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MINI-REVIEW

Cardio-Oncology in the Era of the COVID-19 Pandemic and Beyond

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ABSTRACT: Coronavirus disease 2019 (COVID-19) has emerged as a global pandemic and public health crisis. Increasing waves of intermittent infectious outbreaks have dramatically influenced care among broad populations. Over the past 2 decades, there has been a rapid increase in cancer survival, with >400 000 new survivors each year. The increasingly common presence of cardiovascular disease in patients during or after cancer treatment led to the rapid growth of the field of cardio-oncology with a mandate of identifying, treating, and preventing the various forms of cardiovascular disease seen among this population. This review evaluates the implications of the pandemic on the practice and study of cardio-oncology. The evolving understanding of the relationship between comorbid disease and clinical outcomes among this population is assessed. With the impetus of the pandemic, cardio-oncology can be deliberate in embracing changes to cardiac screening, monitoring, and intervention during oncology care. Bridging 2 specialties, consideration of the lessons learned in cancer and cardiovascular may pivotally inform ongoing therapeutic efforts. Further, the development of multicenter registries focused on understanding and optimizing outcomes among these patients should be considered. Together, these insights may critically inform strategies for the care of cardio-oncology patients in future phases of the COVID-19 pandemic and beyond.

Key Words: cancer ■ cardiac imaging ■ cardio-oncology ■ COVID-19 ■ targeted therapies

Coronavirus has emerged as a global pandemic and public health crisis.[1–3] Increasing waves of intermittent infectious outbreaks have influenced care among broad populations. However, coronavirus disease 2019 (COVID-19) has much further reaching implications than many of the previous contagious outbreaks. As of late May, the virus has already resulted in the death of over 350 000 patients worldwide.

Over the past 2 decades, there has been a rapid increase in cancer survival, with >400 000 new survivors each year. Much of this survivorship has been driven by the use of novel anticancer therapies, including the nearly 160 new therapies approved since 2000 alone.[4] However, this population, particularly those with comorbid or complicating cardiovascular disease (CVD), is susceptible to adverse outcomes.

The common presence of CVD in patients during or after cancer treatment led to the development of the field of cardio-oncology with a mandate of identifying, treating, and preventing the high burden of CVD seen among this population. The growing interest in this new subspecialty of medicine has led to the formation of national and international cardio-oncology groups, peer-reviewed journals, and research initiatives aimed at meeting the needs of oncology patients in the 21st century. Moreover, available data have suggested that these patients may be among those at disproportionate risk for adverse outcomes after COVID-19 infection.[5–9] Providing optimal care for patients with cancer, particularly those infected with COVID-19, is challenging, given that our understanding of the COVID-19 pandemic and its effects

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Nonstandard Abbreviations and Acronyms

COVID-19	coronavirus disease 2019
CTLA-4	cytotoxic T-lymphocyte-associated protein 4
PD-1	programmed cell death protein 1
PD-L1	programmed death ligand 1

on various populations continues to evolve on a daily basis.

Barring any game-changing therapy and until a vaccine is widely available, the COVID-19 pandemic may remain a constant within medicine for the near future, and the need to develop policies to provide safe clinical care under the ongoing specter of COVID-19 is paramount. Many changes implemented will persist after the initial phase of the pandemic is over. As we continue to progress through the subsequent phases of this crisis, a more comprehensive cardio-oncology strategy is clearly needed.

Within this review, we evaluate the implications of the pandemic for the practice and study of cardio-oncology. We specifically focus on the evolving understanding of the relationship between comorbid disease and clinical outcomes among this population. We also discuss potential insights gained, which may critically inform strategies for the care of cardio-oncology patients in future phases of the COVID-19 pandemic and beyond.

VULNERABILITY OF PATIENTS WITH CANCER AND CARDIOVASCULAR DISEASE TO COVID-19

The populations with cancer and CVD are particularly vulnerable to COVID-19 because of increased healthcare exposure and infection risk. Patients with cancer have an ongoing need for anticancer therapy irrespective of the COVID-19 pandemic necessitating frequent interactions with health care. Patients with CVD have ongoing healthcare needs with the development of acute cardiovascular events and routine surveillance visits. Patients with cancer and underlying CVD and/or treated with potentially cardiotoxic cancer therapies are vulnerable to both short- and long-term adverse cardiac events, needing increased healthcare interactions for risk mitigation. Increased healthcare interactions amplify potential exposure to COVID-19. In addition, patients with underlying cancer or CVD are generally considered more susceptible to infections. The majority of infection risk in cancer is attributed to cancer types and cancer treatments that result in immunosuppression.[10,11] For instance, cytotoxic therapies for hematological malignancies diminish lymphocyte populations. Cardiovascular disease is exacerbated by infection. Recent studies have linked acute myocardial infarction to respiratory infections, especially influenza.[12] In addition, an increase in heart failure hospitalizations is linked to influenza illness.[13] Yearly flu shots are offered annually in recognition of this increased risk in patient populations with CVD and cancer. Based on this underlying vulnerability to infection and poor outcomes, initial publications have emphasized the susceptibility to COVID-19 of both patients with cancer and with CVD.[5,14] Multiple governments have issued guidance that categorizes patients with cancer and patients with CVD as high risk for severe COVID-19 illness.[15–18] These guidelines recommend increased diligence in shielding these patients from unnecessary exposures.

