

Heart Disease Risk Higher in Cancer Survivors

BY SHARON WORCESTER
Southeast Bureau

Compared with their healthy siblings, survivors of childhood cancers have a substantially increased risk of developing heart disease in early adulthood, new findings from the Childhood Cancer Survivor Study show.

The investigators analyzed data from 14,358 5-year survivors of eight childhood cancers and 3,899 sibling controls. Increased risk in survivors ranged from 5 times more likely to suffer a heart attack to 10 times more likely to have atherosclerosis at an early age.

Anthracycline exposure and radiation to the heart also increased the risk of heart disease in early adulthood when exposed survivors were compared with survivors who had not received anthracycline drugs or radiation to the heart. Compared with survivors not given these treatments, the relative risk of heart failure, for example, was 4.1 in survivors exposed to more than 250 mg/m² of anthracycline and 2.0 in those who had radiation to the heart.

The data were presented at the annual meeting of the American Society of Clinical Oncology (ASCO). An abstract was posted on the society's Web site (www.asco.org) and discussed by Dr. Daniel A. Mulrooney, lead author, during a press briefing Webcast.

Survivors in the study had been diagnosed with

leukemia, central nervous system tumors, Hodgkin's or non-Hodgkin's lymphoma, renal tumors, neuroblastoma, soft-tissue sarcoma, or bone cancer between 1970 and 1986 before reaching 21 years of age. Their mean age was 7.8 years at diagnosis, and 27.5 years at follow-up.

After adjustment for age, gender, race, sociodemographic factors, and smoking status, survivors were more likely than were their siblings to report heart failure (relative risk 5.7), myocardial infarction (RR 4.9), atherosclerosis (RR 10), pericardial and valvular disease (RR 6.3 and 4.8, respectively), and coronary angiography (RR 8.2), reported Dr. Mulrooney of the University of Minnesota, Minneapolis.

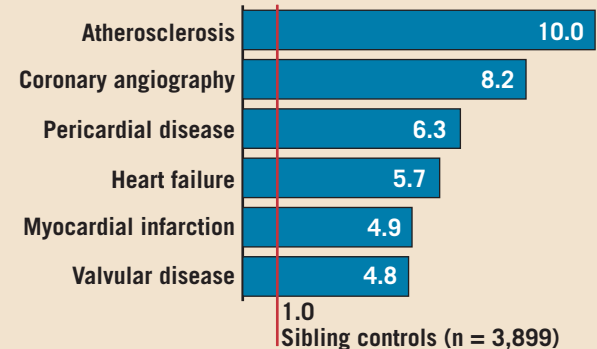
"We found that 5-year survivors of childhood cancers are at elevated risk of early cardiovascular disease," he said, noting that cardiac toxicity can occur years following the cancer diagnosis, and that incidence increases steadily over time.

"Cardiovascular monitoring of early childhood cancer survivors should begin early and be lifelong," he concluded.

Dr. Richard L. Schilsky, president-elect of ASCO and professor of medicine at the University of Chicago, said the findings add to the increasing knowledge of the effects of childhood cancer on later health outcomes, and that they underscore the need for appropriate monitoring of survivors.

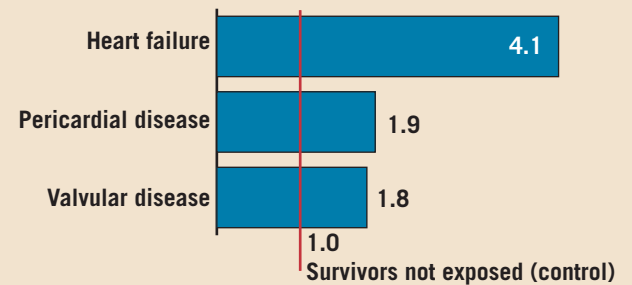
Previous studies have shown childhood cancer treatments have consequences on bone health, fertility, thyroid health, and mental health, and that survivors are also at increased risk of developing another malignancy. These findings have become increasingly important given the improvements in cancer treatments—and thus the increasing number of childhood cancer survivors. Currently there are more than 11 million cancer survivors in the United States; among them, about 270,000 are survivors of childhood cancers, Dr. Mulrooney said.

