Hodgkin's lymphoma survivors have higher risk for cardiovascular diseases

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Survivors of Hodgkin lymphoma appear to be at higher risk for cardiovascular diseases and both physicians and patients need to be aware of this increased risk, according to an article published online by *JAMA Internal Medicine*.

Hodgkin lymphoma (HL) is a curable cancer with 10-year survival rates exceeding 80 percent. Treatment for HL has been associated with increased risks for other cancers and cardiovascular diseases, and those later cardiovascular complications may be the consequence of radiotherapy and chemotherapy in HL treatment, according to the study background.

Flora E. van Leeuwen, Ph.D., of the Netherlands Cancer Institute, Amsterdam, and coauthors examined the risk for cardiovascular disease in survivors up to 40 years after HL treatment and compared it with the general population. They also studied treatment-related risk factors.

The study included 2,524 Dutch patients diagnosed with HL at younger than 51 years (median age was 27.3 years), who were treated from 1965 through 1995 and had survived for five years after diagnosis. The treatment for HL included mediastinal (chest area) radiotherapy and anthracycline agents for chemotherapy.

Of the 2,524 patients in the analyses, 2,052 patients (81.3 percent) had received mediastinal radiotherapy and 773 patients (30.6 percent) had received chemotherapy containing an anthracycline. After follow-up that lasted a median of 20.3 years, there were 1,713 cardiovascular events in 797 patients and 410 of those patients (51.4 percent) had developed two events or more.

The most frequently occurring cardiovascular disease was coronary heart disease (CHD), with 401 patients developing it as their first event, followed by valvular heart disease (VHD, 374 events) and heart failure (HF, 140 events). The median times between Hodgkin lymphoma treatment and first cardiovascular disease events were 18 years for CHD, 24 years for VHD and 19 years for HF, according to the results.

Compared with the general population, the authors observed 4-fold to 7-fold increased risks of CHD or HF 35 years or more after treatment for Hodgkin lymphoma, which resulted in 857 more cardiovascular events per 10,000 person years, according to the results.

The cumulative risk of any type of cardiovascular disease was 50 percent at 40 years after Hodgkin lymphoma diagnosis. For patients treated for Hodgkin lymphoma before they were 25, the cumulative risk at 60 years of age or older for CHD was 20 percent, 31 percent for VHD and 11 percent for HF as first events, the result indicate.

The study also found that mediastinal radiotherapy increased the risk of CHD, VHD and HF, while anthracycline-containing chemotherapy increased the risks of VHD and HF as first events compared with patients who did not receive those cancer treatments.

"Treating physicians and patients should be aware of the persistently increased risk of cardiovascular diseases throughout life, and the results of our study may direct guidelines for follow-up of patients with HL [Hodgkin lymphoma]," the study concludes.

In a related commentary, Emily Tonorezos, M.D., M.P.H., of the Weill Cornell Medical College, New York, and Linda Overholser, M.D., of the University of Colorado Denver School of Medicine, Aurora, write: "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, 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," the commentary continues.

"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," the commentary concludes.

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