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Research paper

Cardio-oncology and COVID 19: Lessons learned, past reflections and future deliberations

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1. Introduction

In cardio-oncology, a myriad of cardiovascular toxicities can result from cancer therapies, primarily radiation therapy and pharmacologic cancer therapies [1] (Fig. 1). The valves, pericardium, myocardium, coronary arteries, and conduction system of the heart can all be affected. The peripheral vasculature can also be affected by systemic hypertension, pulmonary hypertension, vasospasm, thrombosis stenosis, and vasculitis, yielding a breadth of cardiovascular toxicities in cardio-oncology [1]. Interestingly, there is also a range of cardiovascular toxicities in coronavirus disease of 2019 (COVID-19) [2,3]. Indeed, the etiology of COVID-19 is different from that of cardio-oncology. In COVID-19, the source of cardiovascular toxicity is severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In cardio-oncology, the source of cardiovascular toxicity is cancer therapies. Yet the toxicities in cardio-oncology and COVID-19 are similar in terms of thromboembolism, takotsubo, myocarditis, arrhythmia, heart failure, and acute coronary syndrome [2]. Not only are there commonalities in toxicities between COVID-19 and cardio-oncology, but also there are commonalities in pathophysiology in terms of cytokine release, inflammation, hypoxia, and hypercoagulability [2]. Similarly, dexamethasone, tocilizumab, and bembcentinib are drugs that can be used to treat COVID-19, and have also been used in the treatment of cancer in cardio-oncology [2]. Therapeutic anticoagulation has been studied to treat components of COVID-19 and is also used in cardio-oncology [2]. These all represent lessons we have learned by reflecting on cardio-oncology in the COVID-19 pandemic and have led to the following future deliberations.

2. Health disparities and risk prediction

As we move forward in studying, understanding, caring for patients in, and educating others and each other regarding cardio-oncology and COVID-19, the continued assessment of underlying factors and solutions to address health disparities in cardiovascular toxicities observed in cardio-oncology and COVID-19 is necessary [2] (Table 1). Additionally, more precise risk prediction in cardio-oncology and COVID-19 patients belonging to communities and populations that experience health disparities, as well as in the general population, needs to take place [2]. We must consider how to predict who is most at risk for developing cardiovascular toxicity from cancer therapies, as well as who is most at risk for severe illness or death from COVID-19. Other important points to consider in both cardio-oncology and COVID-19 are the short-term and long-term sequelae of inflammation, endothelial dysfunction, macrovascular and microvascular dysfunction, among others, that exist [2].

3. Survivorship

Along the path of survivorship and understanding survivorship, we are much further along in cardio-oncology than we are in COVID-19, yet there is much further for us to advance. As we learn more about how to screen, approach surveillance, and manage long-term survivorship in cardio-oncology, we must do the same in COVID-19, as we learn more about both conditions, moving forward, together. We must therefore consider the need to build more clinics across our practices for cardio-oncology, that are also cognizant of the effects of COVID-19 [4]. To accomplish this, a three-pronged virtual hybrid approach can be used [4]. This virtual hybrid approach includes information seeking, information gathering, and information sharing. Information seeking focuses

