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CARDIO-ONCOLOGY (EH YANG, SECTION EDITOR)

Targeting Barriers of Systems of Care in a Growing Multi-disciplinary Field

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Abstract

Purpose of Review Cardio-oncology is a growing multi-disciplinary field that focuses on treating and preventing cardiovascular complications in cancer survivors and patients. This review summarizes the current clinical needs and system-based approaches to target barriers of care.

Recent Findings The field of cardio-oncology has experienced significant growth in recent years, and an increasing number of programs have been developed across the nation to provide improved and multi-disciplinary care to this patient population. Despite this burgeoning growth, practitioners in the field continue to face important challenges which include lack of administrative and departmental support, funding limitations, and gaps in the areas of mentoring, education, and research.

Summary Despite continued growth, cardio-oncology providers continue to face a multitude of challenges. Early inclusion of multi-disciplinary stakeholders, oncologists, cardiovascular team members, and administrative leadership provides an opportunity to collaborate and achieve unique patient care and health system benefits, such as prevention of adverse cardiovascular outcomes, and facilitates the delivery of optimal oncologic treatment.

Keywords Cardio-oncology · Cardiovascular disease · Oncology · Chemotherapy · Radiation therapy · Targeted therapy

Introduction

Advances in the diagnosis and treatment of a range of malignancies over the past several decades have led to a decrease in cancer-related mortality and an increase in cancer survivorship. There is increasing recognition that patients are at risk of experiencing cardiovascular (CV) complications of cancer therapies sometimes with events occurring several decades after completion of treatment [1, 2, 3•]. According to the American Cancer Society, there will be an estimated 20 million cancer survivors in the USA by 2026 and with this growing number of survivors, now living to advanced ages with pre-existing CV disease and risk factors, there is a growing need for cardio-oncology experts [4, 5•].

Collaborations between cardiologists and oncologists in the management of patient co-morbidities during and after cancer have occurred for decades; however, the multi-disciplinary assessment and management of cancer patients with a greater focus on preventive care in a dedicated environment have evolved more recently, in particular outside of tertiary cancer

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referral centers [6]. The armamentarium of treatment for a variety of cancers has increased substantially and the list continues to grow as do the number of potential on- and off-target effects of these therapies [7]. Additionally, new targeted therapies are being developed at a rapid pace, many of which have recognized or unrecognized CV toxicities.

With the growing clinical need, the landscape of cardio-oncology in the USA has changed. National societies in cardiology and oncology have published position statements [8–10], and the number of cardio-oncology programs continues to grow both at academic institutions and in community settings [6, 11]. There has also been an interest in training with rare but increasing opportunities for fellowships at tertiary institutions. Despite this growth, several barriers remain to establishing successful multi-disciplinary cardio-oncology programs including challenges in clinical practice, education, and research. In this article, we discuss the development of a cardio-oncology program in a health care organization with a focus on the different needs and perspectives of multi-disciplinary team members including cardiovascular and oncology specialists as well as health care administrators.

Part 1: Cardiovascular Needs During the Continuum of Cancer Care

Chemotherapy and radiation therapy continue to be the cornerstones for the treatment of cancer, but unfortunately, some of these regimens have also been shown to have undesirable cardiac effects. The most notable first-line agents that cause cumulative dose-dependent cardiotoxicity are the anthracyclines which continue to have an important role in the treatment of solid tumors such as breast cancer and hematologic malignancies. Higher cumulative anthracycline dose, female gender, underlying CV disease, and both younger and older age groups have been associated with a higher risk of cardiomyopathy [2, 8, 12]. Trastuzumab, used in the treatment of HER2-positive breast cancer, has been shown to cause an often reversible cardiomyopathy with reported rates of heart failure between 1 and 28% [13, 14]. Systemic hypertension, QT prolongation, arrhythmias, myocardial ischemia, pulmonary hypertension, thrombo-embolic events, accelerated atherosclerosis, and pericardial and valvular heart disease are other cardiovascular toxicities that have been described but are not systematically followed or captured during oncology care [15]. Immune checkpoint inhibitors are another class of cancer therapies that are transforming the care of patients with previously limited options, and they have become the first line of therapy in multiple cancer types including renal cell carcinoma, melanoma, urothelial, and lung cancer. The immune adverse effects associated with immune checkpoint inhibitors can affect multiple organ systems, and while reports of cardiac manifestations have been overall rare, they include fatal myocarditis, refractory ventricular arrhythmias, heart block, and cardiogenic shock [16, 17]. The extent of both short- and long-term cardiotoxicities of many novel therapies remains unclear given the rapid rate of development of new agents as well as frequent use of combination therapies either in a concomitant or sequential manner. Radiation therapy is similarly associated with a myriad of potential adverse effects, many of which are delayed, and these include injury to the myocardium, valves, pericardium, and the coronary arteries [7].

