

The Burgeoning Field of Cardio-Oncology

Barry H. Trachtenberg, MD

HOUSTON METHODIST DEBAKEY HEART & VASCULAR CENTER, HOUSTON METHODIST HOSPITAL, HOUSTON, TEXAS

The extraordinary success of cancer treatment, particularly in the past two decades, has boosted cancer survivorship to an all-time high. It is estimated that there are more than 15.5 million cancer survivors in the United States alone (approximately 4% of the population!), and the number of long-term survivors continues to grow.¹ However, the success of cancer treatment comes with a cardiovascular cost.

While it is widely known that one in eight women will develop breast cancer, most people are unaware that nearly one in ten women treated with the most common breast cancer chemotherapy regimen (anthracyclines) will develop cardiotoxicity. Survivors of childhood cancer are 15 times more likely to have heart failure and 8 times more likely to die of heart disease compared to their peers without a history of cancer.² Although the cardiovascular risks of anthracycline-based chemotherapies and radiation have been known throughout the medical community, the explosion of new chemotherapeutic agents and targeted therapies has done nothing to decrease this risk. In fact, many of these agents have been associated with diverse cardiovascular events that have contributed to patient morbidity and mortality. This is why the burgeoning field of cardio-oncology is of prime importance to practicing cardiologists.

Because the number of cancer survivors is continuing to grow at an unprecedented rate, it is highly likely that cardiologists will encounter these patients in their practices. With this in mind, we have devoted this issue of the *Methodist DeBakey Cardiovascular Journal* to the field of cardio-oncology and have recruited several leading experts to weigh in on the topic. It is our intention to provide a broad overview of cardio-oncology and highlight the specific and unique cardiovascular issues that physicians should be aware of when treating patients who are battling or surviving cancer.

The first topic, by Drs. Tolulope Agunbiade, Raja Zaghlol, and Ana Barac from the MedStar Heart and Vascular Institute, is a two-part article on heart failure related to various chemotherapeutic agents. In part one, the authors provide a comprehensive review of anthracycline-based cardiotoxicity, discussing the incidence, risk factors (including emerging concepts of genetic risks), proposed pathophysiology, and current clinical guidelines for assessing cardiotoxicity. In part two, they review a select list of tumor-targeted and immunotherapies that can cause heart failure, with a focus

on human epidermal growth factor 2 (HER2) antagonists. Trastuzumab and newer HER2 antagonists are used to treat approximately 20% of breast cancer patients, and while they have revolutionized treatment for these women, they are associated with a decrease in left ventricular ejection fraction. The authors highlight the incidence and risk factors for the development of trastuzumab-related cardiomyopathy and explore the cardiotoxic potential of other types of agents, including vascular endothelial growth factor (VEGF) inhibitors and proteasome inhibitors (especially carfilzomib). They conclude with an overview of immune checkpoint inhibitors, a Nobel prize-awarded invention that has dramatically improved survival in many types of cancer but can cause a potentially fatal and fulminant myocarditis of which cardiologists and oncologists should be aware.

From understanding the scope, pathophysiology, and clinical manifestations of these various chemo- and immunotherapies, we move to diagnosing cardiotoxicity with a review by Drs. Ali Agha, Juan Lopez-Mattei, and their colleagues from the MD Anderson Cancer Center. The authors discuss the advantages and disadvantages of various imaging modalities—including 2- and 3-dimensional transthoracic echocardiogram, radionuclide angiography, and cardiac magnetic resonance imaging—and explain the role of cardiac biomarkers for detecting cardiotoxicity. They conclude with guidelines from various societies on best approaches for cardiotoxicity monitoring.

Once cardiotoxicity is diagnosed, there are unique challenges in treating this population since they may still require ongoing cancer treatment. Drs. Monica Avila, Edimar Bocchi, and their colleagues from the Heart Institute do Hospital das Clinicas da Faculdade de Medicina da Universidade in Sao Paulo, Brazil, review the treatment for patients who manifest cardiotoxicity from various agents—including anthracyclines, trastuzumab, and immune checkpoint inhibitors—and thoroughly review the literature regarding preventive and cardioprotective strategies.

Next, Dr. Gary Lewis from the University of Texas Medical Branch in Galveston and Dr. Andrew Farach from Houston Methodist Hospital shift gears to focus on cardiotoxicity related to radiation therapy. They review the physiology of radiation therapy, its myriad potential cardiovascular manifestations, risk factors for CV toxicity, and strategies that have been shown to mitigate the risk.

While heart failure and cardiotoxicity have been the major focus in the field of cardio-oncology, there are many other clinical manifestations to consider. Drs. Hae Lee, Sanjay Chandrashekhar, and Michael Fradley from the H. Lee Moffitt Cancer Center and Research Institute in Tampa, Florida, review the common cardiac-related electrophysiological manifestations of cancer treatments, including atrial and ventricular arrhythmias and associated thromboembolism, the clinical significance of QT interval prolongation, and the unique circumstances in balancing the benefits of anticoagulation with the risks of bleeding in the cancer population.

In the last invited review, cardiologists Jose Alvarez-Cardona, Joshua Mitchell, and Daniel Lenihan from Washington University in St. Louis, Missouri, remind us that vascular complications—such as thrombosis, accelerated atherosclerosis, and vasospasm—are also common with cancer treatment and that cardiologists and vascular surgeons should have increased awareness. Through a series of cases, the authors illustrate the various ways vascular toxicity can manifest in patients with cancer, offer scientific evidence that supports clinical decision making, raise questions about the complex management of these patients, and explore future research in this growing field.

To close out this issue, I wanted to highlight some exciting developments in the field of cardio-oncology by focusing on new paradigms of genetic predisposition and genomic biomarkers, potential imaging advances—such as positron emission topography and novel techniques using cardiac MRI—and the potential role for stem cell therapies.

We hope this overview of cardio-oncology is informative and clinically useful and that it emphasizes the growing importance of identifying and treating treatment-related cardiotoxicity in the context of increasing cancer survivorship. We are very grateful to our readers for their continued interest and support, and to our expert authors for providing up-to-date, insightful content.

REFERENCES

1. Bluethmann SM, Mariotto AB, Rowland JH. Anticipating the “Silver Tsunami”: Prevalence Trajectories and Comorbidity Burden among Older Cancer Survivors in the United States. *Cancer Epidemiol Biomarkers Prev*. 2016 Jul;25(7):1029-36.
2. Oeffinger KC, Mertens A, Sklar CA, et al.; Childhood Cancer Survivor Study. Chronic health conditions in adult survivors of childhood cancer. *N Engl J Med*. 2006 Oct 12;355(15):1572-82.