Cardiotoxicity Looms After Breast Cancer Therapy

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HOLLYWOOD, FLA. — Advances in the treatment of breast cancer have been significant, but they have come at a price: increased toxicity to the heart. The most important step in minimizing this cardiotoxicity is to be aware that it does occur, Dr. William J. Gradishar said at the annual conference of the National Comprehensive Cancer Network.

"Women with breast cancer are living longer and, as time passes, some of the long-term side effects as a result of therapy may become apparent. That is certainly an issue with some of the systemic therapies we use," said Dr. Gradishar, professor of medicine at Northwestern University, Chicago.

Factors that may raise the risk of cardiotoxicity include age, with women aged 70 years and older at particularly high risk; mediastinal radiotherapy; and preexisting heart disease.

Dr. Gradishar said outcomes for patients receiving radiation have improved over the past 10 years, largely because of better planning and technology. However, while this has occurred, there has been an increase in non–breast cancer mortality, and heart disease has risen by 27%. He cautioned that clinicians must recognize that there is a small but real risk of cardiac side effects related to radiation therapy, particularly when it is left sided. "We have to balance this risk against the incremental improvement in outcome that comes with adjuvant radiation therapy."

As time passes, some of the long-term side effects of breast cancer therapy may become apparent.

DR. GRADISHAR

Dr. Gradishar also talked about the perils of systemic therapy. Here, the anthracyclines, most notably doxorubicin, are the main cardiotoxicity culprits. Doxorubicin lowers left ventricular ejection fraction, and some patients develop heart failure as a result. Dr. Gradishar said these drops in ejection fraction can be asymptomatic.

Treatment with ACE inhibitors and calcium channel blockers can help these patients recover their cardiac function, but left to its own devices, anthracycline-induced heart failure will not resolve spontaneously, he said.

Dexrazoxane (Zinecard, Pfizer Inc.) is an iron chelator that counteracts the cardiotoxic effects of the anthracyclines. It is approved for reducing the incidence and severity of doxorubicin-associated cardiomyopathy in women with metastatic breast cancer who have received a cumulative doxorubicin dose of 300 mg/m^2 and who, in their doctor's opinion, would benefit from continuing therapy with taking doxorubicin. However, it is not recommended for use at the start of doxorubicin therapy, Dr. Gradishar said.

"There was concern that dexrazoxane might attenuate some of the antitumor effect of the doxorubicin if it was started from the get-go as opposed to starting it later. So for those patients you think would benefit from doxorubicin beyond 300 mg/m^2, consider using dexrazoxane."

More recently, concerns have been raised about the cardiotoxicity of targeted therapy with trastuzumab. This risk is justified, given the dramatic 25% improvement in overall survival in poor prognosis HER2-positive breast cancer seen with the drug, Dr. Gradishar said.

He noted that about 4% of patients getting chemotherapy with concurrent trastuzumab develop heart failure. "Most of the events occur relatively early on so we are not seeing—at least with the follow-up we have to date—a large spike in [heart failure] after therapy is discontinued," he said, adding most of the cardiac toxicity occurs in the midst of therapy.

Predicting who will develop cardiac problems from their therapy remains difficult. Symptoms are not the most sensitive way of detecting or predicting who is going to have a problem, Dr. Gradishar said.

Similarly, electrocardiographic changes are not always predictive, he said.

Biomarkers such as troponin and brain natriuretic peptide are being investigated as indicators of developing cardiotoxicity or cardiovascular risk but are not standard of care, Dr. Gradishar said. He stated that he had no conflicts of interest to declare. ■