Most cardio-oncology efforts initially focused on patients receiving high doses of anthracyclines, but over the past several decades, there have been substantial advances in cancer biology and the field has expanded to include many new treatments which include targeted and immune-modulating therapies. With these novel therapies and the rapid pace of development of new anti-cancer agents, the list of cardiac toxicity is only expected to grow. These changes serve to underscore the importance of having specialists that are knowledgeable about cancer therapies, their toxicities and management. Additionally, this patient population has needs that cross two major specialties, and their care must encompass not just the treatment period but their lifetime of oncologic and CV risk. This highlights the importance of a multi-disciplinary approach with appropriate long-term follow-up that will successfully manage this patient population along the entire continuum of their care.

The continuum of care for oncology patients includes the time of diagnosis (pre-treatment phase), on-treatment phase, and the post-treatment period often referred to as survivorship [8]. In the pre-treatment phase, the focus is geared towards assessment of baseline cardiovascular risk and the onus lies on the oncologist to identify patients at increased risk who would benefit from a cardio-oncology referral particularly when therapies with potential CV toxicity are being considered. The patients with risk factors as shown in Table 1, when referred to cardio-oncology, will benefit from a comprehensive CV evaluation that includes a baseline ECG and cardiac imaging (echocardiogram or advanced cardiac imaging) as well as symptom or CV condition specific evaluation. Optimization of CV treatment for existing risk factors (such as hypertension and hyperlipidemia) as well as patient counseling and education about symptoms that should raise concern is an important part of the pre-treatment cardio-oncology encounter. Depending on the planned treatment, primary cardiopreventive strategies, such as use of beta-blockers, angiotensin receptor blockers (ARBs), or ACE inhibitors, can be considered [18, 19].

While on therapy, one enters a more reactive phase and cardio-oncology referrals often occur when problems are detected or concerns arise. One of the goals of establishing multi-disciplinary cardio-oncology programs is to enable the prompt

Table 1 Clinical criteria and risk factors along the continuum care that should prompt a referral to cardio-oncology clinic

Point in cancer treatment continuum	Clinical referrals examples	Examples of cardio-oncology evaluation and plan
Pre-treatment	History of CVD Previous high-dose anthracycline treatment (> 250 mg/m^2)	Comprehensive CV assessment ECG
	Prior exposure to low dose anthracycline (< 250 mg/m^2) and radiation with heart in treatment field	ECHO and/or cardiac MRI Consider serum biomarkers in high risk patients
	Prior low dose anthracycline exposure AND ≥ 2 CV risk factors	Initiation of therapy (e.g., ACE inhibitor, beta blocker)
	Abnormal ECHO or cardiac imaging (EF ≤ 50%)	Develop plan for further surveillance while on therapy
	HER2 therapy with past or planned anthracycline treatment	
	Planned HER2 therapy with ≥ 2 CV risk factors	
	Elevated BP prior to or during VEGF inhibitor therapy	
	Baseline prolonged QT with planned exposure to QT prolonging regimens	
	Decrease in EF by 5% or more to < 55%with symptoms	
	Asymptomatic decrease in EF by ≥ 10% to < 55%	
During treatment	Decrease in strain of 10–15% Pericardial effusion	Comprehensive CV assessment ECG
	Cardiac Biomarker elevation	ECHO and/or cardiac MRI
	Chest pain or heart failure symptoms	Initiation of therapy (e.g. ACE inhibitor, beta blocker)
	Arrhythmias	Multi-disciplinary discussions regarding cessation of therapy if indicated
	QT prolongation on ECG > 500 ms	
	Uncontrolled hypertension	
After treatment	History of high-dose anthracycline therapy (> 250 mg/m^2) Past exposure to radiation therapy (> 35 Gy) with new symptoms	Comprehensive CV assessment and counseling ECG
	Past exposure to radiation therapy (> 35 Gy) with heart in treatment field >5 years ago without symptoms	ECHO and/or cardiac MRI Appropriate evaluation of CV conditions (myocardial, vascular and/or valvular dyfunction)
	History of radiation therapy or known cardio toxic therapy with ≥ 2 CV risk factors	Treatment and Management of CV conditions
	History of cardiotoxic chemotherapy or XRT with plans for upcoming pregnancy or prior to starting competitive sports	
	Need for cardiotoxic therapy to treat secondary malignancy	

