi-factorial 70% reduction in age-adjusted CVD death rates in the US, and yet it still remained the leading cause of death [1]. There was a moment when it appeared that heart disease might become the second leading cause of death behind cancer, but the decade of the 2010s has seen stagnation in CVD death rates and accelerating downward trends in cancer death rates (Fig. 1) [2].

With the improved survival of patients after cancer diagnosis, the opportunity for CVD events to occur in these patients has increased as a competing risk [3]. Data from cohorts of survivors of childhood cancers show early mortality risk (in the first two decades after diagnosis) from recurrent cancer that plateaus over time, and later mortality risk (particularly after the third decade) from all other causes (especially CVD) that far exceeds the background risk of the general population at the same ages [4]. One study suggested 10–15-fold higher relative risks for congestive heart failure, coronary heart disease, and stroke among such patients [5].

Likewise, CVD and cancer share a common soil of behavioral, physiological, and environmental risk factors from which they emerge [6], so that individuals at risk for one are also at elevated risk for the other [7]. Cigarette smoking and diet are obvious risk factors for both cancer and CVD incidence. But a number of studies have also shown elevated risks for both CVD and cancer associated with diabetes and even hypertension.

A number of pathophysiological links have been proposed to drive the co-occurrence of elevated risks for cancer and CVD. Among these, several pathways have attracted strong interest. For example, there is tantalizing evidence that inflammatory pathways may play a key role in elevating conjoint risk; and some interventional studies suggest benefit in targeting inflammation reduction to reduce risk for both CVD and cancer. Randomized clinical trial data suggest a modest benefit for aspirin in reducing risk for CVD, as well as significant reductions in colorectal cancer caused by tumors expressing cyclooxygenase-2 [8]. A recent trial using canakinumab (an anti-IL 1β monoclonal antibody), showed modest reductions in both CVD recurrence and incidence and mortality due to lung cancer [9].

Current studies suggest that clonal hematopoiesis, a potential precursor to certain hematologic malignancies, may also be associated independently with risk for CVD through both somatic genetic mutations affecting common disease pathways, as well as common upstream exposures like ambient radiation, smoking, air pollution, dietary factors, and possibly other exposures. The common occurrence of clonal hematopoiesis (seen in up to 20% of 70-year-old individuals) could make this an important risk marker, and possible risk factor, for CVD as well as cancers [10].

There is an elevated risk for incident acute CVD events among patients with cancer. CVD risk appears to be elevated in the first year after cancer diagnosis and then to decline, only to re-emerge at five years and beyond [11,12]. The early risks may be related to enhanced thrombotic and thromboembolic vascular events associated with the cancer [13] and stressors related to cancer diagnosis and acute treatment. Later CVD risk among cancer patients appears to be a consequence of common underlying risk factors and effects of radiation and or chemotherapeutic agents on the cardiovascular system [14].

Fortunately, the successes in survival among cancer patients have spawned a new subspecialty – cardio-oncology (or oncocardiology) – that can address the unique and sometimes challenging aspects of co-managing cardiovascular risks and disease among cancer patients. As a result of important research and growing need for expertise, recent years have seen marked growth in recognition of the discipline by

Abbreviations: CVD, cardiovascular disease.

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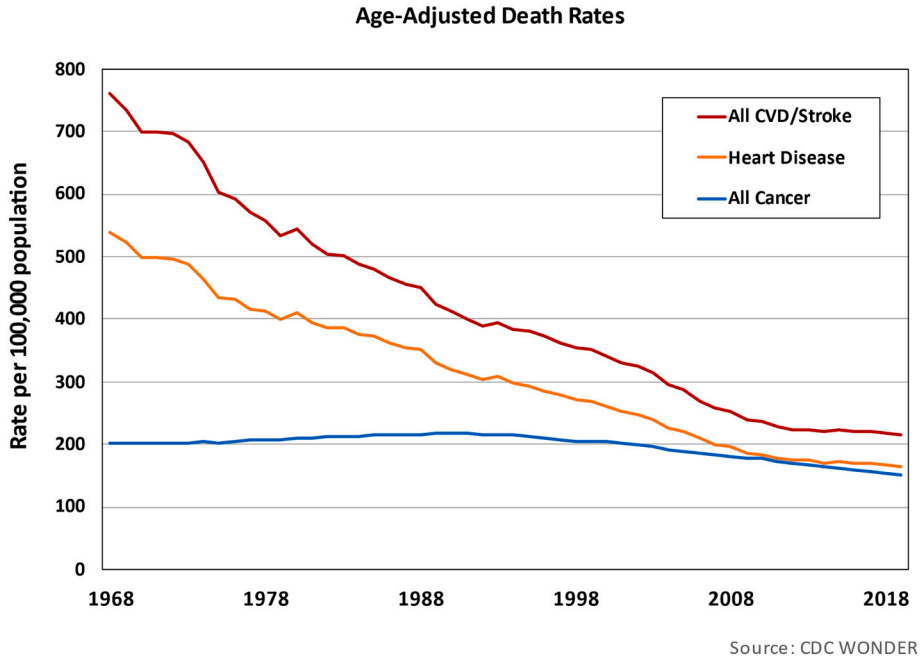

Fig. 1. Cause-specific mortality rates, US, 1968–2019. Heart disease, cardiovascular disease/stroke, cancer. Source: CDC WONDER.

professional societies, increasing attention in the scientific literature (and entire journals dedicated to the field), increased research funding, specific clinical programs, focused training programs, and now board certification. The rapid emergence of this discipline is serving as a model for others (e.g., cardio-obstetrics).

Declaration of competing interest

Unpaid fiduciary officer of the American Heart Association.

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