Patients With Cancer and COVID-19: Susceptibility and Outcomes

The first study of COVID-19 patients with cancer was published by Liang et al.[19] In a prospective cohort, they identified 18 of 1590 (1%) patients with COVID-19 who had a history of cancer, higher than the overall Chinese cancer incidence of 0.29%. Patients with cancer were significantly more likely to have severe clinical courses, defined as requiring invasive ventilation or resulting in death, than the patients without cancer, 39% versus 8%, respectively. Four of the patients had received chemotherapy or surgery within 1 month of their hospitalization, and 3 (75%) had severe clinical courses. Compared with patients without cancer, patients with cancer deteriorated more rapidly, within 13 days compared with 43 days.

Although these cancer cases were heterogenous,[5] subsequent studies have confirmed an increased prevalence of cancer in patients infected with COVID-19 and an increased risk of death.[6,20] Antitumor therapy within 14 days placed patients with cancer at a significantly increased risk of a severe clinical course.[7] In a meta-analysis of 10 studies that included data on patients with cancer and COVID-19, the overall prevalence of cancer in patients with COVID-19 was estimated at 2.0%.[21] In another meta-analysis, the odds ratio of a severe complication was 2.29 for a patient with cancer infected with COVID-19 compared with a patient without cancer.[22]

In the first US COVID-19 and cancer publication, 334 of 5688 (6%) patients, admitted in the Mount Sinai Health System, had a history of cancer.[23] Patients with cancer were more likely to require mechanical ventilation but had no significant difference in mortality. However, cancer stage and cancer treatment data were not available. The results of a New York study found a significant increase in case fatality rate for patients with

cancer: 25% in patients with solid tumors and 37% in patients with hematological malignancies.[24]

A multicenter COVID-19 case-control study of 105 patients with cancer and 536 age-matched patients without cancer showed that patients with hematological malignancies, lung cancer, or metastatic cancer had the highest frequency of severe events.[25] However, patients with nonmetastatic cancer had similar event frequencies compared with patients without cancer. A study of 423 patients with cancer diagnosed with COVID-19 at Memorial Sloan Kettering Cancer Center demonstrated 20% developed severe respiratory illness and 12% died within 30 days.[26] Age older than 65 years and treatment with immune checkpoint inhibitors were predictors of hospitalization and severe disease. An intriguing Italian study found that patients with prostate cancer receiving androgen deprivation therapy were at lower risk of COVID-19 infection.[27] Although based on a small number of patients, these studies overall suggest that patients with cancer are at higher risk of COVID-19 infection and at risk of having an early, severe COVID-19 clinical course.

Patients With Cardiovascular Disease and COVID-19: Susceptibility and Outcomes

The specific impact of underlying cardiovascular disease in patients with COVID-19 was first analyzed by Guo et al.[8] In a retrospective case series of 187 hospitalized patients with COVID-19 at a single hospital in Wuhan, 66 (35.3%) patients had underlying CVD that included hypertension, coronary artery disease, and cardiomyopathy. Patients with underlying CVD were more likely to have elevated troponin levels (54.5% versus 13.2%). Regardless of underlying cardiovascular disease status, patients with elevated troponin levels were significantly more likely to have a severe clinical course, requiring mechanical ventilation or dying (59.5% versus 8.9%). Shi et al[9] evaluated 426 hospitalized patients with COVID-19 in the Wuhan region, identifying 82 (19.7%) patients with cardiac injury and 334 (80.3%) patients without cardiac injury based on troponin I (0.19 versus <0.006 μg/L) and creatine kinase-MB (3.2 versus 0.9 ng/mL) levels. Patients with cardiac injury were older and more likely to have comorbidities, including hypertension, diabetes mellitus, and coronary artery disease. Complications in patients with cardiac injury included significantly more acute respiratory distress syndrome, acute kidney injury, and coagulation disorders. A significantly higher percentage of patients with cardiac injury died compared with those patients without cardiac injury (42 [51.2%] versus 15 [4.5%], respectively).

