Study finds key metabolic changes in patients with chemotherapy-associated cardiotoxicity

July 18 2019

Credit: CC0 Public Domain

More and more patients are being treated successfully for cancer. However, some cancer treatments that are very effective for breast cancer—medications like anthracyclines and trastuzumab—can cause heart dysfunction and lead to heart failure. Heart-related side effects can limit the amount of cancer therapy that patients are eligible to receive.

Currently, there is no effective way of predicting which patients will develop heart dysfunction during or after receiving these medications.

To learn more about the processes that lead to heart toxicity, a team of researchers at Beth Israel Deaconess Medical Center (BIDMC) embarked on a study to investigate whether early changes in energy-related metabolites in the blood—measured shortly after chemotherapy—could be used to identify patients who developed heart toxicity at a later time. The study, published in the *Journal of Cardiovascular Translational Research*, found that metabolites associated with the energy powerhouse of the cell—the mitochondria—changed differently in patients who later developed heart dysfunction compared to those who did not.

Using blood samples obtained from 38 patients treated with anthracyclines and trastuzumab for breast cancer, the researchers measured 71 energy-related metabolites. They then compared metabolite profiles between patients who developed heart toxicity and those who did not, identifying changes in citric acid and aconitic acid that differentiated the two groups of patients.

"In particular, levels of citric acid increased over time in patients who did not develop heart toxicity, but they remained the same or decreased in patients who did develop heart toxicity," said corresponding author Aarti Asnani, MD, Director of the Cardio-Oncology Program at BIDMC. "The ability to augment citric acid and related metabolites may be a protective response that is absent or defective in patients with heart toxicity." The researchers also observed changes in breakdown products of DNA that differentiated the two groups of patients.

"We hope these findings will ultimately lead to the development of biomarkers that could be used to determine which patients are at the highest risk of developing chemotherapy-related heart toxicity," said

Asnani. "Identification of high-risk patients could allow us to consider medications that protect the heart before patients begin chemotherapy, or prompt the use of different chemotherapy regimens that are less toxic to the heart in those patients."

In their next phase of research to follow up on this pilot study, Asnani and colleagues will seek to confirm their results in larger patient populations.

More information: Aarti Asnani et al, Changes in Citric Acid Cycle and Nucleoside Metabolism Are Associated with Anthracycline Cardiotoxicity in Patients with Breast Cancer, *Journal of Cardiovascular Translational Research* (2019). DOI: 10.1007/s12265-019-09897-y

Provided by Beth Israel Deaconess Medical Center