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Cardio-oncology (M Fradley, Section Editor)

Cardio-Oncology Fellowship Training and Education

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Abstract

Purpose of review With the rapid development of novel cancer therapeutics and the growing number of cancer survivors, there is significant demand for cardio-oncology experts to care for these patients. As such, it has become increasingly necessary to develop formalized training in the field of cardio-oncology. This review will focus on the current state of cardio-oncology education, with recommendations for the development of dedicated cardio-oncology fellowships.
Recent findings Cardio-oncology fellowships should be affiliated with high-volume centers that have established cardio-oncology clinical and research programs with dedicated cardio-oncology faculty. Several recent publications have proposed recommendations to develop uniform cardio-oncology training standards, core curricula, and evaluation metrics.
Summary With the rapid evolution of the field and the support of various profession organizations, the number and quality of dedicated cardio-oncology fellowship programs is expected to increase significantly. The adoption of defined training requirements and evaluation standards to measure competency will be essential to ensure the legitimacy and success of the field.

Introduction

The development of novel cancer therapeutics has seen significant growth over the last decade with the focus shifting from cytotoxic chemotherapy to targeted and immunotherapies. These advances, along with improved and intensified screening recommendations have led to significantly improved survival rates for many cancers. As such, the number of cancer survivors is expected to increase to over 22 million by 2024 [1]. It is increasingly recognized however that many cancer treatments have cardiovascular toxicities which may not occur for several decades and can significantly impact both morbidity and mortality [2]. As such, the field of cardio-oncology was

developed to both treat and prevent cardiovascular complications in cancer patients and survivors.

Despite the rapid incorporation of clinical cardio-oncology to many academic and community practices, there remains inconsistency in the cardiovascular care offered to cancer patients. This can be a result of various issues including lack of formalized educational requirements and/or standardized guidelines for the treatment of the various cardiotoxicities encountered. For example, only 11% of surveyed cardiology fellowship programs included cardio-oncology lectures as part of their core curriculum, and no data exists about cardio-oncology training within oncology fellowships [3••]. Beyond incorporating cardio-oncology education into both cardiology and medical oncology fellowship programs, there is increasing interest in developing dedicated cardio-oncology training programs. While several fellowships exist throughout North America and Europe, this number is expected to grow significantly and therefore, it will be essential to develop standardized cardio-oncology training requirements along with metrics to measure outcomes [4•].

Cardio-oncology faculty and training environment

In order to support cardio-oncology education and training, an established cardio-oncology clinical and research program should already exist within the organization. This will allow trainees to have adequate exposure to the variety of cardio-oncology issues in both the inpatient and outpatient setting. The cardio-oncology program should be routinely evaluating patients with both solid and liquid tumors, as well as those undergoing stem cell transplantation, oncologic surgery, and/or radiation therapy. The members of the cardio-oncology team should have familiarity with all modern medical oncologic treatments ranging from traditional cytotoxic chemotherapeutics, to targeted and immunotherapies. In addition, exposure to active oncologic clinical trials is also recommended as is integration with survivorship programs [5, 6].

Cardiovascular imaging is an important component of cardiotoxicity monitoring, and therefore, cardio-oncology trainees must have robust and comprehensive exposure to multimodality cardiovascular imaging [7]. Echocardiographic evaluation using both 3-dimensional and global longitudinal strain analysis should be regularly utilized in the cardio-oncology workflow, and trainees should feel comfortable analyzing and incorporating the findings into the management of their patients [8]. Additionally, exposure to cardiac magnetic resonance imaging (MRI) as well as cardiac computed tomography (CT) is recommended. For example, cardiac MRI has become invaluable in the evaluation and management of cardiac masses, cardiac amyloidosis, and checkpoint inhibitor myocarditis [9]. Cardio-oncology trainees will benefit from a robust, multidisciplinary group of practitioners including cardiologists, hematologist-oncologists, pharmacists, and nurses. Cardiologists with expertise and knowledge of the various cancer therapeutics and their potential cardiotoxic effects must play a primary role in the education of the trainees as cardio-oncology is clinically a cardiology-focused specialty. Nonetheless, oncologists interested in the field of cardio-oncology should also play a significant role in training as their expertise in oncology treatment planning is invaluable to the improved understanding of cardiotoxicity risk mitigation. In addition, subspecialty cardiologists including interventionalists, electrophysiologists, and heart failure specialists should be identified to augment the clinical and educational experience [4•, 5, 6, 10••].