In a larger risk factor analysis, underlying CVD had an odds ratio (OR) of 5.19, and hypertension had an OR of 2.72 for critical care need or death after COVID-19 infection.[28] A meta-analysis of 6 studies demonstrated a 2- and 3-fold increased risk of severe COVID-19 infection in patients with hypertension and cardiovascular disease, respectively.[29] Together this early data highlights the increased risk of patients with underlying cardiovascular disease of having a more severe disease course and risk of death.[30,31]

Severe acute respiratory syndrome coronavirus 2, the virus causing COVID-19, binds the angiotensin-converting enzyme 2 (ACE) receptor to enter host cells.[32] Given the increased risk of death in patients with CVD and hypertension infected with COVID-19, there has been concern about ACE inhibitor use.[33,34] A smaller, retrospective study of 1128 patients in China found that inpatient use of ACE inhibitor or angiotensin receptor blocker was associated with lower risk of all-cause mortality compared to non-users among hospitalized patients with COVID-19 and coexisting hypertension.[35] A retrospective study of 18 472 patients within the Cleveland Clinic Health System found no association with ACE inhibitor or angiotensin receptor blocker use and the likelihood of a positive COVID-19 test.[36] In another study of 12 594 patients in New York, there was no increase in the likelihood of a positive COVID-19 test nor a risk of severe COVID-19 infection with previous treatment with ACE inhibitors, angiotensin receptor blocker, beta blockers, calcium-channel blockers, or thiazide diuretics.[37]

Healthcare Utilization for Patients With Cancer and Cardiovascular Disease in COVID-19

Beyond the immediate medical complications of COVID-19 infections, the sweeping changes to our healthcare system likely will have unintended consequences. As nonemergent screening tests are postponed, delays in cancer diagnosis are inevitable. Given the increased risk of COVID-19 infection and death, any nonurgent treatments are being deferred. Clinical trial enrollment has, in many instances, has been halted. Patients with cancer are avoiding hospitals to limit COVID-19 exposure but also may be delaying appropriate care for cancer-related complications. The pandemic largely has put a pause on cancer care across the country. Decreased access will unavoidably result in increased cancer-related deaths by up to 20% according to 1 study.[38]

Changes to cardiac care as a result of the COVID-19 pandemic have already emerged. There is a decline in ST-segment–elevation myocardial infarction presenting to the hospital.[39,40] Subsequently, there has been a rise in late presentation myocardial infarctions with increased fatality and complication rates.[41]

The hypothesis is that fear of contracting COVID-19 from the hospital is deterring patients from calling the ambulance or going to the emergency room when they experience chest pain or other symptoms. In addition, nonemergent cardiovascular studies such as stress tests or echocardiograms have been delayed. The extent of these delays has not yet been fully determined and may result in a subset of our clinic population with more advanced cancer and cardiovascular disease than before the pandemic era. The true impact of delayed care has yet to be fully appreciated.

STRATEGIES IN CLINICAL CARE OF THE CARDIO-ONCOLOGY PATIENT

During the pandemic, medicine has undergone an unprecedented upheaval in the face of COVID-19. With the cancellation of routine appointments and procedures, initial hospital lockdown measures have resulted in a plateau of new COVID-19 infections, the opportunity to obtain appropriate personal protective equipment, and the time to develop long-term measures to mitigate risk. Nonemergent care has been postponed. The emergence of this crisis has led to acute alterations in the care of many patient populations, with limited evidence available to guide the management of disease in the era of this rapidly spreading infection. Increasingly societies and authors have moved to provide guidance through general statements and recommendations to attempt to mitigate adverse outcomes among at-risk patient populations.[8,9,42–46] Chief among these groups have been patients with preexisting or newly diagnosed cancers as well as CVD.

Cardio-Oncology Specific Considerations

Cardiology, oncology, and cardio-oncology patient populations are at increased risk not only directly from COVID-19 but also from disruption of their routine care. Creative ways to address this care gap are essential. As an emerging field that is not bound by traditional, inflexible patient-care pathways, cardio-oncology has been a beacon of innovation in developing multispecialty clinics, creating novel clinical care pathways, and designing collaborative research to address the unmet need of the cardiovascular care of the oncology patient. This flexibility provides the opportunity for the field of cardio-oncology to lead by example—not only for other models of multidisciplinary care—but for medicine as a whole.

At some institutions, cardio-oncology clinics have had difficulty gaining traction given logistical issues. Patients with cancer travel from near and far for oncology appointments. Appointment days can be filled with imaging, blood draws, and therapy infusions. Adding additional specialty appointments and tests can require more time, energy, and financial investment from the patient and the healthcare systems standpoint. Clinic time and testing increase contact with the healthcare system, which increases their risk of healthcare-acquired infection.

