Determining Cause-Specific Mortality in Cancer Survivors
A Daunting Task?*

Linda A. Jacobs, PhD, CRNP

Evidence continues to emerge linking cardiovascular disease (CVD) and cancer, the 2 leading causes of mortality and morbidity worldwide. Cancer survivors are at risk for CVD on the basis of individual characteristics, modifiable cardiovascular risk factors, and the acute and long-term effects of cancer treatment. First, CVD and cancer share a number of common risk factors, such as older age, sex, poor nutrition, obesity, smoking status, and lack of physical activity. Modifiable risk factors such as diabetes, hypertension, and hyperlipidemia are associated with an increased risk for CVD in cancer survivors. Risk for cancer treatment–related cardiotoxicity is also well established, including short and long-term effects of radiation and many of the systemic chemotherapies, targeted therapies, and immune therapies patients receive as part of their treatment. Moreover, evidence also links the pathogenesis of both diseases with common molecular, cellular, genetic, and signaling pathways.1,2

In prior work by Strongman et al,3 the risks for specific CVD in a population-based cohort study of survivors of 20 adult cancers were examined during a follow-up period of 1 to 13 years. The investigators concluded that survivors of most site-specific cancers had higher risks for CVD compared with those of people without cancer diagnoses. They also noted that there were insufficient data on the long-term CVD risk of systemic anticancer drugs and radiotherapy with techniques in the modern treatment era. The investigators further commented that an important issue with managing postcancer risk for CVD has been that the long-term follow-up is typically shared by cancer specialists and primary care providers with insufficient focus on potential CVD. Also, most survivors with site-specific cancers had higher risks for CVD compared with patients without cancer.

In this issue of JACC: CardioOncology,4 these same investigators estimate age-stratified mortality rates from CVD or cancer and determine the time point at which risk for cardiovascular mortality overtook risk for mortality from cancer (both all and primary malignancy) in survivors of the 9 most common cancers in England. They propose that to raise awareness of the risk for CVD in cancer survivors, and to inform patient counseling and decisions about monitoring and priorities for disease prevention, we should know how risk for death from CVD competes with risk for death from cancer over time.

Mortality over time due to CVD, the primary cancer, and all cancers was reported for patients stratified by age at diagnosis (40–59, 60–79, and ≥80 years). Mortality rates from the primary cancer decreased over time for all cancer survivors, and there was a clear pattern of increasing mortality from CVD by age, most pronounced in patients ≥80 years of age. This stands to reason given that people in this age group are more likely to have underlying CVD and comorbidities that place them at increased risk for CVD, in addition to the possibility of CVD resulting from cancer treatment. The observation times ranged from 2 to 11 years and 6 to 17 years after treatment for specific cancers, which makes the survivors in this age group, in particular, an elderly age group and at
even higher risk for CVD. In addition, survivors with prostate and breast cancer diagnosed at ≥80 years of age may be more likely to survive their disease for longer periods of time.

For patients diagnosed between 40 and 59 years of age, CVD mortality remained low for most of the cancers examined. Patients of this age group were less likely to have underlying cardiac disease and comorbidities that would increase CVD risk. Not surprisingly, with advancing age at cancer diagnosis, the risk for CVD mortality increased beyond that due to cancer mortality, particularly for patients with cancers associated with longer survival: breast and prostate.

The large sample size is a strength of the study; however, as noted as a limitation of the study, comparisons were not made with a population without cancer or CVD, matched for age, sex, race, comorbidities, and other factors in order to determine norms in the age groups. The lack of cancer characteristics and treatment data is a significant limitation as well. Insufficient data to stratify grade, stage, and treatment data prove to be an important flaw, as these variables must be considered when determining mortality rates as a result of cancer versus CVD. Consequently, it is difficult to draw definitive conclusions from these data.

However, Strongman et al. are to be commended for the large analyses they undertook. The importance of postcancer monitoring with care focused on risk for cancer relapse is crucial. Posttreatment cardiovascular monitoring and follow-up care as well as lifelong monitoring for all late effects of the treatment received must be a priority in cancer care as well. Furthering our understanding requires additional information on CVD mortality in these patients compared with age-matched control subjects without cancer, as well as detailed data on cancer treatments received, which will help providers best care for these patients.

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ADDRESS FOR CORRESPONDENCE: Dr Linda A. Jacobs, 133 Valley Road, Ardmore, Pennsylvania 19003, USA. E-mail: linda.jacobs@pennmedicine.upenn.edu.

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