As with any training program, there should be at least one individual focusing on the educational needs of trainees in the field of cardio-oncology. If a formal cardio-oncology fellowship is established, this individual should be a designated program director with interest and training in graduate medical education and provided with protected time to grow and refine the educational mission of the fellowship. If the cardio-oncology training is incorporated into the curricula of general cardiology or oncology fellowships, then the general fellowship program director will ensure that adequate education is delivered by the cardio-oncology program staff [11].

Non-physician members of the cardio-oncology program can also play a substantial role in the education of cardio-oncology trainees. Pharmacists can be an especially useful resource given their knowledge about different cancer therapeutics. Nurses and specifically nurse coordinators can educate the cardio-oncology trainee about the complexities of coordinating care for this patient population as well as the psycho-social challenges many of these patients are facing on a regular basis [4•, 5, 6, 10••].

Cardio-oncology curriculum and educational recommendations

There remains a great degree of variability in cardio-oncology training recommendations as it relates to core curricula, training duration, and prerequisite experience. This is largely due to a lack of pre-defined training standards. For example, in the USA, the Core Cardiology Training Statement (COCATS-4) does not include cardio-oncology exposure during general the CV fellowship [12], while the European Society of Cardiology Committee for Education has incorporated formal cardio-oncology education into its training recommendations for the general cardiologist [13]. Ideally, standardized educational requirements will be established as a result of collaboration with cardio-oncology professional organizations such as the International Cardio-Oncology Society (ICOS) and the American College of Cardiology (ACC) Cardio-Oncology Council along with the Accreditation Council for Graduate Medical Education (ACGME) and the various oncology societies.

In 2016, the International Cardio-Oncology Society (ICOS) and the Canadian Cardiac Oncology Network (CCON) published a conceptual framework with comprehensive training goals and standards for this growing subspecialty [10••]. They recommend a minimum of 100 unique patient experiences to successfully complete the equivalent of level III training associated with a cardio-oncology fellowship. It should be recognized that metrics for evaluation of graduate medical education training are shifting from a focus on discreet numbers to a competency-based evaluation focused on achieving specific milestones.

Regardless of the approach, there are several specific topics within cardio-oncology that require mastery in order to successfully complete the educational training program (Fig. 1):

1. Pre-chemotherapy Cardiovascular Risk Assessment: Multiple cancer therapeutics are associated with the development of cardiovascular complications ranging from heart failure to arrhythmias [14]. Moreover, with the aging population, many patients begin their cancer treatments with underlying CV disease and risk factors. As such, it is important to screen patients prior to their cancer treatments to minimize their potential risk for toxicity. A frequently

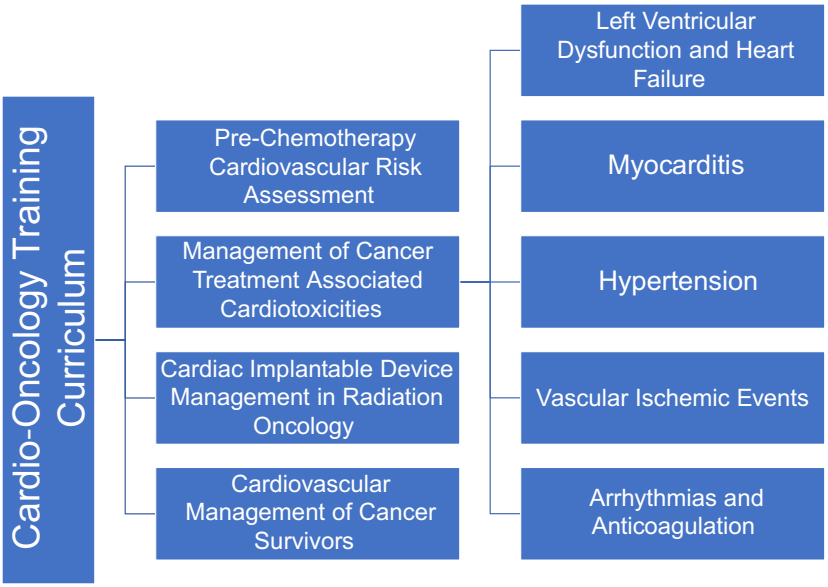

Fig. 1. Cardio-oncology Training Curriculum.

utilized and validated approach is the "ABCDE" method focusing on blood pressure control, lipids, and lifestyle modifications [15]. In addition, pre-treatment CV testing may also be necessary. For example, assessment of cardiac function is essential for patients receiving anthracyclines and HER2-targeted therapies [7], whereas ankle-brachial indices may be helpful to screen for high-risk patients receiving the targeted agents nilotinib and ponatinib [16, 17]. Finally, pre-treatment assessment allows for the baseline evaluation of cardiac biomarkers (troponin and brain natriuretic peptide) which can be helpful to predict those at higher risk for dysfunction especially in the setting of anthracycline use [18, 19].

