EDITORIAL COMMENT
Cardiac Complications of Mediastinal Radiotherapy
The Other Side of the Coin*
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The heart and great vessels were once thought to be relatively resistant to the damaging effects of radiation therapy (1,2). But there is now clear evidence that thoracic irradiation may cause acute inflammation and progressive fibrosis of the pericardial, myocardial, and endocardial (valvular and arterial) tissues (3–6). As new therapies have improved survival, many patients with cancer are now at risk for the cardiovascular complications of radiation therapy administered years or even decades earlier (7).

Most clinical information about the cardiac effects of thoracic radiation is based on studies of patients with breast cancer or Hodgkin's disease who developed symptomatic disease during the course of treatment or during follow-up. Pericardial disease is one of the most common manifestations of radiation-induced cardiac injury. Acute pericarditis may occur early in the course of treatment, but constractive or effusive pericarditis may also develop months to years after therapy (5,6,8). Other late complications include myocardial fibrosis and cardiomyopathy, accelerated coronary artery disease, conduction abnormalities, and valvular dysfunction (8–11).

The overall incidence of clinically detectable heart injury after thoracic irradiation is approximately 30%, although patients treated with mantle radiation for Hodgkin's disease are at highest risk for developing cardiac complications because of the proximity of the radiation field to cardiac structures (6). In one large study of 2,232 survivors of Hodgkin’s disease (mean age 29 years at treatment) the risk of death from heart disease after a mean follow-up of 9.5 years was 3.9% (12). Of the 88 cardiac deaths 55 were due to myocardial infarction. The average age at death from myocardial infarction was 49 years, with 22 deaths in patients to myocardial infarction. The average age at death from heart disease after a mean follow-up of 9.5 years was 3.9% (12). Of the 88 cardiac deaths 55 were due to myocardial infarction (8–11).

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How does this new information help the clinician evaluate the asymptomatic patient who has received thoracic radiation? This study clearly shows that a significant percentage of patients with Hodgkin's disease who were treated with mediastinal radiation developed significant valvular disease or mild left ventricular dysfunction, two abnormalities that are easily detected by echocardiography and may benefit from therapy (19). Importantly, the prevalence and severity of these abnormalities increased considerably over...
time, making a strong argument for screening because they remained clinically unrecognized. On the other hand, as the authors note, radiation therapy has been modified in the past 30 years to reduce the total radiation dose administered and to better shield the cardiac structures. The prevalence of these cardiac abnormalities will thus likely decrease in patients treated more recently. More patients will have to be screened in the future to identify those that might potentially benefit from intervention.

In addition, although resting echocardiography is an excellent tool for evaluating valve or ventricular dysfunction, it is less useful for diagnosing coronary artery disease or pericardial thickening. More sensitive techniques, such as computerized tomography or magnetic resonance imaging, may prove much more effective in detecting such pathologies. Prognostic assessment of coronary arterial disease with exercise echocardiography to reduce the substantial cardiovascular mortality among these young patients also deserves investigation.

These data may not be applicable to patients who received thoracic radiation for other types of malignancies in which the degree of cardiac exposure and the use of concomitant chemotherapy differ significantly from the present study. However, the high prevalence of cardiac disease argues for close observation of patients with Hodgkin’s disease who have received mediastinal radiation. A yearly history and physical examination with close attention to symptoms and signs of heart disease that might otherwise be overlooked in this generally young population is essential. In patients who remain asymptomatic, screening echocardiography 10 years after treatment appears reasonable given the high likelihood of diagnosing significant cardiac pathology. The study by Heidenreich et al. (18) does not address whether treatment of asymptomatic disease will prevent progression of disease or future cardiac events; but these patients may derive benefit from therapies such as antibiotic prophylaxis for significant valve disease and angiotensin II-converting enzyme inhibitors for the treatment of left ventricular dysfunction. Aggressive treatment of cardiac risk factors, especially hyperlipidemia, both at the time of cardiac therapy and during follow-up, may reduce the degree of initial cardiac injury and slow the progression of vascular, myocardial, and valvular fibrosis (19). Finally, newer treatment strategies that use lower total radiation doses, minimize cardiac exposure by subcarinal shielding techniques, and avoid concurrent cardiotoxic chemotherapeutic agents may help reduce the incidence of serious cardiac disease in the future.

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