recognition of cardiotoxicity and to have a streamlined approach towards the patient's care. Some of the symptoms/findings while on therapy that should trigger a cardio-oncology referral during this period of treatment are highlighted in Table 1.

The final phase of this continuum is the survivorship phase which becomes even more crucial as people age and develop other CV risk factors which are compounded with the increased risk imparted by prior chemotherapy/radiation exposure. Survivors are at increased risk of cardiometabolic complications which include hypertension, hyperlipidemia, stroke, diabetes, and coronary artery disease among others. This is highlighted in data published from the Childhood Cancer Survivor Study which has shown that the risk of CV disease can be up to 10 times higher in cancer survivors than in siblings [20], and these differences in the incidence of serious cardiac events have been observed despite baseline similarities in cardiovascular risk factors [21]. In the survivorship cohort, referrals to cardio-oncology should be considered for those with multiple cardiovascular risk factors, history of cardiotoxic therapy with plans to participate in competitive sports, prior to pregnancy, prior to treatment for new or recurrent malignancies with cardiotoxic therapies, and in those who develop any concerning symptoms. With the establishment of cardio-oncology programs comes a greater opportunity for post-treatment counseling regarding the risk of future complications and the establishment of a concrete plan for future monitoring.

PART 2: Structure and Organization of Cardio-Oncology Services

The field of cardio-oncology is gaining momentum, and the number of cardio-oncology clinics in the USA and globally is increasing [5•, 7, 11, 15, 22]. The structure and organization of

cardio-oncology programs are crucial to developing an effective service line that provides efficient, streamlined, and comprehensive care to cancer patients. Various models of cardio-oncology services exist depending upon the structures of the local health service, hospitals, resources, and their specialization [5•]. In larger tertiary care centers, one is more likely to find mutlidisciplinary teams that consist of cardiologists, oncologists, radiation oncologists, pharmacists, nurses, administrators, and other support staff. These institutions may provide both outpatient and inpatient consultative services by cardio-oncology experts. In smaller institutions or those with less expansive resources, the cardio-oncology program may consist of an oncologist and a cardiologist with expertise in this area without the more extensive ancillary support. While outpatient consultations will be readily available, often the provision of inpatient consults will be through the inpatient general cardiology service.

Each member of the cardio-oncology team serves a key role, and it is important to have clearly defined expectations. The oncologist is charged with the responsibility of selecting the patients that will be referred to the cardiology clinic. The cardiologist's role is in facilitating the cardiac evaluation, diagnostic testing, initiation of preventive or therapeutic interventions, and participating in multi-disciplinary discussions surrounding any changes to the oncologic treatment plan such as cessation, modification, or resumption. Oncologic nurses often play a key role in identifying patients with new symptoms that may be picked up during their chemotherapy infusions in-between doctor visits. Oncology and cardiology pharmacists are integral parts of the cardio-oncology team and may lead the development of cancer treatment-specific pathways. Ongoing surveillance is primarily provided by the oncologic team given more frequent contact with those providers. Care tracks or service lines adapted to the different cancer types, risk factors, and planned therapies should be developed among the care teams to help streamline referrals and minimize delays in detection and implementation of appropriate therapies or treatment decisions. Table 1 shows examples of referral pathways/algorithms based on the cancer agent and the time point in the cancer treatment continuum.