2. Management of Cancer Treatment Associated Cardiotoxicities: At the completion of cardio-oncology training, familiarity with a vast array of cardiotoxicities is essential. While there has traditionally been a focus on heart failure, it is increasingly recognized that many other CV complications exist especially with newer targeted and immunotherapies [14].
    a. Left Ventricular Dysfunction and Heart Failure: Anthracyclines and HER2-targeted therapies are most commonly associated with the development of systolic dysfunction and heart failure; however, multiple other therapeutics have been associated with this toxicity including the proteasome inhibitor, carfilzomib, and the tyrosine kinase inhibitor (TKI), sunitinib [20–24]. Understanding the complexities of these cancer treatments will help to guide the cardiovascular treatment plan. Although the treatment of chemotherapy-induced cardiomyopathy and heart failure is similar to any other etiology, the complexities of cancer patients can make management more challenging [25, 26]. Long-term management options including device-based therapies must be appropriately utilized in the context of the oncologic prognosis [25].

b. Myocarditis: There is increasing evidence that certain cancer immunotherapies, particularly checkpoint inhibitors, may lead to myocarditis [27, 28]. These events can range from mild episodes without significant dysfunction, to life-threatening and even fatal events. Evaluation and monitoring can be challenging and trainees must learn to incorporate multiple diagnostic modalities including biomarkers, echocardiography, and cardiac MRI into the evaluation of these patients [27, 29]. Treatment also requires advanced knowledge and may require immune modulating therapies ranging from steroids to antithymocyte globulin or infliximab [30].

c. Hypertension: Accelerated hypertension is a common complication of a class of targeted therapeutics known as vascular endothelial growth factor (VEGF) inhibitors [31]. Although hypertension is considered a marker of drug efficacy, it is important to treat the blood pressure in order to minimize long-term CV disease morbidity and mortality [32]. Angiotensin system inhibitors confer a survival advantage and are the preferred antihypertensive agents in this population [33]. Other cancer therapeutics are also associated with hypertension including MEK inhibitors, ibrutinib, a TKI used for certain B cell malignancies, and carfilzomib; however, neither the mechanism nor the preferred treatment regimens are well established with these agents [24, 34, 35].

d. Vascular Ischemic Events: There is increasing evidence that vascular toxicities can occur with a variety of cancer therapeutics. For example, 5-fluorouracil can lead to coronary vasospasm and myocardial ischemia [36]. Several TKIs, including nilotinib and ponatinib are associated with increased rates of myocardial infarction, stroke, and peripheral arterial occlusive events [16, 37]. Radiation to the chest and vascular beds can have a delayed effect, leading to vascular stenosis many years after the completion of treatment [38]. As such, cardio-oncology trainees must recognize these potential toxicities and develop reasonable risk mitigation strategies. Moreover, the management of cancer patients that develop coronary ischemia may be especially challenging as a result of cancer-associated thrombocytopenia and bleeding diatheses [39].

e. Arrhythmias and Anticoagulation: Atrial arrhythmias, especially atrial fibrillation (AF) are frequently encountered cardiotoxicities. There appears to be an association with incident AF and cancer [40]. Additionally, specific cancer therapies including ibrutinib, doxorubicin, and melphalan are associated with increased rates of arrhythmias [41–43]. Management of these conditions can be challenging in the context of cancer as bleeding concerns and drug-drug interactions can limit the use of both anticoagulants and antiarrhythmic drugs [44]. Ventricular arrhythmias are less frequently encountered; however, there is an association with the TKI, ibrutinib use as well as in the setting of QT prolongation, a common finding with many different cancer therapeutics (arsenic, ribociclib, niltotinib, etc.) [45–47]. QT prolongation in cancer patients is often due to multiple factors ranging from concomitant medications to electrolyte imbalances and

therefore, trainees must be comfortable assessing the QT interval in order to ensure patient safety while minimizing unnecessary treatment disruptions. Bradyarrhythmias are most commonly seen with taxanes and with the TKI crizotinib which targets the anaplastic lymphoma kinase (ALK) [48, 49]. In general, these patients are asymptomatic and no intervention is necessary. Finally, bradyarrhythmais and heart block have been reported as an initial manifestation of checkpoint inhibitor myocarditis [50]. If trainees encounter these issues in patients treated with checkpoint inhibitors, further evaluation for myocarditis is necessary.

