

EDITORIAL COMMENT

Healthy Lifestyle Benefits Both Cancer and Cardiovascular Disease



More Bang for the Buck*

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*Health is a priceless wealth.
Invest while you can.*

—Bryant McGill, author and entrepreneur

A central tenet for population-wide preventive efforts is the compression of morbidity to a shorter duration and a shift to later onset in life. In other words, it is not just simply about extending life but extending years lived free of disease and disability. Notably, individuals with more favorable cardiovascular health (CVH) in middle age have lower levels of cardiovascular and noncardiovascular morbidity decades later, which translates to both longer survival and reduced health care expenditures (1). In a multiethnic cohort, having an optimal CVH score defined by the American Heart Association (AHA) Life's Simple 7 metrics was associated with a 20% lower risk for developing incident cancer over the following 10 years (hazard ratio [HR]: 0.80; 95% confidence interval [CI]: 0.64-0.98) (2).

Cancer and cardiovascular disease (CVD) remain the top 2 leading causes of death in the United States and globally. Cancer and CVD share many risk factors and often coexist in the same individuals, creating synergistic opportunities for shared screening and prevention interventions (3). Among cancer survivors, the leading noncancer cause of death is CVD. In

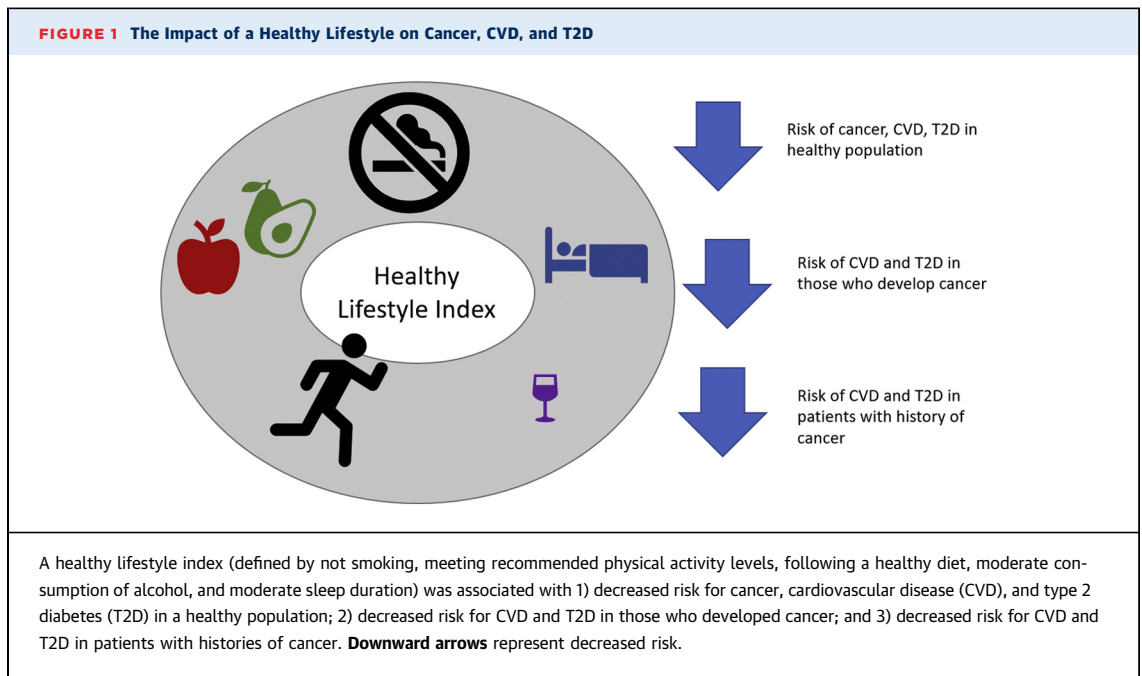
one US cohort of more than 3 million cancer survivors, 38% died of cancer and 11% died of CVD, most of whom had histories of breast, prostate, or bladder cancer (4). CVD mortality was actually highest in the first year after cancer diagnosis compared with the general population but remained elevated throughout the entire follow-up period (4). However, the impact of a healthy lifestyle on the bidirectional interplay between cancer and CVD is complex and had not been previously well elucidated.

In this excellent new analysis by Cao et al. in this issue of *JACC: CardioOncology* (5), the investigators examined the association of a healthy lifestyle index (HLI) on cancer, CVD, and type 2 diabetes (T2D) among more than 432,000 participants of the UK Biobank study recruited from the general population. The principal findings were that healthy living (defined as not smoking, meeting the AHA guidelines for physical activity, a healthy diet, moderate consumption of alcohol, and moderate sleep duration) was associated with a lower risk for incident cancer, CVD, and T2D in a healthy population and a lower risk for CVD and T2D in those who developed cancer or had histories of cancer (Figure 1).