Part 3: Challenges Faced in the Development and Implementation of Cardio-Oncology Programs and Potential Solutions

The field of cardio-oncology has developed significantly in the past decade; however, development and implementation of clinical cardio-oncology programs pose ongoing challenges. At the local health care system level, lack of perceived benefit by the oncology stakeholders, inadequate institutional support, and lack of funding are often noted as the key limiting steps, together with additional burdens such as the availability of expertise, need for clinical staff training, and administrative assistance [6]. At the national level, there is an ongoing lag in development of evidence- and guideline-based clinical care, and need for broad, robust clinical research initiatives, together with the need for education, formalized training, and mentorship. Table 2 summarizes some barriers encountered in the implementation of cardio-oncology programs and proposed solutions.

Challenges from the Perspective of Oncologists Medical oncologists are the main referral source for oncologic patients to cardio-oncology programs as they are prescribing therapies with potential cardiovascular toxicities. While there are well-established guidelines about when an oncologist should not administer a medication, little guidance exists regarding the identification of patients who would benefit from a cardiology intervention to minimize cardiovascular toxicities. Development of treatment-specific algorithms (Fig. 1), which can be readily accessible to a medical oncologist when formulating a treatment plan, facilitates patient flow and referrals. Incorporation of a referral template into electronic medical records (EMRs) is the most efficient way to accomplish this, and this should be followed by a streamlined referral process with defined expectations as to timing of feedback and therapeutic interventions from the cardio-oncology consultant. The EMR is likely an underutilized resource as it can be used to identify individuals at high risk via tracking of their cumulative anthracycline and/or radiation doses, and it can also serve as a platform for ensuring that best practice guidelines established by the program are being followed such as meeting serial imaging recommendations. The EMR can further act as a centralized source for generating referrals based on pre-set criteria and is a useful tool for the identification of abnormal results and findings and communication among multi-disciplinary team members. Once treatment is underway, ideally, treatment plans would incorporate triggers for ordering echocardiograms, relevant labs, and alerts to nurses, pharmacists, and prescribing physicians when there are potentially important changes in cardiovascular parameters.

After completing therapies with curative intent, most oncology programs now provide a Survivorship Plan to patients. It is important to ensure that appropriate monitoring for late CV toxicities is included in these plans. However, patients receiving palliative therapies are living longer and longer, and these patients are not captured by most survivorship programs. We are increasingly recognizing the need for the same CV surveillance in this group of patients, and ongoing cardio-oncology clinic follow-up is recommended. Lastly, it is difficult to stay abreast of emerging data regarding toxicities of new therapies and the involvement of pharmacists, as well as cardiologists, is critical to keep algorithms current.

Table 2 Barriers encountered in implementing cardio-oncology programs and proposed solutions

	Challenges	Proposed solutions
Clinical practice	• Most patients with malignancies are only seen by oncologists in the absence of overt pre-existing heart disease • Lack of awareness about the importance and role of a cardio-oncology program • Building a multi-disciplinary team that has adequate support staff to stream line the cardio-oncology service line	Early inclusion of oncologists in program development with discussion of pre-treatment referrals to cardio-oncology Development of cancer treatment-specific clinical protocols with delineation of risk factors that should prompt referral Dissemination of available educational resources, grand-rounds and tumor-board presentations dedicated to discussion of CV risk prevention and oncology treatment decision making Discussion with administrative leadership from oncology and cardiology about needed resources and support staff Identification of system benefits of the cardio-oncology program and service line to the departments and administration with focus on improved patient care, increased departmental growth and recognition
Education	• Very little formal training in cardio-oncology currently exists • There is little exposure to the field early in medical training • Very few guidelines exist to guide management	Consider applying for the few formal fellowship programs that currently exist Cardiology fellows can rotate with the cardio-oncology experts during training even in the absence of a formal fellowship Medicine residents and fellows in both cardiology and oncology should be integrated into the cardio-oncology programs early to maximize exposure and access to research and mentorship Guideline and position statements have been published by major societies (ASCO, ASE, ESC) and can form the starting point for guiding management Education through dedicated live meetings [23] Develop institution-based protocols Multi-disciplinary discussions for more complex patient cases Collaborations with other established cardio-oncology programs and specialists
Mentorship and research	• The field is still relatively young, and mentorship for interested cardiologists can be challenging • Difficulty identifying research projects to participate in • Difficulty obtaining funding for clinical trials	If no local mentors available, can identify a mentor in one of the major centers with established cardio-oncology program and engage in long distance mentor-mentee relationship Identify research mentors in cardiology, oncology, or both. Mentors can be at local institution or through collaborations with other programs Be creative about funding sources and consider collaborative application that includes oncology and cardiology expertise. Consider NIH funding opportunities [26]