3. Cardiac Implantable Device Management in Radiation Oncology Patients: In a population cohort from Denmark, there was a 199% increase in the annual rate of radiation therapy (RT) in patients with implantable devices from 2003 to 2012 [51]. Effective delivery of RT without compromising the safety of the implantable device can often be challenging and requires refined knowledge of the RT treatment plan [52]. Trainees should have exposure to these patients and help to develop and implement strategies to promote the safe and effective delivery of RT to this patient population.
4. CV Management in Cancer Survivors: The number of cancer survivors living in the USA is estimated to increase dramatically over the next decade. Cancer survivors are at higher risk for all forms of CV disease including heart failure, coronary disease, valvular disease, and arrhythmias [53, 54]. This is due primarily to the treatments themselves which can have a delayed toxic effect on the CV system including anthracyclines and radiation to the heart and other vascular beds. Trainees must learn appropriate screening protocols in this population. For example, the American Society of Echocardiography (ASE) recommends annual CV assessment and stress echocardiogram 5 years after completion of radiation therapy even for asymptomatic patients [7]. In addition, aggressive risk factor screening is necessary to minimize long-term complications.

Didactics

While many of the topics listed above will be addressed through direct patient exposure, dedicated didactics are also an essential part of the cardio-oncology curriculum to ensure trainees possess the knowledge necessary to practice independently. Regular cardio-oncology lectures are essential, and the trainee should be encouraged to attend cardio-oncology-focused scientific meetings including the American College of Cardiology sponsored "Advancing the Cardiovascular Care of the Cancer Patient" or the Global Cardio-Oncology Summit. It is commonplace for oncologists to meet routinely in multidisciplinary "tumor boards" to discuss challenging patient-related topics and formulate appropriate treatment plans. While it is helpful for cardio-oncology trainees to attend these sessions, it is impossible to be at every meeting. As such, we suggest developing a cardio-oncology "tumor board" that will focus on the complex CV issues in cancer patients and invite oncologists to attend if it pertains to their patients, disease process, or treatments. Finally, routine cardio-oncology journal clubs are also encouraged to maintain current knowledge and facilitate discussion [4•, 55•].

Research

Research is the cornerstone of any academic training program. As such, a cardio-oncology trainee should become involved with scholarly activities to advance the current state of knowledge of this developing field. In a training program with an emphasis on clinical exposure, this can be achieved through clinical research projects including retrospective chart review studies as well as prospective evaluations if possible. Collaborations with basic and translational scientists should also be available as mechanistic investigations are essential to our improved understanding of cardio-oncology. Participation in larger scale oncology clinical trials is also recommended as this allows the cardio-oncology trainee to understand patient selection and adjudication of adverse cardiovascular events. A long-term goal would be to obtain a T-32 training grant specifically in the field of cardio-oncology to support the academic endeavors of the cardio-oncology fellowship [56, 57]. There may also be opportunities to collaborate with other more developed fellowships including heart failure and advanced imaging to complete investigations. Cardio-oncology trainees should work towards presenting data at national and international conferences as well as publishing their work in both oncology and cardiology journals. There is increasing interest in promoting research in this field with different NIH funding opportunities as well as journals dedicated to cardio-oncology (*Cardio-Oncology Journal* and the newly developed journal from the American College of Cardiology, *JACC–Cardio-Oncology*).

Conclusions

With the rapid development of the field of cardio-oncology, there has become an increasing need to develop dedicated training programs to educate providers about best practice and to ensure high-quality standardized CV care is provided to cancer patients. Moreover, training programs allow for increased dissemination of knowledge and serve as an excellent platform for the advancement of the field via research and other scholarly endeavors. Despite this, significant challenges remain before their widespread adoption and implementation can occur ranging from a lack of a uniform curriculum and specific training requirements to funding. Nevertheless, with time, it is evident that this specialty will continue to grow, and dedicated training will be necessary to ensure the long-term success of the field.

Compliance with Ethical Standards

Conflict of Interest
Michael G. Fradley is a section editor for *Current Treatment Options in Cardiovascular Medicine*.

Human and Animal Rights and Informed Consent
This article does not contain any studies with human or animal subjects performed by any of the authors.

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