Changes in the Location of Care Delivery and the Use of Telehealth

To mitigate risk, the shift to telehealth visits has been a dominant undertaking for many medical specialties. The switch to virtual visits for cardio-oncology practices minimizes hospital and healthcare worker exposures.[47] Furthermore, it provides an opportunity to integrate into oncology care more seamlessly. For routine follow-ups, virtual visits with different specialists can be scheduled back to back without considering travel time or transportation issues. Cardio-oncology or other specialist telehealth visits could also be incorporated into an otherwise quiet chemotherapy infusion visit—if deemed appropriate by the oncologist. Multidisciplinary survivorship clinics can be conducted more readily in the virtual setting with less coordination of clinic space and clinician workspace.

Virtual visits have many advantages, but they do not fully replace a face-to-face clinical visit. Cardio-oncology can create pathways to appropriately triage patients with cancer into higher risk groups that should be seen for face-to-face consultation or testing. A proposed approach is presented in Figure 1. The specific cardiac triage algorithm can be devised by each institution. Ideally, big data could be leveraged to generate a broadly applicable cardio-oncology risk profile to aid the triage decision, but more research and development are needed. Initial triage can be conducted by the referring physician or the cardio-oncology clinic staff depending on institutional work flow. After this triage, patients with high cardiac risk can be scheduled to be seen virtually by a cardio-oncologist. Patients with low or uncertain risk can be scheduled to be seen virtually by a cardio-oncology nurse navigator first. Depending on the institution, this person may be an advanced practitioner or clinical nurse. The navigator can obtain further clinical information and relevant patient records to appropriately assess the cardiac risk prior to a virtual or in-person cardio-oncologist visit.

SPECIFIC SCENARIOS AND STRATEGIES

Cardiac Imaging

Although cardio-oncology patients are at a high risk of both COVID-19 infection and complications from

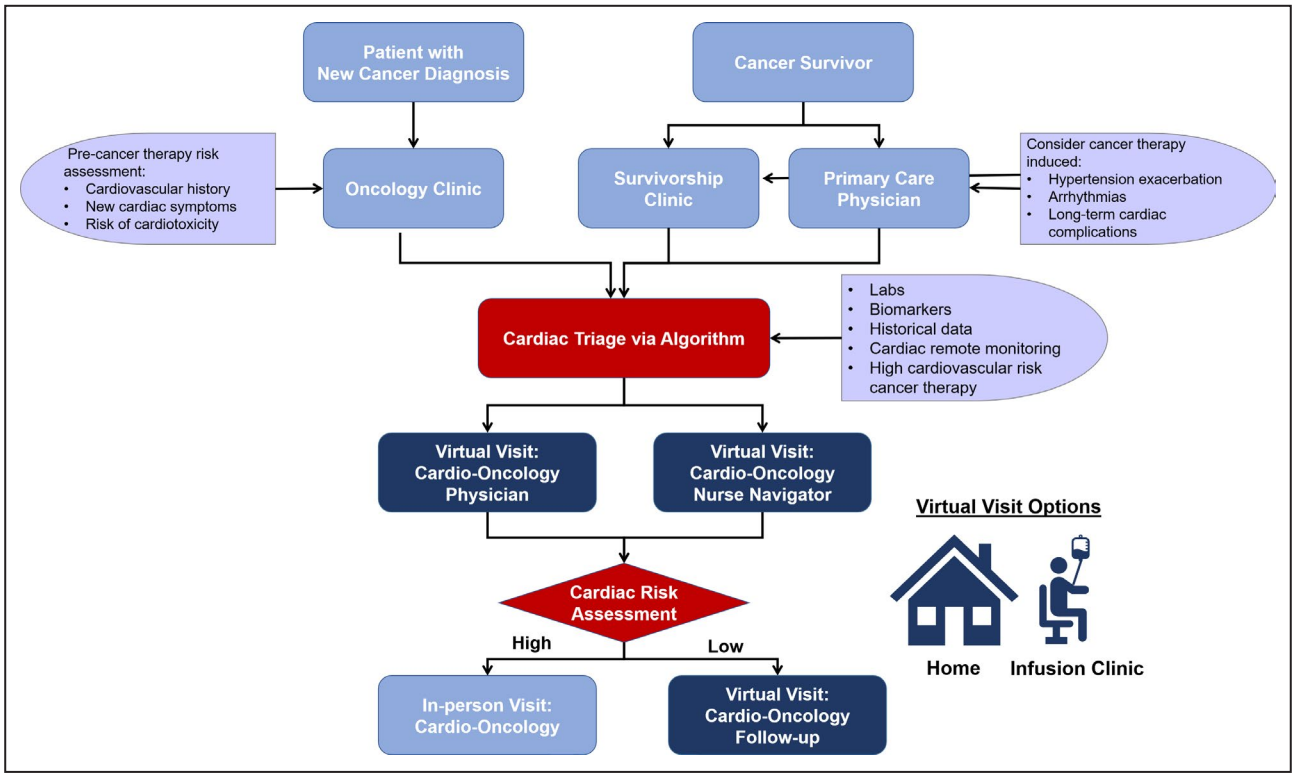

Figure 1. Suggested triage algorithm for cardio-oncology referrals, and care in the coronavirus disease 2019 (COVID-19) pandemic and early recovery.