Administrative Challenges There are several barriers that may be encountered from an administrative perspective in the implementation of cardio-oncology programs. One of the biggest challenges to overcome is bringing together the various service lines in this multi-disciplinary team to foster effective collaboration and facilitate the nuanced management of these at-risk patients. Due to the novel nature of the specialty, there is a lack of awareness of the need for the service. In a large tertiary hospital, the main pipeline for new patient referrals may be the Oncology department. Education sessions to raise awareness about the specialty program and its scope need to be conducted strategically among oncologists or other potential referring providers to ensure effective capture of all patients that may benefit from a cardiology consult. More comprehensive marketing strategies can assist with promoting the program among external referring providers in the catchment areas based on the patient population served.

Due to the rapidly developing nature of this specialty, it may also be challenging to communicate current and updated clinical protocols for patient eligibility for the program to all the referring providers. Dedicated human resources to proactively identify patients at risk with the use of technology such as interoperable electronic medical records and robust algorithms may help alleviate the challenges discussed. Dedicated administrative support is also required for scheduling visits and procedures, obtaining financial authorizations and registering patients among other responsibilities. Early partnership with oncology administrative leadership allows discussion of patient and system benefits of cardio-oncology programs which include prevention of CV toxicity, management of

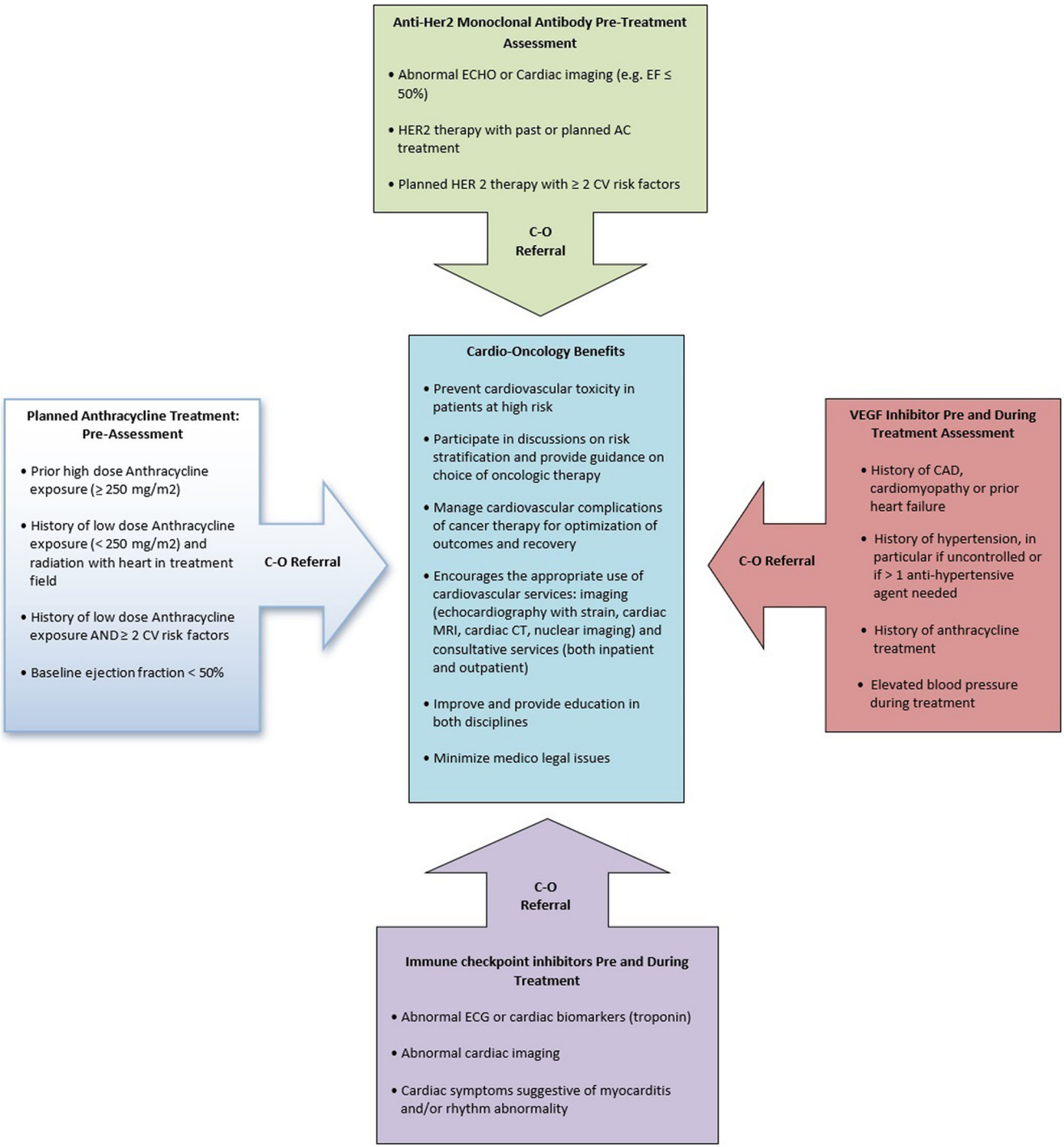

Fig. 1 Examples of the referral criteria for common drug categories with known potential for cardiovascular toxicity. Limited data: ECG and troponin can be considered for patients undergoing combination therapy with immune checkpoint inhibitors in addition to baseline LVEF assessment

CV conditions, and complications, as well as facilitation of oncology care (Fig. 1). These considerations may help justify the investment in additional resources and inform plans for provider education and appropriate use of system resources.

Another Herculean challenge is capturing cancer survivors, especially in areas lacking robust survivorship programs. The effects of cardiotoxicity may develop years after the administration of cancer therapy, especially in cases of radiation therapy. Recently, due to the implementation of electronic health records at health organizations, it has become easier to track and follow patients through time. However, there is limited access to historical patient data predating the use of electronic

health records and, therefore, it is a challenge to proactively identify at-risk survivors who were treated before the implementation of the electronic recording system. Direct patient outreach efforts and provider education, in particular with family practice physicians, may help overcome this challenge.

