

MANAGING CTC IN PEDIATRIC CANCER PATIENTS AND SURVIVORS

Dedicated Cardio-Oncology Program Offers Long-Term Screening

Improvements in childhood cancer therapy have led to a growing number of long-term survivors of childhood cancer. However, pediatric cancer patients are at risk for developing serious cardiac conditions, either during treatment or later in life, as a result of exposure to the class of chemotherapy drugs called anthracyclines. In addition, chest radiation can cause similar risks. Heart issues that result from cancer treatment-related cardiotoxicity, or CTC, are the third leading cause of death post-treatment.

In 2016, recognizing the growing prevalence of CTC concerns, Children's Mercy Kansas City was one of the few pediatric hospitals in the world to create a dedicated cardio-oncology program. Led by Joy M. Fulbright, MD, pediatric oncologist, and Aliessa Barnes, MD, pediatric cardiologist, the cardio-oncology team is fully integrated into the Children's Mercy multidisciplinary oncology clinic.

All patients with changes or concerns during their cardiac work-up are seen in the oncology clinic by a cardio-oncology specialist. This approach of having all specialists come to the patients in their oncology home provides crucial continuity of care, including long-term monitoring as part of the survivorship program.

ACUTE CARDIAC ISSUES DURING THERAPY

During the administration of chemotherapy, approximately 10%-20% of patients experience acute cardiac issues, such as decreased cardiac function, heart dilation or rhythm problems or effusions. Cardio-oncologists work closely with oncologists to determine the best course of action: continue therapy, alter the dose or discontinue the drug.

The risks vary based on the chemotherapy regimen employed. The toxicity of anthracyclines is affected by the number of rounds and the specific dose given. Children's Mercy cardio-oncologists monitor the cumulative exposure to these drugs while considering risk stratification recommendations developed by the Children's Oncology Group.

Dr. Fulbright is the co-chair of the Children's Oncology Group Survivorship and Outcomes Cardiovascular Task Force. This group reviews the most recent literature on late effects and releases updated recommendations every five years. Children's Mercy considers these recommendations to help stratify patients according to their risk level for developing heart failure.

LONG-TERM CONCERNS

Effects from chemotherapy can occur soon after completion of therapy, but cardiac late effects become more prevalent as a person ages, up to 10 to 20 years after therapy is complete. They often emerge as left ventricular or systolic heart failure. Rhythm issues such as bradycardia and QT prolongation also can occur. Hypertension is a modifiable risk factor for the development of heart failure, so blood pressure must be carefully monitored during both the acute and chronic phases. A dietician meets with families at every survivorship visit to coach families on living a healthy lifestyle, emphasizing good nutrition and exercise.

If a patient receives radiation to a field that includes the heart, scarring can occur that leads to valve issues, heart failure or a restrictive physiology that can affect function. Abnormal lipids also can occur as a result of the abdominal radiation. Radiation patients experience a higher risk of coronary issues and myocardial infarction than those who did not receive this type of treatment.

IMPROVING DETECTION OF LATE-ONSET CARDIAC DYSFUNCTION

Children's Mercy is an early adopter of strain imaging with echocardiogram. While the technology is not new, its use in cardio-oncology is recent, thanks to studies that have evaluated its efficacy in the detection of chemotherapy-associated cardiotoxicity.

For example, a recent prospective multicenter study by Sawaya, et al., demonstrated that global longitudinal strain (GLS) <19% was predictive of subsequent cardiotoxicity and was present in all patients who later developed symptoms of heart failure. Another study, by Negishi, et al., similarly showed that a $\geq 11\%$ relative reduction in GLS was predictive of subsequent trastuzumab-associated cardiotoxicity.

These demonstrated outcomes led Children's Mercy to implement strain imaging for its predictive capabilities, with the aim of determining whether earlier intervention can lessen disease burden.

Sanket S. Shah, MD, pediatric cardiologist at Children's Mercy, led a study that compared echocardiographic methods, cardiac MRI and cardiac biomarker testing in adolescent cancer survivors. The study was published in Echocardiography.

EARLY PATIENT TRACKING SUGGESTS IMPROVED OUTCOMES

Patients are referred from primary oncology teams, bone marrow transplant physicians, primary care physicians and from Survive and Thrive, the Children's Mercy survivorship clinic. Of those tracked to date, patients were evaluated for valvular dysfunction, concern

for arrhythmia, global hypokinesis and decreased left ventricular function. One-third of patients with a decrease in left ventricular dysfunction required only close monitoring and two-thirds were started on an ACE inhibitor, which led to improvement or stabilization of function. The team is formalizing a process for tracking all patients evaluated in the cardio-oncology clinic.

THE FUTURE OF THE PROGRAM

Dr. Fulbright and Dr. Shah recently presented a multidisciplinary grand round to help increase regional awareness of the program. They work closely with the University of Kansas Health System (UKHS) to transition pediatric cancer survivors to a team that includes adult cardiologists who have a specific interest in caring for cancer patients. As the cardio-oncology program continues to expand and evolve, the goal is to work more closely with UKHS to expand research efforts and evaluate long-term outcomes for survivors. A registry of adult childhood cancer survivors, established in 2016, will aid in this effort. In addition, Children's Mercy is beginning to focus on collaboration with other pediatric centers, as they create similar programs, to share protocols and learn from successes.

SOURCES

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