delayed care, cardiac imaging is still a critical and essential part of patient management. Multiple societies have developed guidelines for cardiac imaging during COVID-19: European Society of Cardiology, American Society of Echocardiography, Society of Cardiovascular Computed Tomography, and Society of Cardiovascular Magnetic Resonance.[48–51] Specific scenarios for decreasing cardiac imaging in the cardio-oncology population in the short term have been suggested.[52] However, when considering the possible years that the COVID-19 pandemic may disrupt clinical care, establishing new pathways is important. Similarly, surveillance echocardiography is necessary for the capture of early or impending cardiotoxicity. In this pathway, increasing the interval for serial echocardiogram screening for patients at lower cardiotoxicity risk, based on cancer treatment regimen and underlying risk factors, is feasible. For example, the interval between serial echocardiograms could be stretched from 3 to 6 months in stable, asymptomatic patients. This pathway can be supplemented by serial biomarker surveillance during routine lab work with slight elevations prompting subsequent imaging. Cardiac magnetic resonance imaging will continue to remain a growing aid in the understanding and treatment of cancer-treatment associated CVD (Table).[53] We propose the development of "clean" clinical testing pathways for the highest risk patients in recognition of the real threat of the asymptomatic spread of COVID-19. This pathway could be achieved through full personal protective equipment of specific staff that is performing cardiac testing to prevent the potential spread or routine COVID-19 testing of a subset of staff to ensure no asymptomatic viral shedding. A low threshold for pre-outpatient screening for COVID related symptoms should underlie most effective strategies. Additionally, the duration of potential exposure to COVID-19 can be decreased with point-of-care ultrasound and focused echocardiogram.[54] Bedside point-of-care ultrasound by physicians can quickly answer straightforward questions, such as presence or absence of a pericardial effusion, and obviate the need for a formal echocardiogram. In an acute care setting, a focused echocardiogram to answer only the specific clinical question will also limit patient and staff exposure. Patients who have serial echocardiograms, such as patients on anthracyclines or trastuzumab, would benefit from shorter study duration to only assess ejection fraction. These approaches should be considered for patients with cancer or CVD who are high risk.

Cardiac Arrhythmias, Biomarkers, and Monitoring

Cardiac arrhythmias are an increasingly recognized manifestation of cancer therapy-related

Table. General Considerations and Recommendations for Cardio-Oncology Care During the COVID-19 Pandemic

COVID-19 Consideration and Recommendations for Cardio-Oncology	
General clinical care	• Increase telehealth utilization for both inpatient and outpatient care, with the degree of use depending on local healthcare resource allocation and COVID-19 infection risk • Consider consolidation of care with telehealth visit during chemotherapy infusion • Incorporate cardiac risk profiling for triaging and identifying patients who can benefit from telehealth versus in-person visits • Aggressive anti-COVID treatment when hospitalized (ex. remdesivir)
Cardiac imaging	• Assess the risk of cardiotoxicity based on cancer treatment regimen and underlying treatment • Consider increased serial imaging intervals and/or cardiac biomarker prompted imaging • Direct use of definitive imaging in challenging scenarios (ex. cardiac magnetic resonance imaging for low left ventricle ejection fraction), if available • Clean testing pathways with PPE and/or COVID-19 staff testing to mitigate the risk of asymptomatic or presymptomatic spread
Heart failure	• Optimize heart failure therapy • Continue use of ACEi/angiotensin receptor blockers • Assess the likelihood of exacerbation on ongoing anticancer therapy
Arrhythmias	• Remote patch-based rhythm monitoring for cancer treatment arrhythmia side effects • Consider cardiac CT to evaluate for left atrial appendage thrombus before cardioversion for atrial fibrillation versus invasive transesophageal echocardiogram • Consider delaying elective ablations until sufficient hospital PPE
Ischemic disease	• Urgent cardiac catheterization for acute coronary syndrome for cardio-oncology patients—underused even pre-COVID-19 • Consider coronary CT for preoperative evaluation or to exclude ischemia in newly diagnosed cardiomyopathy
Valvular interventions (ie, TAVR, TMVR)	• Severe aortic stenosis can significantly increase mortality of patients with cancer, and many cardio-oncology patients do not quality for surgical aortic valve replacement • Elective TAVR can be delayed at peak COVID-19 hospital resource utilization but should be a priority for rescheduling • Elective TMVR can be delayed at peak COVID-19 hospital resource utilization but should be a priority for rescheduling
Research (COVID-19 related, and cardio-oncology)	• Cardio-oncologists have unique expertise in treating hyper-inflammation related to novel immune-based therapies (ex. chimeric antigen receptor-T cell therapy, immune checkpoint inhibitors, etc) • Cardiotoxicity vigilance needed when repurposing cancer treatments to treat COVID-19 in clinical trials • Vaccine research is paramount; cardio-oncology patients should receive priority for COVID-19 immunization because of enhanced susceptibility to poor outcomes of infection • Multicenter clinical research trials needed to assess and validate cardio-oncology patient COVID-19 risk mitigation strategies while maintaining clinical care excellence • Consider working off site during pandemic peak • Focus on modifying research strategies based on lessons learned during the pandemic