Prospective planning of a cardio-oncology service starts with an understanding of the oncologic, cardiovascular and administrative perspectives and the formation of a multidisciplinary team. The development of such teams is ultimately dictated by the needs of the program, volumes of the cancer center, and the availability of resources. In smaller community programs, the initial team may consist of one cardiologist and one oncologist which would suffice to get the cardio-oncology program started and this can be expanded once more resources become available. For centers where low volumes limit growth, community outreach should be considered given that much of oncologic care is indeed provided by oncologists in the community.

Education and dissemination of knowledge are the foundations for growth of any field and due to the relatively new nature of cardio-oncology; the lack of randomized clinical trials to guide management is not surprising. This need has been at least in part addressed by the professional societies' expert consensus and guideline statements [1, 8, 9] that facilitate the communication between the specialists and CV and oncology health team members. They also provide a platform for successful collaboration and exchange of multidisciplinary data and perspectives in this area. There have been an increasing number of dedicated educational conferences by the professional societies including the American College of Cardiology [23], International Society of Cardio-Oncology, and by comprehensive cancer centers such as Memorial Sloan Kettering and MD Anderson. Regulatory agencies, in particular the Food and Drug Administration (FDA), have a critical role in promoting safety of therapies, and FDA public workshops that focus on diagnosis and monitoring of CV toxicities in oncology trials importantly advance the field [24, 25]. Another critical partnership is with the government and funding agencies where significant progress has been made through the joint work of the National Cancer Institute (NCI) and the National Heart, Lung, and Blood Institute in creating funding opportunities for research into mechanisms, diagnosis, and management of CV effects of cancer therapies [26].

Mentorship and training in this field is a challenge that is faced by many cardiologists, oncologists as well as cardiology and oncology fellows given the limited availability of experts in this area. In recent years, a few cardio-oncology fellowships have been established which will provide formal training to interested parties. Some institutions without a formal fellowship program are attempting to increase exposure to this area during general cardiology fellowship but this is not widely available. For those with an interest but no mentorship at their local institution, collaborations with larger centers with well-established programs or with individual mentors that have experience is an option. This may also foster inter-institutional collaborations that might provide opportunities for research. Earlier exposure of trainees in both cardiology and oncology, while in residency and fellowship, may increase interest in the field over time and will provide a platform for trainees to engage in research projects early in their careers and establish relationships with mentors.

