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Caring for the Adult Survivor of Hodgkin Lymphoma:

Highlighting the Need for Care Coordination

Emily Tonorezos, MD, MPH and

Department of Medicine, Memorial Sloan Kettering Cancer Center, and Department of Medicine, Weill Cornell Medical College, New York, New York

Linda Overholser, MD, MPH

Division of General Internal Medicine, University of Colorado Denver School of Medicine, Aurora

There are currently more than 13 million individuals with a history of cancer living in the United States.¹ Of these, an estimated 400 000 are adult survivors of childhood cancer²; with ongoing progress in cancer treatment and supportive care, that estimate is expected to increase. Cardiovascular events, including coronary heart disease (CHD), cardiomyopathy and congestive heart failure (HF), and valvular heart disease, are the leading noncancer causes of morbidity and mortality in this population.³ Furthermore, we know that few adult survivors of childhood cancer return to their cancer center for adult care,⁴ and care for older adult cancer survivors is often fragmented, such that care for these medically complex patients is typically in the hands of primary care physicians who treat adults.

In this issue of *JAMA Internal Medicine*, van Nimwegen and colleagues⁵ from the Netherlands describe the results of a large retrospective cohort study to assess the long-term risk of clinical diagnosis of CHD, valvular heart disease, and HF among survivors of Hodgkin lymphoma (HL) compared with age-matched general population controls. Patients included survivors of HL diagnosed before 51 years of age and treated in 1 of 5 Dutch university hospitals or cancer centers from 1965 through 1995. Cardiovascular outcomes were identified from medical records and primary care physicians and cardiologists for both the survivors and controls.

van Nimwegen et al report that individuals who were treated for HL were at a significantly higher risk of developing CHD (standardized incidence ratio, 3.2) and HF (standardized incidence ratio, 6.8) than population controls. These estimates correspond to absolute excess risks of 70 and 58 cases of CHD and HF per 10 000 person-years, respectively. Furthermore, the risks were higher with longer follow-up; absolute excess risks for CHD and HF were 475 and 382 events per 10 000 person-years more than 35 years after treatment. The highest risks were among those who were treated at a younger age for their HL. Adjusting for year of diagnosis, sex, and smoking history, mediastinal radiotherapy and anthracycline chemotherapy were identified as relevant risk factors, with overall hazard ratios of 3.6 and

Corresponding Author: Linda Overholser, MD, MPH, University of Colorado Denver School of Medicine, 12631 E 17th Ave, Mail Stop B180, Aurora, CO 80045 (Linda.Overholser@ucdenver.edu).

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1.5, respectively, for any cardiovascular disease diagnosis. With this work, van Nimwegen and colleagues have expanded our understanding of this high-risk population.

What implications does this study have for the primary and secondary prevention of heart disease in individuals with non-traditional risk factors? This study is important because it adds to the increasing body of evidence regarding risk factors in cancer survivorship that do not fit into traditional cardiovascular risk models. It highlights a population (individuals living with a history of HL) for whom the natural history of cardiovascular disease is only beginning to be understood. The authors note that, in this study, individuals were not routinely screened for cardiovascular disease. Furthermore, we do not know the status of other important comorbidities, such as hypertension, obesity, diabetes mellitus, or dyslipidemia. Therefore, these results do not reveal whether screening or early intervention with traditional approaches would be effective at reducing morbidity or mortality from cardiovascular disease. In addition, the pathophysiologic mechanism of cardiovascular disease among these cancer survivors may be different than the general population; although traditional risk reduction strategies are recommended,^{6,7} effectiveness is not fully known. Ultimately, we will need large, long-term prospective studies and randomized clinical trials to guide evidence-based practice in regard to defining the best approaches, taking into account potential benefits and harms. How we incorporate additional risk factors attributable to past exposures into consideration of treatment recommendations for our patients and use of currently available guidelines needs to be tailored to each clinical scenario and to take into account patient preferences. However, we are learning more about important long-term risks associated with past cancer treatment and which individuals may be at higher risk.

A considerable strength of this study is that individuals diagnosed as having HL as young adults or adults were included in the cohort, building on what we have learned from the childhood cancer survivor population. Research that helps develop best evidence-based practices for prevention of future morbidity and mortality in these older populations has been lacking. This study is also important because it found that tobacco smoking was an additive risk factor for the development of heart disease on top of the risk attributed to radiotherapy and/or anthracycline therapy. On the basis of these results, tobacco cessation appears especially important for HL survivors.

Previous work has suggested that primary care physicians may not be comfortable caring for adult survivors of childhood cancer and have gaps in knowledge regarding what additional screening and surveillance this population may require.⁸ Furthermore, the oncology field has not increased to match demand, such that ongoing care in an oncologic setting will not be possible for most survivors (<http://www.asco.org/practice-research/workforce-initiatives>). It is clear that, although the best models for follow-up care for cancer survivors may vary with the context of individual care settings and local resources, there is a role for specialists involved in cancer care and primary care to address the comprehensive needs of cancer survivors. It is a matter of providing the right care at the right time. In this context, it is necessary for primary care physicians to rise to the challenge of health promotion in cancer survivors.

This work by van Nimwegen et al can specifically help physicians identify their highest-risk patients: those with a history of HL who were treated at a younger age and those who are the longest from treatment. For most encounters, starting by asking a few key cancer history questions will help identify these patients: (1) What kind of cancer did you have? (2) How old were you when your lymphoma was diagnosed? (3) Did you receive chest radiotherapy? (4) Did you receive doxorubicin (many patients know it by the brand name Adriamycin [the red medicine])? Our clinical experience has been that patients typically know the answers to these basic questions, and these responses will go a long way toward identifying at-risk patients. Nonetheless, the future of good care for cancer survivors will require establishment of the evidence-based best practices for this population.

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