ACEi indicates angiotensin-converting enzyme inhibitor; COVID-19, coronavirus disease 2019; CT, computed tomography; PPE, personal protective equipment; TAVR, transvalvular aortic valve replacement; and TMVR, transcutaneous mitral valve repair or replacement.

cardiotoxicity.[55,56] For common complaints of palpitations or syncope, monitoring for potential arrhythmias is standard of care. To socially distance from patients, patch-based cardiac rhythm monitors are an excellent approach to monitoring for arrhythmic side effects of cancer treatment.[57] The whole process of placing the patch, monitoring, interpretation, and debriefing can be done from the comfort of the patient's home. Beyond arrhythmias, patch monitoring can also be used for QT interval monitoring to identify patients at risk for fatal arrhythmia, torsades de pointes. Confirmation that the patch monitor available is appropriate for QT interval assessment is important. Patients with baseline prolonged QT interval, a history of induced QT prolongation, or started on cancer treatment that may prolong QT interval may benefit from remote patched based monitoring rather than in-person 12 lead electrocardiogram. In addition, rhythm monitors can be used as surrogates for measuring physical activity. Assessing the R-R dispersion and chronotropic changes may provide insight into patient activity level when direct assessment with the 6-minute walk test and other exams are not feasible.

From the standpoint of social distancing and meaningful use while not compromising care, incorporating a cardiovascular biomarker-based monitoring strategy into existing imaging monitoring system should be considered.[58–60] These lab tests, such as troponin or NT-proBNP (N-terminal pro-B-type natriuretic peptide), may be able to replace or allow spacing out of the serial echocardiograms, which are standard cardio-oncology practice. Biomarkers are relatively lower cost, lower risk, less invasive, and less COVID-19 exposure approach compared with imaging. Obtaining labs during oncology or chemotherapy infusion visits would reduce the burden on the patient. Nevertheless, current data show only a modest correlation between biomarkers increases and ejection fraction decreases in cardiotoxicity surveillance. Moving to a primarily biomarker-based monitoring could compromise sensitivity and specificity of cardiotoxicity detection. Further research is needed on biomarkers to detect cardiotoxicity. This strategy can be considered on an individual basis, balancing risk of COVID-19 exposure and the patient's cardiotoxicity risk. Patients with known immunocompromise due to cancer therapy or have lower

relative risk of cardiotoxicity may benefit more from more biomarker-based screening than primarily imaging-based screening.

Invasive Cardiac Procedures

The most common invasive procedures for cardio-oncology patients are transesophageal echocardiogram and cardiac catheterization. Patients with cancer are at high risk of arrhythmia and thromboembolic complications. In the setting of atrial fibrillation, this scenario often means a transesophageal echocardiogram to rule out left atrial appendage thrombus to minimize stroke risk before a direct cardioversion to achieve sinus rhythm. To avoid an invasive procedure, we suggest shifting to computed tomography imaging to evaluate for left atrial appendage thrombus, if this option is available at one's institution.[61,62] Furthermore, cardiac catheterization is often used to assess patients with cancer, whether after an abnormal stress test result during preoperative evaluation or to exclude coronary disease in a newly diagnosed cardiomyopathy. Transition to coronary computed tomography to evaluate for coronary perfusion when able can further decrease cardio-oncology patient exposure to healthcare staff. Nevertheless, urgent cardiac catheterization for acute coronary syndrome for this population should still be considered. Noninvasive therapy for acute coronary syndrome in patients with cancer is associated with worse overall survival.[63] The Society for Cardiovascular Angiography and Interventions has published COVID-19 guidance.[64]

Valve replacement in aortic stenosis can be considered an elective procedure, but in severe aortic stenosis, intervention becomes more urgent. Options for intervention include surgical aortic valve replacement and transcatheter aortic valve replacement. These cases may be delayed at the peak of COVID-19 hospital resource usage but should be a priority for rescheduling. Many patients with cancer are not eligible for surgical aortic valve replacement. Transcatheter aortic valve replacement is associated with lower periprocedural complications and better disposition in patients with cancer and should be pursued where feasible.[65]

RESEARCH CONSIDERATIONS

COVID-19 Investigational Treatments

Cytokine storm-like syndromes are thought to contribute significantly to the morbidity of COVID-19.[66] Some cancer therapies and immunomodulatory agents are being considered for COVID-19 treatment and are under investigation in ongoing clinical trials, such as ibrutinib (NCT04375397), imatinib (NCT04394416), thalidomide (NCT04273529), baricitinib (NCT04421027), and tocilizumab (NCT04331795).[67–69] Previous experience in treating hyper-inflammation associated myocardial injury with immune checkpoint inhibitors and chimeric antigen receptor T cell therapy positions cardio-oncologists as unique experts.[70] In addition, the use of anticancer therapies to treat COVID-19 can have cardiotoxic side effects such as hypertension, arrhythmia, and venous thromboembolism. Cardiac vigilance must be maintained when using these therapies in this novel infectious setting.

