JACC: CARDIOONCOLOGY VOL. 5, NO. 1, 2023

EDITORIAL COMMENT

The Cause of Death in Patients With Cancer*

Michael C. LeCompte, MD, MS,[a] Otis W. Brawley, MD[b,c]

Cardiovascular disease (CVD) and cancer are the most common and second most common causes of death in the United States, respectively.[1] Despite advances toward improved outcomes in both diseases, health disparities exist and in some cases have widened, as certain groups have less access to quality health care. As the number of cancer survivors grows, better characterization of what causes death is important.

In this issue, Zhu et al[2] report their study of data from the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute, identifying groups of patients with cancer, particularly those with early-stage disease, younger age, and better prognosis disease, who have a higher risk for CVD death. Black patients with cancer had a higher risk for both all-cause and CVD mortality compared with non-Hispanic (NH) White patients. NH White patients had higher mortality rates than Hispanic and NH Asian/Pacific Islander patients. This increased risk persisted on multivariable analysis, adjusting for sociodemographic and clinical characteristics.

It is of note that this paper is published at a time when cancer is starting to surpass CVD as the leading cause of death in most Western countries.[3] This is projected to occur in the United States in the near future. Indeed, cancer is already the leading cause of death among Asian Americans, Hispanic Americans, and the U.S. population aged 45 to 64 years.[4]

When studying cancer outcomes and disparities in outcomes, researchers often quote cancer-specific death rates. It is important to remember that our purpose is not just to control cancer but to prolong life. As we improve our abilities to control cancer, we need to be more holistic and focus on reducing all-cause mortality. This means identifying and focusing on the control of other common causes of death for patients with cancer. Compared with persons of the same age, patients with cancer have a 4-fold greater risk for dying of CVD within the first year of cancer diagnosis and remain at elevated risk throughout the rest of their lives.[2,5] CVD is caused or exacerbated by common causes of cancer, such as tobacco use and obesity. Some cancer therapies can also exacerbate CVD. Indeed, there is ongoing research to better understand how toxicities of cancer therapies, physiological effects of cancer (eg, inflammation, oxidative stress), and shared biological predisposition may contribute to CVD death in patients with cancer.[6-8]

As outcomes research has matured, it has become evident that some populations suffer from disparities in outcome. Disparities are avoidable differences in incidence, mortality, or quality of life. Populations can be defined in a number of ways: by gender, area of geographic origin, race, ethnicity, socioeconomic status, and area of residence.[9] Realizing these differences helps more appropriately target efforts and reduce disparities.

Zhu et al[2] assess differences in CVD death among patients with cancer by race and ethnicity. These are commonly used population categorizations, and it is appropriate to use them. However, one must remember what they are and what they are not. Race is a concept of population categorization developed

*Editorials published in *JACC: CardioOncology* reflect the views of the authors and do not necessarily represent the views of *JACC: CardioOncology* or the American College of Cardiology.

From the [a]Department of Radiation Oncology and Molecular Radiation Sciences, Johns Hopkins University, Baltimore, Maryland, USA; [b]Department of Oncology, Johns Hopkins University, Baltimore, Maryland, USA; and the [c]Department of Epidemiology, Johns Hopkins University, Baltimore, Maryland, USA.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

ISSN 2666-0873 https://doi.org/10.1016/j.jaccao.2023.01.004

JACC: CARDIOONCOLOGY, VOL. 5, NO. 1, 2023
FEBRUARY 2023:67–69

about 300 years ago to justify European colonialism.[9] Today, the anthropological community views race as a complex sociopolitical construct rather than a biological categorization.[10] There are no discrete biological boundaries among races. Recently, the American Medical Association has been outspoken, saying that race should not be a proxy for biology in medical education, research, and clinical practice.[11] In contrast, ethnicity is distinct from race and loosely refers to culture. Both can correlate with societal influences that cause disease.

Race is often linked to area of geographic origin. The forces of natural selection have led to human differentiation. Although these forces operate in ecologic or geographic areas, the areas often do not coincide with population or racial boundaries. There are some biologic variables, including some genetic traits, that loosely parallel area of geographic origin, but even so, this is complicated by significant population admixture.

The racial categories in SEER are defined by the U.S. Office of Management and Budget,[1] which defines race for all demographic data collected by the federal government. The definitions are typically published about 2 years before every decennial census, and the definitions do change. For example, people originating in the Indian subcontinent were once considered White or Caucasian but more recently have been categorized as Asian subcontinent, Asian/Pacific Islander, and now Asian. Since the 2000 census, the categories used are Black or African American, White or Caucasian, Asian, Native Hawaiian or other Pacific Islander, and Native American or Alaskan Native.[12] The U.S. government recognizes 2 ethnicities: Hispanic and NH. Also, beginning in 2000, individuals surveyed for the census are encouraged to self-identify and to choose all that apply.

An example of race as a social construct is the fact that Black or African American race generally correlates with a population in the United States that is more likely to be socioeconomically underprivileged, which in turn leads to reduced access to quality health care (preventive, screening, diagnostic, and treatment).[9] Social influences or social determinants that parallel with race can influence the entire spectrum of disease from pathogenesis to disease biology or aggressiveness and, of course, access to care and outcomes. The disease can be cancer, diabetes, CVD, or a number of other diseases. Indeed, it is important to note that social deprivation does not discriminate by race. Impoverished White Americans have higher rates of these diseases compared with middle-class White Americans.