Accessibility to cardio-oncology services, not only at tertiary centers but also in the community, is of paramount importance and can be a limitation, particularly in larger programs. Large tertiary centers often service large geographical regions, but it is not always feasible for patients in the community to travel to these centers for their care. This can be improved by having experts in cardio-oncology at different sites in the community or with the establishment of outreach clinics when feasible. In situations where resources may be limited, telemedicine and e-consultative services can be utilized to expand the reach of the cardio-oncology team, but this will be dependent on the capabilities of the program and the degree of support afforded to them.

Conclusion

The number of cardio-oncology programs has increased across the nation and while structures may vary, a multidisciplinary approach remains a key component. Important challenges continue to exist and at the local level, this often includes lack of administrative and departmental support and funding limitations. Early inclusion of multi-disciplinary stakeholders, oncology, and CV team members, as well as administrative leadership, provides an opportunity to present unique patient care and health system benefits, including prevention of CV adverse outcomes and facilitation of optimal oncology treatment. Joint development and implementation of cancer treatment-specific protocols represent the cornerstone of cardio-oncology programs and creates a platform for collaborative clinical care. National-level efforts by the professional societies, government, and regulatory agencies continue to make advances in education and clinical training, as well as in mentorship opportunities through cardiology and oncology partnership.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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.

References

Papers of particular interest, published recently, have been highlighted as:
- Of importance

