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FELLOWS-IN-TRAINING & EARLY CAREER PAGE

Cardio-Oncology for GenNext

A Missing Piece of the Training Puzzle

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An aging population and an increase in cancer survivors has led to significant overlap between comorbid cardiovascular disease (CVD) and cancer (1). Despite growing recognition of the importance and complexity of the relationship among cancer, its treatment, and CVD, the vast majority of cardiovascular (CV) professionals have little exposure to the field of cancer therapeutics and its effect on CV health (2). The number of centers and physicians providing specialized care for this growing cohort remains insufficient (2), and the need for incorporating training in cardio-oncology into CV fellowship programs remains unmet. Here, we argue for providing structured training in cardio-oncology, suggest specific core educational topics, and discuss barriers to incorporating cardio-oncology in the CV fellowship core curriculum.

ARGUMENT FOR STRUCTURED TRAINING IN CARDIO-ONCOLOGY FOR CV FELLOWS-IN-TRAINING

Cancer and CVD are interlinked through common risk factors, co-occurrence in an aging population, and the deleterious effects of cancer treatment on CV health. The relationship between cancer and CVD is bidirectional. Well-known risk factors for CVD, such as tobacco, obesity, physical inactivity, poor nutrition, diabetes, alcohol, hypertension, and hyperlipidemia, are also risk factors for many cancers (3). Chemotherapeutic agents have been associated with a wide spectrum of short- and long-term cardiotoxic effects, with cardiomyopathy resulting from anthracyclines as a classic example. An explosion of novel cancer therapies has revolutionized the field and dramatically altered cancer prognosis. However, these therapies have introduced unexpected CV complications beyond cardiomyopathy. Ironically, increases in CV morbidity and mortality now threaten to offset the advances in cancer-related survival (4,5). Moreover, the epidemiological impact of cancer therapy-related cardiotoxicity is growing, and the number of cancer survivors and aging patients with various CV comorbidities at risk for cancer is increasing.

Oncologists are thus increasingly reliant on CV specialists to risk-stratify and to address a myriad of comorbidities and the adverse effects of novel cancer therapeutics, the mechanisms of which are often poorly understood. CV specialists need to have a thorough understanding of the complex pathophysiology that links cancer and CVD and the mechanisms of novel chemotherapeutic agents. Familiarity with the modalities to risk-stratify and detect early CV effects of cancer treatment is among the skills required for optimal care of the cancer patient; however, these topics are not addressed in current training core curriculum.

Cardio-oncology (or onco-cardiology) is emerging as a field of expertise that aims to usher patients safely through cancer therapy and into survivorship while tempering CVD and minimizing risks of cancer therapy as competing causes of morbidity and mortality. With growing clinical demand, there are a small but increasing number of cardio-oncology training programs across the United States, located mainly at tertiary/quaternary referral centers with both comprehensive cancer centers and heart failure programs. However, the majority of patients with cancer are cared for by community-based practices and cardiologists without specialized training. It is thus important for general cardiologists to acquire knowledge that pertains to this patient population during fellowship training.

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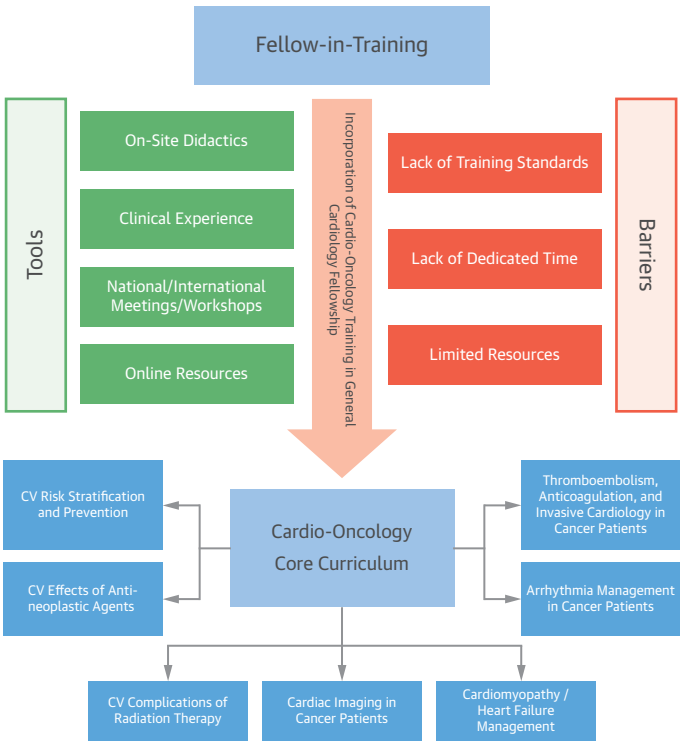
FIGURE 1 Cardio-Oncology Training in General Cardiology Fellowship



The figure illustrates the tools and barriers of incorporating cardio-oncology training in general cardiology fellowship along with a proposed cardio-oncology core curriculum. CV = cardiovascular.

