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EDITORIAL COMMENT

Addressing the "Common Soil" of Risk Factors for Cardiovascular Disease and Cancer*

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The American Heart Association (AHA) and the American Cancer Society both promote the importance of a healthy lifestyle as a central strategy for primordial and primary prevention of cardiovascular disease (CVD) and cancer. CVD and cancer are the leading causes of death in the United States, and there is significant overlap in shared modifiable risk factors and, potentially, in molecular mechanisms of disease (1). Some earlier epidemiologic studies noted this "common soil" of underlying risk factors from which these 2 chronic diseases of aging may spring. Individual patients are at risk for both CVD and cancer simultaneously as a result of common risk factors, but mechanisms of these joint risks, beyond the biologically obvious risk factors as in cigarette smoking, remain somewhat obscure.

Lau et al. (2) provide a helpful contribution to the field in this issue of *JACC: CardioOncology* by exploring the temporal associations and influence of CVD risk factors on cancer incidence. Their study was conducted among 20,305 participants of the Framingham Heart Study and the PREVEND (Prevention of Renal and Vascular End-State Disease) study, which are both community-based longitudinal cohort studies focused on cardiovascular epidemiology (but with collection, adjudication, and confirmation of histologically proven major cancer diagnoses). Lau et al. (2) evaluated cancer incidence associated with individual CVD risk factors, as well as with a widely used atherosclerotic CVD risk estimation score (3) that used clinical risk factors as a basis and the AHA's cardiovascular health (CVH) assessment score (4) that also includes lifestyle factors and body mass index. Lau et al. (2) further examined 2 CVD biomarkers, natriuretic peptides and troponin, for associations. During a mean follow-up period of 15.0 years (range 13.3 to 15.0 years), they observed 2,548 cases of incident cancer in any tissue, excluding nonmelanoma skin cancers, and specific subtypes of cancer including breast, lung, prostate, and gastrointestinal cancers. Overall, Lau et al. (2) observed previously described univariable associations with incident cancer for most of the individual traditional CVD risk factors, including age, male sex, cigarette smoking, hypertension, diabetes, and dyslipidemia. In multivariable analyses, using stringent thresholds for statistical significance resulting from multiple tests, age, sex, and smoking status remained significantly associated with a higher risk of any cancer, and associations for other risk factors were in the expected directions. Of interest, both the atherosclerotic CVD risk score of clinical risk factors (weighted for prediction of CVD events) and the unweighted CVH score used to describe both risk factors and lifestyle variables showed strong dose-response associations with incident cancer. Natriuretic peptide levels, but not troponin levels, were also associated with a modestly higher risk for cancer. Neither prevalent CVD nor interim CVD events during follow-up were associated with cancer incidence. Overall results were similar in both the Framingham and PREVEND cohorts, thus lending credence to the findings.

Strengths of the study by Lau et al. (2) include the large size of the sample and the well-characterized participants, as well as careful follow-up and adjudication of endpoints using histological diagnoses and not just administrative diagnosis codes. Both Framingham and PREVEND, however, included only

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White individuals of European ancestry. Nonetheless, the results merit our attention. As noted by Lau et al. (2), Rasmussen-Torvik et al. (5) previously took a similar approach to examine individual lifestyle and risk factors, as well as the CVH score, in White and Black Americans in the Atherosclerotic Risk in Communities Study and found similar associations. A very large study of more than 575,000 European individuals showed robust associations of blood pressure levels with overall cancer incidence in men and with specific cancer subtypes in men and women (6). The consistency of the results across these cohorts and the earlier published reports should reinforce the concept of "common soil," which offers opportunities in research, clinical practice, and public health.

It is clearly important to examine the risk of cancer by distinct subtypes, not just by tissue, as was done by Lau et al. (2), but also by molecular subtypes of breast cancer or colorectal versus stomach cancer, given their unique risk factors and risk of mortality. The current results raise important and lingering questions about genetic and epigenetic changes in target tissues potentially induced by risk factors and lifestyles that may use common pathways to disease through inflammation, clonal hematopoiesis, or other mechanisms. Furthermore, variation in risk of cancers in many tissues is known to vary by sex, and it may have a biological basis related to exposure to hormonal factors and risk factors across the life course (7). Sex-specific findings of associations with cancer were not presented in the current study (other than for prostate and breast cancers). In addition, the incidence of young and early onset cancer is increasing among adults younger than 50 years of age, particularly for breast and colorectal cancers (8). Future studies should examine stratified analyses to account for heterogeneity and provide evidence for potentially unique risk factors in these groups.

As clinicians, we must break down silos in consideration of preventing CVD and cancer using separate approaches. The common soil of the 2 diseases (and other chronic diseases of aging, such as lung diseases, degenerative joint diseases, among others) necessitates holistic and comprehensive approaches to communication and implementation of health promotion and disease prevention strategies. Before the onset of either disease, we must use all of our tools in counseling and safe interventions to improve lifestyle and control existing risk factors, with medication use when safe and necessary. In this vein, primary CVD prevention is well ahead of the cancer prevention field. Moving forward, we must nurture the concept in our patients' minds of joint benefit to forestall both CVD and cancer, particularly through lifestyle interventions of healthier eating patterns and participation in more physical activity. The AHA and the American Cancer Society, primary care and pediatric professional societies, and government agencies should play a larger role in speaking with a unified voice about common goals for health promotion and prevention of all chronic diseases of aging by addressing the common soil of risk factors and behaviors. Even in the setting of existing CVD and cancer, a focus on these modifiable risk factors remains appropriate. Although Lau et al. (2) observed that prevalent and interim CVD events were not associated with cancer incidence, this finding reinforces the fact that it is the underlying risk factors, not CVD itself, that create the joint risk.

Another important consideration for future clinical research is the impact of early life CVD risk factors on cancer survivorship. As survival from cancer increases, CVD in survivors has become increasingly prevalent. This is likely the result of shared modifiable risk factors and overlapping molecular mechanisms (1,9). Another reason is that commonly used cancer chemotherapies are cardiotoxic, which is a risk factor for subsequent development of heart failure (9).

From a public health perspective, the case for primordial prevention, that is, prevention of the development of risk factors in the first place, has never been stronger. Once risk factors have developed, restoration of truly low risk for CVD and cancer becomes unlikely if not impossible (10). Unifying concepts such as the AHA's Cardiovascular Health construct (4) can provide a framework to help the public sector and patients work on structural barriers and implement incremental individual goals that will provide real benefits in terms of longer life span, longer health span, and avoidance of these major diseases (11). The impact on individual quality of life, systemic health care use, and overall health care costs would be substantial (12,13).

We know what to do. Now we must go out and till this common soil to promote health, not generate disease.

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