Cardio-Oncology Basic Science Research Considerations

The pandemic has dramatically shifted basic science research focuses toward COVID-19. Vaccine development is at the forefront of the current efforts. The contrast of an often mild viral response phase followed by a more potent host immune response phase has inspired novel ways of thinking about inflammation. Recent advances in cancer therapies have used the immune system to attack malignant cells specifically. Chimeric antigen receptor T cells are genetically modified autologous T cells.[71] Current iterations target CD-19, a B-lymphocyte antigen commonly expressed in diffuse large B cell lymphoma. Immune checkpoint inhibitors are monoclonal antibodies directed at PD-1 (programmed cell death protein 1), PD-L1 (programmed death ligand 1), and CTLA-4 (cytotoxic T-lymphocyte-associated protein 4) receptors.[72] Immune checkpoint inhibitors remove the brakes placed on T cell–mediated response and increase the immune system's ability to scavenge for and identify foreign cells. Yet each of these therapies can have the side effect of overactivation of the immune system, which shares similarities with the inflammatory response seen in some cases of COVID-19.[42] The treatment of immune checkpoint inhibitor-induced inflammation may also ameliorate COVID-19 induced inflammation. In addition, the pathways targeted to stop cancer angiogenesis, such as vascular endothelial growth factor, may also play a role in vascular permeability resulting in increased tissue inflammation in the lung.[73]

Cardio-Oncology Clinical Research Considerations

During the pandemic, all caution should be taken to minimize unnecessary visits, particularly where a COVID-19 conscientious approach is not in place. However, much of the work central to cardio-oncology will continue in the face of the need for continued anticancer care. When approaching these situations, risks and benefits must be routinely considered. If a patient or subject is without clear symptoms or recently tested negative, inclusion in an ongoing study

may be considered. Some clinical trial enrollment was put on hold at the beginning of the pandemic. Cardio-oncology as a field can advocate for clinical trial resumption in the pandemic era and the inclusion of cardiotoxicity vigilance.

With the impetus of the pandemic, cardio-oncology can be deliberate in embracing changes to cardiac monitoring during oncology care. Ongoing development of multicenter biomarker-based trials to mitigate risk without comprising patient care should be a priority. In addition, uniform care pathways should be validated in a research context. Big data will be essential in assessing the success of cardiotoxicity monitoring, modified care pathways in cardio-oncology care, and the impact of COVID-19 mitigation efforts. The pandemic should inspire innovation to develop new ways to overcome barriers to ongoing research and to develop new research to address patient risk.

SUBSEQUENT PANDEMIC PHASES (INCLUDING RECOVERY)

In the face of the ongoing COVID-19 pandemic, cardio-oncology can emerge with flexible, uniform care strategies. These approaches can be stratified into phases (Figure 2). As local outbreak levels ebb and flow, plans to shift from urgent-only care to the recovery phases and back again should be in place. Plans for subsequent waves of COVID-19 infections are essential. This postsurge recovery phase will consist of a new normal with routine mask use and the embracing of telehealth options. Careful accounting of deferred cardiac testing should be made to keep patients from slipping through new COVID-19-created cracks. A concerted outreach effort by administrative and clinical staff in educating patients, along with making cardiovascular appointments, will help close these gaps.

Given the high infection risk and morbidity of cardio-oncology patients infected with COVID-19, these patients, along with healthcare workers, should be a top priority and at the front of the line for a COVID-19 vaccine, once developed. Cardio-oncology patients are vulnerable and have a frequent need for healthcare utilization. Protecting this population early with a vaccine will mitigate risk throughout the healthcare system.