CORE CURRICULUM TOPICS

Managing patients diagnosed with, undergoing, or who have completed treatment for cancer requires a broad understanding of the various clinical and pathophysiological aspects pertaining to both CVD and cancer. We propose the following topics as components for the training of the cardio-oncologist (6) (**Figure 1**):

1. *CV risk stratification and prevention strategies in patients with cancer* entails identifying patients who would benefit from specific chemotherapeutic regimens based on their risk profile and known adverse effects of the antineoplastic agents. It also includes optimizing their CV profile pre-therapy.
2. *CV effects of antineoplastic agents* extend beyond cardiomyopathy resulting from anthracyclines. A myriad of CV effects, extending from arrhythmias, to malignant hypertension, arterial and venous thrombosis, coronary artery spasm, and myocarditis, are observed with novel antineoplastics and biologics, warranting a thorough understanding of pathophysiology, monitoring, prevention, and treatment strategies.
3. *CV complications of radiation therapy*, including premature coronary artery disease, valvular disease, conduction system disease, pericardial disease, and autonomic dysfunction, have been well studied.
4. *Cardiac imaging in patients with cancer* using modalities such as strain echocardiography, 3-dimensional echocardiography, and cardiac magnetic resonance imaging for cardiotoxicity surveillance, early diagnosis, and treatment-related decisions. Indications, advantages, and shortcomings of each modality in this patient population should be incorporated into the curriculum.
5. *Management of cardiomyopathy in patients with cancer* is particularly challenging given their inability to tolerate higher doses of neurohormonal antagonists due to frequent episodes of hypotension, fluctuation in kidney function, and drug interactions. Advanced mechanical support in these patients requires special considerations involving overall prognosis.
6. *Arrhythmias in patients with cancer* occur commonly, whether related to surgery, chronic inflammation, autonomic nervous system imbalance, paraneoplastic manifestations, metabolic abnormalities, cardiac metastasis, or chemotherapy. The treatment is challenging, given the proarrhythmic nature of many chemotherapeutic agents and multiple drug interactions.
7. *Thromboembolism, anticoagulation, and percutaneous coronary interventions in patients with cancer* require complex decision-making to balance the increased bleeding risks due to bone marrow suppression and thrombocytopenia, multiorgan dysfunction, and the thrombotic tendencies associated with malignancy and antineoplastic agents (7).

INCORPORATING CARDIO-ONCOLOGY TRAINING INTO THE GENERAL CARDIOLOGY FELLOWSHIP

Training programs can incorporate cardio-oncology in the formal curriculum in various ways (6):

1. *On-site didactics* to cover core topics over the course of training are essential. Fellows-in-training (FITs) should also be encouraged to present on these topics as they do in other core areas of the training.
2. *Clinical experience* can be incorporated either on- or off-site depending on availability of expert faculty and structured cardio-oncology

clinics/program. Close collaboration with oncology would provide an opportunity for shared decision making and robust involvement of FITs in the CV care of cancer patients.

3. *National and international meetings or workshops* on cardio-oncology provide comprehensive and up-to-date reviews on the topic. For example, the American College of Cardiology's cardio-oncology council organizes annual workshops to cover the breadth and width of several important topics. FITs should be provided an opportunity to participate in such meetings.
4. *Online resources*, such as the American College of Cardiology's cardio-oncology section website, which is a portal for FITs to find opportunities to train in cardio-oncology and provide learning resources such as guidelines and the latest scientific updates.

BARRIERS TO TRAINING AND WAYS TO OVERCOME THEM

Several barriers exist to incorporating cardio-oncology as a part of core curriculum for CV FITs (2):

1. *Cardio-oncology remains an ill-defined field,* with an unclear scope of practice and lack of guidelines. How much clinical experience is required and how to measure competency are both difficult to define in the absence of strong evidence-based approaches to the challenges in cancer patients. As the field evolves, objective assessment of predefined core competencies and milestones set by the Accreditation Council for Graduate Medical Education and American Board of Medical Specialties should be easier to define and adopt.
2. *There is a lack of dedicated time for cardio-oncology* in the current Core Cardiology Training Symposium (COCATS-4), as the current structure of training programs allows pursuing cardio-oncology only during limited elective-time. The 3-year length of CV training programs, however, should allow for incorporating exposure to cardio-oncology. The ultimate solution would be recognition and incorporation of cardio-oncology as a part of the core curriculum by upcoming COCATS-5 Task Force. But, in the meantime, fellowship programs may have to be creative in providing formal education and training in this emerging field. One option is inclusion of cardio-oncology during mandatory heart failure and other subspecialty rotations.
3. *Institutional differences in the availability of cardio-oncology services and specialists* represent major barriers, as most programs still do not provide these services. Partnerships with other centers and local experts may be an acceptable alternative. Adult congenital heart disease and advanced heart failure rotations are the prime examples of such collaborative work.