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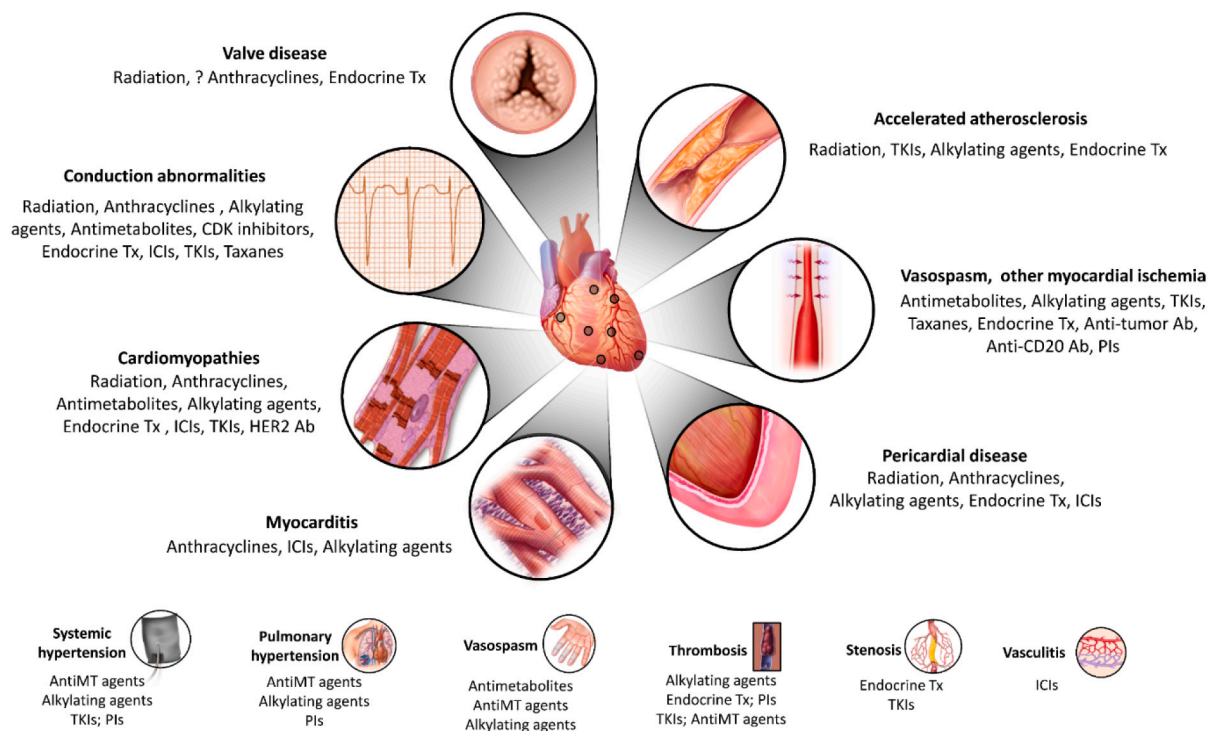


Fig. 1. Cardiovascular toxic effects of cancer therapies. A wide range of cancer therapies can harm or aggravate a variety of cardiac (top) and vascular (bottom) system components, and understanding these effects can help with diligent monitoring, avoidance, and appropriate early diagnosis; used with permission [1].

Table 1
Concepts and topics to study common to cardio-oncology and COVID-19.

Common topic	Cardio-oncology	COVID-19
Mechanisms of left ventricular cardiomyopathy	Elucidate mechanisms and optimal management of left ventricular systolic dysfunction in Cardio-Oncology	Elucidate mechanisms and optimal management of left ventricular systolic dysfunction in COVID-19
Immune system activation	Analyze pathophysiology and optimal management of immune response, cytokine release syndrome, and autoimmune adverse effects from ICl or CAR-T cell therapy	Analyze pathophysiology and optimal management of immune response, cytokine release syndrome, and related adverse effects in COVID-19
Long-term sequelae of inflammation	Investigate long-term implications of inflammation induced by neoplastic agents	Investigate long-term implications of myocardial inflammation in COVID-19
Endothelial dysfunction	Interrogate role of endothelial dysfunction in ischemic and cardiomyopathic cardiovascular injuries from cancer drugs	Interrogate role of endothelial dysfunction in ischemic and cardiomyopathic cardiovascular injuries from COVID-19
Coagulopathy and anticoagulation	Study the burden, mechanisms, and optimal management of coagulopathy (arterial or venous) with need for anticoagulation or antiplatelet therapy in Cardio-Oncology	Study the burden, mechanisms, and optimal management of coagulopathy and microthrombosis with beneficial response to anticoagulation in COVID-19
Role of RV and RVAD	Explore significance of RV systolic dysfunction after anthracycline therapy	Explore significance of RV systolic dysfunction in severe COVID-19 infection
Prognostic value of RV strain	Evaluate utility of RV strain to predict outcomes following anthracycline therapy	Evaluate utility of RV strain to predict COVID-19 severity/mortality
Utility of steroid therapy and biologics	Determine the effectiveness and timing of steroid treatment and monoclonal antibodies for inflammation- or immune-related adverse events from ICl or CAR-T cells	Determine the effectiveness and timing of steroid treatment and monoclonal antibodies for inflammation-related adverse CV events in COVID-19
Neurohormonal therapy	Establish cardioprotective contributions of neurohormonal therapies	Establish whether neurohormonal therapies are protective in COVID-19
Potential drug interactions	Appraise the extent and impact of potential drug interactions between Cardiology drugs and Oncology drugs	Appraise the extent and impact of potential drug interactions between Cardiology drugs and COVID-19 drugs
Impact of health disparities	Assess underlying factors and solutions to address health disparities in cardiovascular toxicities observed in Cardio-Oncology	Assess underlying factors and solutions to address health disparities observed in cardiovascular injuries in COVID-19
Precision of risk prediction	Develop precise methods of predicting cardiovascular toxicities and prognosis	Develop precise methods of predicting risk and overall prognosis in COVID-19