1. Bovelli D, Plataniotis G, Roila F. Cardiotoxicity of chemotherapeutic agents and radiotherapy-related heart disease: ESMO clinical practice guidelines. Ann Oncol : official journal of the European Society for Medical Oncology. 2010;21(Suppl 5):v277–82.
2. Yeh ET, Bickford CL. Cardiovascular complications of cancer therapy: incidence, pathogenesis, diagnosis, and management. J Am Coll Cardiol. 2009;53(24):2231–47.
3. • Fradley MG, Brown AC, Shields B, Viganego F, Damrongwatanasuk R, Patel AA, et al. Developing a comprehensive cardio-oncology program at a cancer institute: the Moffitt Cancer Center Experience. Oncol Rev. 2017;11(2):340 **This article details the experience of developing a cardio-oncology program and provides an overview of the challenges faced and practical solution suggestions.**
4. American Cancer Society. Cancer Treatment & Survivorship Facts & Figures 2016–2017. Atlanta: American Cancer Society; 2016.
5. • Lancellotti P, Suter TM, López-Fernández T, Galderisi M, Lyon AR, Van der Meer P, et al. Cardio-oncology services: rationale, organization, and implementation. A report from the ESC Cardio-Oncology council. Eur Heart J. 2018;2018:ehy453 **A comprehensive review article by the European Society of Cardiology Cardio-Oncology Council that discusses the rationale, organization, and implementation of cardio-oncology services.**
6. Barac A, Murtagh G, Carver JR, Chen MH, Freeman AM, Herrmann J, et al. Cardiovascular health of patients with cancer and cancer survivors: a roadmap to the next level. J Am Coll Cardiol. 2015;65(25):2739–46.
7. Herrmann J, Lerman A, Sandhu NP, Villarraga HR, Mulvagh SL, Kohli M. Evaluation and management of patients with heart disease and cancer: cardio-oncology. Mayo Clin Proc. 2014;89(9):1287–306.
8. Armenian SH, Lacchetti C, Barac A, Carver J, Constine LS, Denduluri N, et al. Prevention and monitoring of cardiac dysfunction in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol : official journal of the American Society of Clinical Oncology. 2017;35(8):893–911.
9. Zamorano JL, Lancellotti P, Rodriguez Munoz D, Aboyans V, Asteggiano R, Galderisi M, et al. 2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines: the Task Force for cancer treatments and cardiovascular toxicity of the European Society of Cardiology (ESC). Eur Heart J. 2016;37(36):2768–801.
10. Plana JC, Galderisi M, Barac A, Ewer MS, Ky B, Scherrer-Crosbie M, et al. Expert consensus for multimodality imaging evaluation of adult patients during and after cancer therapy: a report from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging. 2014;15(10):1063–93.
11. Okwuosa TM, Barac A. Burgeoning cardio-oncology programs: challenges and opportunities for early career cardiologists/faculty directors. J Am Coll Cardiol. 2015;66(10):1193–7.
12. Swain SM, Whaley FS, Ewer MS. Congestive heart failure in patients treated with doxorubicin: a retrospective analysis of three trials. Cancer. 2003;97(11):2869–79.
13. Suter TM, Procter M, van Veldhuisen DJ, Muscholl M, Bergh J, Carlomagno C, et al. Trastuzumab-associated cardiac adverse effects in the herceptin adjuvant trial. J Clin Oncol : official journal of the American Society of Clinical Oncology. 2007;25(25):3859–65.
14. Guarneri V, Lenihan DJ, Valero V, Durand JB, Broglio K, Hess KR, et al. Long-term cardiac tolerability of trastuzumab in metastatic breast cancer: the M.D. Anderson Cancer Center experience. J Clin Oncol : official journal of the American Society of Clinical Oncology. 2006;24(25):4107–15.
15. Jovenaux L, Cautela J, Resseguier N, Pibarot M, Taouqi M, Orabona M, et al. Practices in management of cancer treatment-related cardiovascular toxicity: a cardio-oncology survey. Int J Cardiol. 2017;241:387–92.
16. Salem JE, Manouchehri A, Moey M, Lebrun-Vignes B, Bastarache L, Pariente A, et al. Cardiovascular toxicities associated with immune checkpoint inhibitors: an observational, retrospective, pharmacovigilance study. Lancet Oncol. 2018;19(12):1579–89.
17. Johnson DB, Balko JM, Compton ML, Chalkias S, Gorham J, Xu Y, et al. Fulminant myocarditis with combination immune checkpoint blockade. N Engl J Med. 2016;375(18):1749–55.
18. Gulati G, Heck SL, Ree AH, Hoffmann P, Schulz-Menger J, Fagerland MW, et al. Prevention of cardiac dysfunction during adjuvant breast cancer therapy (PRADA): a 2 x 2 factorial, randomized, placebo-controlled, double-blind clinical trial of candesartan and metoprolol. Eur Heart J. 2016;37(21):1671–80.
19. Avila MS, Ayub-Ferreira SM, de Barros Wanderley MR Jr, das Dores Cruz F, Goncalves Brandao SM, Rigaud VOC, et al. Carvedilol for prevention of chemotherapy-related cardiotoxicity: the CECCY trial. J Am Coll Cardiol. 2018;71(20):2281–90.
20. Oeffinger KC, Mertens AC, Sklar CA, Kawashima T, Hudson MM, Meadows AT, et al. Chronic health conditions in adult survivors of childhood cancer. N Engl J Med. 2006;355(15):1572–82.
21. Armstrong GT, Oeffinger KC, Chen Y, Kawashima T, Yasui Y, Leisenring W, et al. Modifiable risk factors and major cardiac events among adult survivors of childhood cancer. J Clin Oncol : official journal of the American Society of Clinical Oncology. 2013;31(29):3673–80.
22. Kenigsberg B, Wellstein A, Barac A. Left ventricular dysfunction in cancer treatment: is it relevant? JACC Heart Fail. 2018;6(2):87–95.
23. American College of Cardiology. Advancing the Cardiovascular Care of the Oncology Patient [Available from: https://www.acc.org/education-and-meetings/meetings/meeting-items/2018/06/06/06/54/2019-cardio-oncology. Accessed 10 Dec 2018.
24. United States Food and Drug Administration. FDA Public Workshop: cardiovascular toxicity assessment in oncology trials [Available from: https://www.fda.gov/drugs/newsevents/ucm513031.htm. Accessed 10 Dec 2018.
25. United States Food and Drug Administration. FDA Public Workshop: assessment of cardiovascular toxicities in immuno-oncology trials [Available from: https://www.fda.gov/Drugs/NewsEvents/ucm574741.htm. Accessed 10 Dec 2018.
26. NIH. Department of Health and Human Services [Available from: https://grants.nih.gov/grants/guide/pa-files/pa-16-035.html. Accessed 10 Dec 2018.