Women treated with radiotherapy for cancer of the left breast are more likely to develop cardiac disease years later than women whose right breast was irradiated, according to a study in the *Journal of Clinical Oncology* (2006;24:4100–4106).

Researchers from the University of Pennsylvania noted significantly higher rates of chest pain ($P < 0.001$), coronary artery disease ($P < 0.001$), and myocardial infarction ($P = 0.002$) in left breast patients (484 women) compared to right breast patients (477 women). Participants were treated at the institution between 1977 and 1994 with lumpectomy and radiation for Stage I or II breast cancer. All were free of heart disease when diagnosed.

Women in both groups had a higher risk of developing coronary artery disease if they also had hypertension, and those with left breast cancer and hypertension had the highest risk of all (hazard ratio [HR] = 11.4).

Nevertheless, women in the study group had lower rates of coronary artery disease than women in the general US population, and the study found no significantly increased risk of cardiac death among left breast cancer patients, even after 20 years.

Lead study author Eleanor Harris, MD, says the higher rate of cardiac morbidity seen in the research should not discourage women and physicians from using adjuvant radiation, but should spur radiation oncologists to strive even harder to protect the heart during treatment.

“Fortunately, we do have new technology and new treatment modalities, so we are better able to do that now than during the era of the study,” said Harris, who is now Clinical Director of Radiation Oncology at the H. Lee Moffitt Cancer Center and Research Institute in Florida.

As examples, she cited 3-dimensional planning with CT scans and intensity modulated radiation therapy (IMRT). Partial breast radiation may also be appropriate, she said, particularly once results of the NSABP B-39/RTOG 0413 trial give a better indication of which patients are best suited to this treatment.

On the other hand, Harris also noted that cardiotoxic drugs like Adriamycin and Herceptin are more commonly used today than during the study period. “What we need to do is look at that issue and see if there’s any interaction, but to be cautious I would assume that anyone who had a cardiotoxic drug might be at higher risk for heart disease as well,” she said.

Edward Yeh, MD, Chair of Cardiology at The University of Texas MD Anderson Cancer Center, agreed that minimizing radiation exposure of the heart is important.
But it’s equally critical to continue monitoring and treating patients for other cardiac risk factors (smoking, diabetes, etc.) during cancer treatment, he said.

Harris said women treated for breast cancer do not need any more intense cardiac surveillance than other women, but that they should be screened for cardiac symptoms and risk factors, such as blood pressure, cholesterol, and smoking, according to routine recommendations.

Yeh emphasized that regular checkups are important for breast cancer survivors regardless of whether they had radiation therapy because all women should be monitored for heart disease as they age.

**ANDROGEN DEPRIVATION RAISES RISK OF DIABETES, HEART DISEASE**

Certain types of androgen deprivation therapy (ADT) for prostate cancer may make men more susceptible to diabetes and heart disease, researchers from Harvard Medical School reported in the *Journal of Clinical Oncology* (2006;24:4448–4456). They suggest physicians and patients take this possibility into account when considering therapy with a gonadotropin-releasing hormone (GnRH) agonist.

“Doctors should think twice about prescribing GnRH agonists in situations for which studies have not demonstrated improved survival until we better understand the risks of treatment,” study co-author Matthew R. Smith, MD, PhD, Associate Professor of Medicine, said in a statement.

Smith and colleagues conducted an observational study of more than 73,000 Medicare enrollees age 66 years and older diagnosed with locoregional prostate cancer, with a median 4.55 years of follow up. Their aim was to evaluate possible associations of ADT with the incidence of diabetes and heart disease.

Overall, 36.3% of men received a GnRH agonist, and 6.9% underwent bilateral orchiectomy. In men without preexisting diabetes or heart disease, those treated with a GnRH agonist had a significantly higher risk of developing diabetes (Hazard Ratio [HR] 1.44, *P* < 0.001), coronary heart disease (HR 1.16, *P* < 0.001), myocardial infarction (HR 1.11, *P* = 0.03), and sudden cardiac death (HR 1.16, *P* = 0.004) than men not on hormone therapy. The elevated risk began as soon as 1 to 4 months after treatment and remained elevated among those who continued treatment for longer periods. Men treated with orchiectomy had a significantly higher risk of diabetes (HR 1.34, *P* < 0.001).

Based on known side effects of GnRH agonists—increased body fat and insulin resistance—these results seem biologically plausible. However, the authors suggest caution in interpreting their results. Because this was an observational study, differences between men who received ADT and those who did not may have contributed to differing outcomes. Also, the researchers did not have information on other oral medications (including antiandrogens); the validity of disease outcomes identified from administrative datasets is difficult to evaluate; and the small number of men who underwent orchiectomy limits conclusions regarding that procedure.

Nevertheless, the findings should give physicians who routinely prescribe these treatments some pause, other experts agree.

“It should make us more cautious in starting men on this therapy, but not preclude starting those who need it,” said David Smith, MD, Professor of Internal Medicine and Urology at the University of Michigan, who was not involved in the study.

Smith said men with metastatic disease are obvious candidates for hormone therapy, but he suggested that average patients with newly diagnosed disease usually are not. And deciding how to treat the average patient with biochemical recurrence is difficult, he added.

“I would argue that you really ought to follow PSA trends for some time and only start [ADT] if the PSA rate of rise starts to increase into that logarithmic phase,” said Smith, explaining that a PSA rising from 0 to 10 in 10 years may not be of concern, whereas the same rise within 10 months should be.

Both Smith and the study authors agreed that men beginning ADT should be counseled about exercise and weight loss to reduce their risk for diabetes and heart disease.

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