CAR-T Cells = Chimeric Antigen Receptor T-Cells; COVID-19 = Coronavirus Diseases of 2019; CV = cardiovascular; ICI = Immune Checkpoint Inhibitor; RV = Right Ventricle; RVAD = Right Ventricular Assist Device.
Used with permission [2].

on where there are clinics already in place. Focus should be placed on literature reviews on how others have built their cardio-oncology clinics, as well as networking and attending regional and national meetings. Information gathering addresses where the clinic will be built,

learning about existing resources and the needs and patients in the partnering cancer center, and networking with stakeholders. Once the clinic has been built, information sharing is key. Share qualitative data and quantitative data about how you have been able to build and

incorporate virtual health into your hybrid cardio-oncology practice, recognizing that some of your patients will also be coming in who currently, previously, or in the future would have COVID-19 [4]. To protect our patients, we must minimize in-person visits, making most visits virtual and safe, to protect the patient from COVID-19, and to protect each other, as well as our trainees [5]. Thus, as trainees learn, they are learning in virtual didactics and conferences, from social media “Tweeterials”, learning by experiencing telemedicine and remote monitoring, and by individualizing cardiotoxicity surveillance, whether in the inpatient or outpatient setting [5,6]. Therefore, virtual care for our patients, telemedicine and remote monitoring, partnering with virtual communication, can expand the capacity of each other and our trainees to collaborate across each institution, across institutions, and across the world [4]. Truly, we are all in this inevitable dance between cardio-oncology and COVID-19, and between cardio-oncology and oncology [7], together. We must work together in research and innovation, education, awareness, support, collaboration, and community, to improve the health, healing, and well-being of all of our patients in cardio-oncology or COVID-19, or both.

Author contributions

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References

- [1] S.A. Brown, Preventive cardio-oncology: the time has come, *Front. Cardiovasc. Med.* 6 (2020) 187.
- [2] S.A. Brown, S. Zaharova, P. Mason, J. Thompson, B. Thapa, D. Ishizawar, et al., Pandemic perspective: commonalities between COVID-19 and cardio-oncology, *Front. Cardiovasc. Med.* 7 (2020), 568720.
- [3] I. Bisceglia, D. Gabrielli, M.L. Canale, G. Gallucci, I. Parrini, F.M. Turazza, et al., ANMCO POSITION PAPER: cardio-oncology in the COVID era (CO and CO), *Eur. Heart J. Suppl.* 23 (Suppl C) (2021) C128–C153.
- [4] S.A. Brown, S. Patel, D. Rayan, S. Zaharova, M. Lin, T. Nafee, et al., A virtual-hybrid approach to launching a cardio-oncology clinic during a pandemic, *Cardiooncology* 7 (1) (2021) 2.
- [5] S. Feldman, J. Liu, R. Steingart, D. Gupta, Cardio-oncology training in the COVID-19 era, *Curr. Treat. Options in Oncol.* 22 (7) (2021) 58.
- [6] S. Brown, E. Yang, M. Branch, C. Beavers, A. Blaes, M. Fradley, et al., Training & Career Development in Cardio-Oncology Translational and Implementation Science, *Heart Fail. Clin.* (2022). In Press.
- [7] S.-A. Brown, in: *Cancer And The Heart: The Inevitable Dance*. Your Heart and Cancer, Dr. Brown Cares LLC, Cheyenne, WY, 2020, pp. 10–22.