The poor, known to include many racial and ethnic minorities, are more prone to receive care in resource-poor clinical environments.[13] Largely because of education and economic deprivation, healthful behaviors are less likely to be adopted in these populations. Throughout life, preventive services are more often lacking. More emphasis should be put on the fact that there are significant disparities in disease influences, which in turn cause disparity in disease development and in some cases even disparities in the aggressiveness of disease. The influences that cause disease are often pressures over years and even decades.

The SEER program has been a vital resource in the study of health disparities. Although the SEER database provides essential information, it does have limitations. It does not collect data on insurance status or individual sociodemographics, such as education level, income, or occupation.[14] In their analysis, Zhu et al[2] observed a higher risk among Black patients with cancer for CVD death, when looking at those <55 years of age. A large portion of patients older than 55 years are insured through Medicare (which enrolls most U.S. residents at 65 years of age). One could believe access to insurance to be a confounding variable. The investigators do try to adjust for socioeconomic status using county median income level. This is an extremely coarse adjustment that cannot fully adjust for socioeconomic status. Indeed, it is impossible to fully adjust for all sociodemographic and clinical characteristics even when using individual-level data.

SEER reflects cause of death as indicated on a patient's death certificate. This information is placed on the death certificate by the physician certifying the death. This process can be subjective and thus is susceptible to biases toward inaccurately attributing death to CVD, especially among the socially deprived, when the doctor completing a death certificate may not have known the deceased individual in life. Because of our health care system, poorer patients are more likely to be unknown to physicians completing death certificates. This might lead to some patients' true causes of death being missed and attributed to CVD. Similarly, self-declared race may not be on the death certificate. Indeed, the physician often assumes the race and ethnicity of the individual on the basis of physical characteristics or the individual's name.

We agree that data by race/ethnicity should be published, realizing the limitations in the data. It is important to recognize disparities, realize who suffers from them, and assess the reasons for those disparities in order to develop a plan to overcome them. Ironically, we are endorsing a sort of benevolent

racial profiling, but we also encourage open-mindedness and attention to all patients' social determinants of health.

When we see disparities by race/ethnicity, it is important to recognize what the racial categories are and what they are not. Race is not a biological or an inherent genetic categorization. Race is a social construct. That being said, social determinants of health associated with race can influence biology and lead to higher risk for certain diseases. This is especially true for the major chronic diseases, cancer, diabetes, and CVD.

Zhu et al[2] clearly show that the cancer control effort cannot be waged in a vacuum. Health equality cannot be achieved without significant efforts to identify and control comorbid diseases. These efforts involve prevention and risk reduction, appropriate screening, diagnostics, and treatment.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

Dr Brawley is a consultant to Grail, Agilent, Incyte, PDS Biotech, Lyell, Genentech, and EQRx. Dr LeCompte has reported that he has no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr Otis W. Brawley, Department of Oncology, Department of Epidemiology, Johns Hopkins University, 1550 Orleans Street, Suite 1M16, Baltimore, Maryland 21287, USA. E-mail: otis.brawley@jhu.edu. Twitter: @OtisBrawley.

REFERENCES

1. Siegel RL, Miller KD, Fuchs HE, et al. Cancer statistics, 2022. *CA Cancer J Clin*. 2022;72:7-33.

2. Zhu C, Shi T, Jiang C, et al. Racial and ethnic disparities in all-cause and cardiovascular mortality among cancer patients in the US. *J Am Coll Cardiol CardioOnc*. 2023;5(1):55-66.

3. Bray F, Laversanne M, Cao B, et al. *Comparing cancer and cardiovascular disease trends in 20 middle- or high-income countries 2000-19: a pointer to national trajectories towards achieving Sustainable Development Goal Target 3.4*. 100. Cancer Treat Rev; 2021:102290.

4. Heron M. Deaths: leading causes for 2019. *Natl Vital Stat Rep*. 2021;70:1-114.

5. Sturgeon KM, Deng L, Bluethmann SM, et al. A population-based study of cardiovascular disease mortality risk in US cancer patients. *Eur Heart J*. 2019;40:3889-3897.

6. Panova-Noeva M, Schulz A, Arnold N, et al. Coagulation and inflammation in long-term cancer survivors: results from the adult population. *J Thromb Haemost*. 2018;16:699-708.

7. Lenneman CG, Sawyer DB. Cardio-oncology: an update on cardiotoxicity of cancer-related treatment. *Circ Res*. 2016;118:1008-1020.

8. Masoudkabir F, Sarrafzadegan N, Gotay C, et al. Cardiovascular disease and cancer: Evidence for shared disease pathways and pharmacologic prevention. *Atherosclerosis*. 2017;263:343-351.

9. Williams DR, Lavizzo-Mourey R, Warren RC. The concept of race and health status in America. *Public Health Rep*. 1994;109:26-41.

10. Benn Torres J. Anthropological perspectives on genomic data, genetic ancestry, and race. *Am J Phys Anthropol*. 2020;171(suppl 70):74-86.

11. Flanagin A, Frey T, Christiansen SL, et al. Updated guidance on the reporting of race and ethnicity in medical and science journals. *JAMA*. 2021;326:621-627.

12. Friedman DJ, Cohen BB, Averbach AR, et al. Race/ethnicity and OMB Directive 15: implications for state public health practice. *Am J Public Health*. 2000;90:1714-1719.

13. Bach PB, Schrag D, Brawley OW, et al. Survival of Blacks and Whites after a cancer diagnosis. *JAMA*. 2002;287:2106-2113.

14. Johnstone PA. NCI Surveillance, Epidemiology & End Results (SEER) registry. Foreword. *Curr Probl Cancer*. 2012;36:182.

KEY WORDS cardiovascular disease, cause of death, health disparities, overall mortality, race