FUTURE DIRECTIONS

The field of cardio-oncology has emerged in response to the need to provide optimal cancer care without jeopardizing CV health. However, there is an unmet need of high-quality research in this field as patients with cancer are usually excluded from clinical trials examining therapeutic interventions for CVD, and similarly, patients with CVD are often excluded from cancer therapy trials. As a result, the current practice recommendations are mainly based on expert consensus and small studies rather than robust evidence-based guidelines. Translational and clinical research is the key to advance basic understanding of the interactions of the heart with cancer and cancer therapy. Eventually, subspecialization in this field after general cardiology fellowship and board certification might be helpful given the complexity and dynamicity of the field.

CONCLUSIONS

With the growing number of cancer survivors and older patients with comorbid CVD receiving treatment for cancer, the CVD burden in this population is larger than ever. Although the field of cardio-oncology is emerging at a fast pace, it is mainly restricted to a limited number of academic centers, while the majority of patients with cancer and survivors are cared for by community-based practices that lack the necessary expertise. Providing the next generation of FITs with knowledge and training in cardio-oncology is necessary to address what is a major challenge in improving the care and quality of life of patients with cancer.

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RESPONSE: A Call to Action for Established Cardio-Oncologists

Time to Train the Future

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Although the cardiotoxic effects of anthracyclines and radiation have been known since the 1970s, and important papers were published during the late '70s and early '80s using radionuclide angiography monitoring, patients with concomitant cancer and cardiovascular diseases were, until recently, mainly followed by internists or general cardiologists. There has been a growing call for the 2 specialties of oncology and cardiology to grow closer as patients survive longer and develop both comorbidities. This increasing awareness was considerably boosted by the seminal paper by Slamon et al. (1) in 2001, which reported both the prognostic-changing effect of trastuzumab on the very aggressive HER2-positive breast cancers and a rate of 27% of impaired left ventricular ejection fraction in patients receiving this treatment. There are now >600 tyrosine kinases in development, many of which, by direct or off-target effects, affect the cardiac or vascular system, and novel immunotherapies carry specific cardiac myocarditis risks.

Additionally, underlining the need for a cardio-oncology subspecialty, the patients referred by the oncologists are complex, with multiple comorbidities. These patients have an extensive list of medications, many of which are unknown to the general cardiologists, most of them with side effects and pharmacological interactions. The oncology treatments that they have received result in specific conditions that may require different treatment than other patients, as is the case for radiation-induced valvular disease.

Ganatra and Hayek make a case for structured training for fellows interested in cardio-oncology, and they are absolutely on target. To develop the cardio-oncology subspecialty, we need standardized accredited training. The authors are correct that barriers remain. As principal investigators and mid-career or senior faculty, we still have many fundamental questions about how to best manage cardio-oncology patients, such as what the usefulness and the ideal method and frequency are of cardiac function monitoring during and after potentially cardiotoxic anticancer treatment, and which therapeutic route to follow when there are differing results from monitoring. Many cardio-oncology programs have their homegrown common-sense approach to these questions, creating variability in the approach. We are still missing the large clinical trials to answer these questions.

A very important factor that is crucial to cardio-oncology is the necessity to have a multidisciplinary team and a multidisciplinary approach to cardio-oncology patients. The buy-in and involvement of oncologists are necessary, and the time in the oncology wards should be considered. Close collaborations with cardiology subspecialties (electrophysiology, heart failure, and so on), cardiovascular surgery, and other specialists (neurologists,

nephrologists, and so on) are necessary for successful cardio-oncology program implementation. Multidisciplinary meetings and rounds need to be incorporated in the fellowship.

Although the number of cardio-oncology programs is growing, there are presently only a handful of homegrown fellowships in cardio-oncology. As Ganatra and Hayek remind us, fellows-in-training are eager to enter the cardio-oncology subspecialty. The ACC's cardio-oncology council and all established cardio-oncologists should recognize the enthusiasm of fellows-in-training. We should work to structure and standardize the education of future cardio-oncologists who will develop and improve this important field.

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