The investigators included 2 populations: patients who developed incident (new) cancer (thus examining the impact of lifestyle prior to cancer diagnosis) and those who previously had cancer (thus examining the impact of a healthy lifestyle after diagnosis). Among individuals initially cancer free, each 1-point increment in the HLI (range: 0-5) was associated with an 8% decreased risk for incident cancer (HR: 0.92; 95% CI: 0.91-0.93) and a 12% lower risk for incident CVD (HR: 0.88; 95% CI: 0.87-0.89) (5). Even after incident cancer diagnosis, a similar increment in HLI was associated with a 10% reduction in incident CVD. Among those with prevalent cancer at baseline, a 1-point increment in HLI was

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similarly associated with a 10% lower risk for incident CVD (HR: 0.90; 95% CI: 0.87-0.93) and a 13% reduction in incident T2D (HR: 0.87; 95% CI: 0.83-0.91). These favorable associations with healthy living were dose dependent, with cancer survivors who achieved all 5 measures of healthy lifestyle being at 44% and 38% reduced risk for subsequent CVD and T2D, respectively, compared with cancer survivors with only 0 or 1 healthy lifestyle measure. Other notable findings were that the beneficial effect of healthy living on CVD risk in cancer survivors appeared stronger in women than in men, and higher HLI was associated with lower risk for CVD and T2D regardless of age.

This study has many strengths, including the use of a large, robust dataset with low rates of missing data. By including patients who were both cancer free and with prevalent cancer, the investigators captured many different types of patients and cancer diagnoses. However, some caveats should be considered. First, the median age of the cancer prevalent group was 59 years, so the cancers diagnosed in that group (breast, cervical, and melanoma) were not surprisingly different from the incident cancers that developed in the baseline healthy group (breast, prostate, and colorectal), which had a median age of 55 years at entry into the cohort. For context, the median age at prostate cancer diagnosis in the United States is 66, and the median age at lung cancer diagnosis is about 70 years (6).

Perhaps more controversial is that in this analysis, moderate intake of alcohol was considered a healthy lifestyle factor. Although light to moderate alcohol consumption has been shown to be associated with favorable CVH in some cohort studies, higher alcohol intake has been associated with poor CVH, and associations with cardiovascular risk differ by sex and alcohol type (7,8). Alcohol use increases the risk for accidents and for atrial fibrillation. Alcohol is also a risk factor for many cancers, even moderate alcohol use (9). Thus, it was somewhat surprising in this cohort that alcohol use was associated with lower risk for transition to cancer. The investigators did not examine the association between alcohol and incidence of secondary cancer occurrence in patients with prevalent cancer. The AHA does not endorse alcohol as a preventive strategy or consider alcohol as one of its favorable CVH metrics. The American Society of Clinical Oncology similarly does not support alcohol use as a preventive strategy.

Another perhaps surprising finding was that a healthy lifestyle was associated with an increased risk for prostate cancer (HR: 1.04 per 1-point increment in HLI; 95% CI: 1.01-1.06) and melanoma (HR: 1.09; 95% CI: 1.04-1.15), the former perhaps due to screening practices, as has been suggested previously (10), and the latter perhaps due to ultraviolet exposure from outdoor physical activity. Although this certainly does not negate the overwhelming benefits of a healthy lifestyle overall, this finding does point out

that there is significant heterogeneity between lifestyle factors and certain cancers.

Some additional questions remain, which hopefully can be addressed by future studies. Lifestyle and behavioral change can be challenging to implement; we need a better understanding of tools that can help support it and the impact of policy changes. Additionally, studies are needed to help identify optimal strategies to screen for CVD risk among cancer survivors, such as the incorporation of cardiorespiratory fitness testing or the assessment of coronary artery calcium scores (3). Although many cancer therapies have detrimental effects on the cardiovascular system, drug development in oncology is currently at an all-time high. Further work should be conducted to identify therapies that will improve both CVH and cancer outcomes. For example, in prostate cancer, a novel treatment strategy of bipolar androgen therapy seems to have some beneficial effects on CVD risk factors (11). Another example of this is through targeting inflammation, a shared mechanistic explanation for overlap between the 2 diseases. The CANTOS (Cardiovascular Risk Reduction Study [Reduction in Recurrent Major CV Disease Events]) trial showed that the anti-inflammatory agent canakinumab, inhibiting interleukin-1 β , reduced the risk for both

CVD events and fatal cancers (12). Further research on this and other agents is ongoing in cancer.

In sum, the analysis by Cao et al (5) highlights the importance of a healthy lifestyle for prevention of the 2 leading causes of death. Healthy living factors related to favorable diet, exercise patterns, not smoking, and adequate sleep should be encouraged for everyone. Notably, the benefit of a healthy lifestyle extends even after a cancer diagnosis. Health is wealth, and investment in healthy living throughout the life span can help mitigate 2 of the greatest health threats of a global population.

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