Genetic biomarker IDs patients with increased risk for heart damage by anthracycline chemo

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Bottom Line: Among women with breast cancer who received a type of chemotherapy called an anthracycline, those who had a certain genetic biomarker had a significantly increased risk for having anthracycline-induced congestive heart failure.

The study was published in *Clinical Cancer Research*, by Bryan P. Schneider, MD, associate professor of medicine at the Indiana University Melvin and Bren Simon Cancer Center in Indianapolis, and colleagues.

Schneider explained that the decision to undergo chemotherapy for breast cancer is not always clear cut because each patient has a different risk of relapse and different tolerance to potential adverse effects of treatment. As a result, the more information a patient and his or her oncologist have about the potential risks and benefits of treatment the better prepared they are to make good treatment decisions, he noted.

"Anthracyclines such as doxorubicin, which are widely used chemotherapeutic agents, cause congestive heart failure in about 1 to 2 percent of patients," continued Schneider. "Knowing which patients are at increased risk for this life-threatening effect of anthracycline chemotherapy is important to help oncologists counsel patients about their personal risks and benefits of such treatment."

Schneider and colleagues analyzed genome-wide association data from 3,431 women with breast cancer who received doxorubicin as part of treatment received through enrollment in the phase III Eastern Cooperative Oncology Group (ECOG) 5103 clinical trial and for whom heart assessment data were available. Among these patients, 68 (2 percent) had cardiologist-adjudicated congestive heart failure.

Because the majority of those who had cardiologist-adjudicated congestive heart failure (51) were European-American, the researchers limited the genetic association analysis to European-Americans. They identified several SNPs associated with risk of anthracycline-induced congestive heart failure.

After looking at the chromosomal location of the SNPs, the researchers chose two of the top SNPs for validation in independent data sets.

One of the two SNPs, rs28714259 was associated with risk of anthracycline-induced congestive heart failure among 2,415 women with breast cancer who received doxorubicin as part of treatment received through enrollment in the phase III ECOG 1199 clinical trial. It was also associated with low ventricular ejection fraction, which is a sign of heart damage, among 828 women with breast cancer who received doxorubicin as part of treatment through enrollment in the phase III BEATRICE clinical trial.

"We found that the A allele of the single nucleotide polymorphism (SNP) rs28714259 was associated with increased risk of anthracycline-induced congestive heart failure among women with breast cancer," said Schneider. "Adding information gained from testing for this SNP to currently used clinical information could help oncologists provide a more precise prediction of the risks and benefits of anthracycline chemotherapy for patients with breast cancer. We are currently further testing this finding in patients receiving anthracyclines at the Indiana

University Melvin and Bren Simon Cancer Center to better understand its contribution to heart failure risk in the face of other known risk factors and comorbidities."

According to Schneider, the study has two main limitations. First, not all of the clinical trials used the same method for assessing heart damage with corresponding long-term data. Second, the number of patients who had heart damage was relatively low because it is a rare adverse event. "As a result, additional studies in other patient groups and in the real-world setting of the clinic, as we are doing, are needed to confirm the association," Schneider said.

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