Cardio-Oncology in 2020: Prime for Translation

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Everything should be made as simple as possible, but not simpler.

(Albert Einstein)

Cardiology and oncology have traditionally existed as separate and largely non-overlapping disciplines. Both fields have seen unprecedented successes in diagnosis and treatment options; however, cross-talk and communication have lagged between the subspecialists. Routine cardiovascular (CV) assessment in clinical oncology practice has remained limited to a fraction of patients with focus on left ventricular ejection fraction (LVEF) as a single parameter [1, 2]. At the same time, spectrum of CV effects of cancer therapeutics has exploded and relevance of CV health has become paramount for millions of cancer survivors. This *JCTR* special issue (SI) highlights the growing needs for translation of CV biology into clinical tools for diagnosis and management of oncology patients.

Starting the SI is the elegant, proof-of-concept study by Asnani et al. [3], which investigates mitochondrial metabolic responses in women with breast cancer receiving anthracycline and trastuzumab therapy. The investigators compared changes in metabolite profiles during cancer treatment using targeted mass spectrometry. They found an association between increased levels of circulating citric and aconitic acid and absence of LVEF decline, suggesting that upregulation of citric acid cycle metabolites may serve in protection against cardiotoxicity. A comprehensive review of mitochondrial biology and cardiac metabolic imaging [4] will provide the reader with a broader perspective of these findings.

Genomic studies, including cohort-based candidate gene association studies (CGAS) and genome-wide association studies (GWAS), have also been used to understand

individual susceptibility to cardiotoxicity. BurrIDGE et al. [5] summarize a wealth of GWAS and CGAS data in the context of newer human-induced pluripotent stem cell (hiPSC) technology. The hiPSCs allow the investigation of cancer therapies in different CV cell types and assessment of distinct cellular functions, including, for example, electrical properties relevant for QT prolongation, atrial fibrillation, and ventricular arrhythmias [6].

In contrast to cardiomyocyte toxicity, cardiometabolic side effects have traditionally received less attention. Androgen deprivation therapy used in the treatment of prostate cancer has been associated with increased risk of insulin resistance, diabetes, and dyslipidemia, as well as increased CV mortality. Melloni and Nelson [7] review contradicting data from observational and randomized studies and identify a path toward improved CV screening and treatment among patients with prostate cancer.

An important focus of the SI are the approaches to diagnosis and management of CV effects of tyrosine kinase inhibitors and immune checkpoint inhibitors [8]. These two classes of agents have grown exponentially in the recent years, giving us a fascinating insight into the effects of “targetable,” tumor-relevant pathways on CV homeostasis. CV presentations span from hypertension and cardiomyopathy with vascular endothelial growth factor (VEGF) inhibitors, to metabolic and vascular events with chronic myelogenous leukemia agents, and atrial fibrillation with ibrutinib. Heterogeneous and hard to predict, they have also provided an opportunity for reverse translation, bringing questions from clinical findings “back to the bench” of basic CV science.

Cardio-oncology, field that bridges cardiovascular function and cancer treatment, has come full circle. From (over)simplified definition of LVEF as a single marker of drug safety, it has grown into a collaborative science linking oncology and cardiology, and basic and clinical investigators. It has also shown that a path to answers, to simple questions, requires deep dives into complexities of the CV system, cancer, and cancer treatment interactions. My hope is that this SI stimulates new and exciting research collaborations and advances the practice of cardio-oncology.

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