Higher Relative Risk for Adverse Cardiac Events in Childhood Cancer Survivors



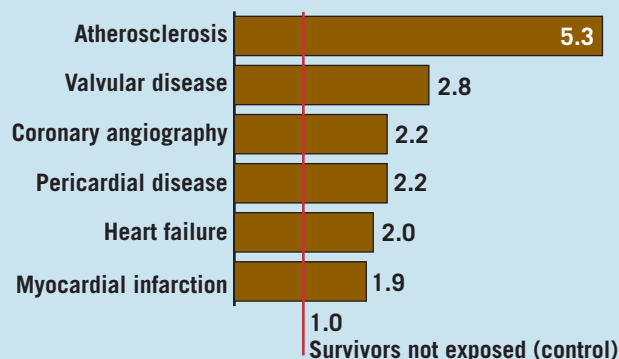
Notes: Based on an approximate 20-year follow-up of 14,358 5-year survivors of childhood cancer. Adjusted for age, gender, race, sociodemographic factors, and smoking status.
Source: Dr. Mulrooney

Relative Risk of Cardiac Disease With Anthracycline Exposure >250 mg/m²



Notes: Based on an approximate 20-year follow-up of 14,358 5-year survivors of childhood cancer. Adjusted for age, gender, race, sociodemographic factors, and smoking status.
Source: Dr. Mulrooney

Relative Risk of Adverse Cardiac Events Increased With Radiation to the Heart



Notes: Based on an approximate 20-year follow-up of 14,358 5-year survivors of childhood cancer. Adjusted for age, gender, race, sociodemographic factors, and smoking status.
Source: Dr. Mulrooney

Some Cancers Need Prolonged, High-Dose VTE Prophylaxis

BY MITCHEL L. ZOLER
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NEW YORK — Cancer patients with certain tumor types face a high risk for recurrent venous thromboembolism, and may benefit from an extended course of intensive prophylactic treatment with a low-molecular-weight heparin.

Patients with cancer of the pancreas, gastroesophageal tract, lung, or advanced metastatic disease (especially with an unknown primary cancer) were most likely to have recurrent venous thromboembolism (VTE) despite low-intensity anticoagulant therapy with a low-molecular-weight heparin (LMWH), according to a major study in 2003, Dr. Agnes Y.Y. Lee said at a symposium on cardiovascular disease in cancer patients sponsored by the University of Texas M.D. Anderson Cancer Center, among others.

Because of this experience, Dr. Lee usually treats patients with these cancers and a recent history of VTE with a high-dose regimen of dalteparin for at least 6 months. After daily treatment with 200 IU/kg dalteparin, patients are reevaluated to assess their need to continue on this regimen, switch to a lower dalteparin dose, switch to warfarin, or stop prophylactic treatment, said Dr. Lee, a physician specializing in VTE at McMaster University, Hamilton, Ont. She stressed that using a high-dose LMWH for this long in these patients was not based on findings from a prespecified analysis in the 2003 study. Dr. Lee has received research support from Pfizer Inc., which markets dalteparin (Fragmin).

Dr. Lee ran the study that led to this practice and that proved the superiority of dalteparin over warfarin for preventing recurrent VTE in cancer patients (*N. Engl. J. Med.* 2003;349:146-53). Patients random-

ized to dalteparin received the intensive regimen (200 IU/kg daily) for the first 30 days, but then were switched to a lower dosage, about 150 IU/kg per day, to reduce their risk of bleeding complications. The results suggested this dosage reduction led to a small but discernible uptick in the overall incidence of recurrent VTE episodes. "Breakthrough" VTEs, despite ongoing dalteparin treatment at the reduced dosage, were particularly a problem in patients with the higher-risk cancer types.

Prophylaxis with an LMWH for cancer patients with a history of VTE has since been endorsed in guidelines issued by the American Society of Clinical Oncology, the National Comprehensive Cancer Network, and the American College of Chest Physicians, Dr. Lee said at the meeting, sponsored by the American College of Cardiology and the Society for Geriatric Cardiology. VTE is a common problem in

cancer patients, with an incidence of 1%-30% in patients not on prophylaxis, depending on their tumor type.

Results from several studies also have hinted that treatment with an LMWH might have a direct anticancer effect. One suggestion of this effect appeared in a post hoc analysis of data that they had collected in their 2003 study by Dr. Lee and her associates. The analysis showed a statistically significant 50% drop in mortality in patients without metastatic disease treated with dalteparin versus warfarin (*J. Clin. Oncol.* 2005;23:2123-9). Similar links between improved survival and treatment with an LMWH have been seen in other studies, Dr. Lee said at the symposium. The reduction in deaths is not explained by a reduction in VTE alone because the mortality effect continues when the LMWH is stopped. More studies are needed, Dr. Lee said.