As we move into the postpandemic world, the ripple effects of the COVID-19 pandemic with its collateral damage will affect our patients for years to come. These costs cannot be underestimated. Medical consequences of deferred testing, imaging, screening, and procedures will be appreciated fully only in retrospect. Economic losses such as job losses, decreased incomes, and loss of health insurance can severely limit many patients' ability to afford medication, screening tests, and doctors' appointments. Concerted sociopolitical measures and policies at local, national, and

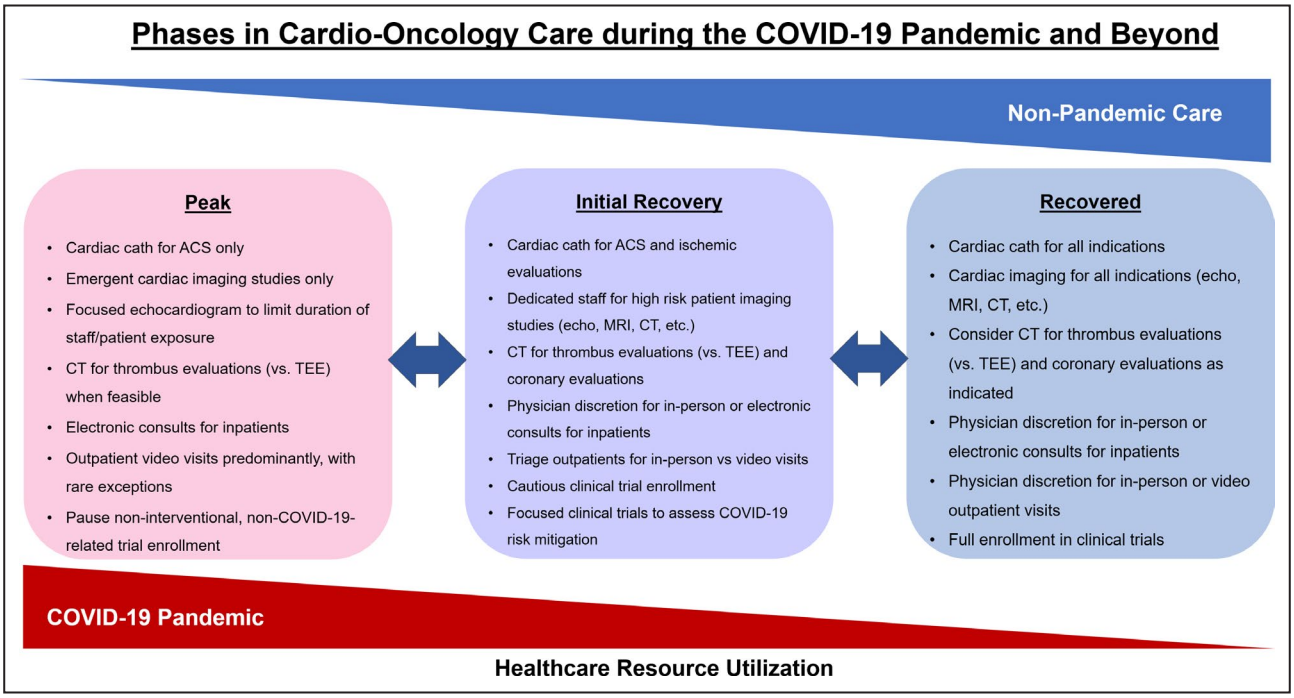

Figure 2. General phases (stages) in cardio-oncology care during the coronavirus disease 2019 (COVID-19) pandemic and recovery.
ACS indicates acute coronary syndrome; CT, computed tomography; echo, echocardiogram; MRI, magnetic resonance imaging; and TEE, transesophageal echocardiogram.

international levels may assist with such aftermath. Cardio-oncology practitioners should continue to advocate for patient's access to health care and affordable treatment options.

The cardio-oncology field will be transformed after the COVID-19 pandemic. Telehealth use will become routine, particularly for follow-up visits, routine cardiac monitoring, and patients who live far away from healthcare centers.[42] Clinical trials will address disease phenotypes and therapeutic responses in the face of the COVID-19 pandemic. Basic science will explore COVID-19's impact on cellular mechanisms and predisposition to infection.

CONCLUSIONS

Despite initial challenges, the era of COVID-19 is teaching us new paradigms of medicine that will change the face of how we practice. Now is the time to implement some of our learnings into making cardio-oncology endeavors more effective, easy, and far reaching. Vigilance and planning will help alleviate downstream consequences of delayed and deferred cardio-oncology care. As these new paradigms emerge as part of our daily practice, it will be important to evaluate the effectiveness of these new strategies.

ARTICLE INFORMATION

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REFERENCES

1. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395:1054–1062.
2. Holshue ML, DeBolt C, Lindquist S, Lofy KH, Wiesman J, Bruce H, Spitters C, Ericson K, Wilkerson S, Tural A, et al. First case of 2019 novel coronavirus in the United States. *N Engl J Med*. 2020;382:929–936.
3. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*. 2020;323:1061–1069.
4. Bonsu JM, Guha A, Charles L, Yildiz VO, Wei L, Baker B, Brammer JE, Awan F, Lustberg M, Reinbolt R, et al. Reporting of cardiovascular events in clinical trials supporting FDA approval of contemporary cancer therapies. *J Am Coll Cardiol*. 2020;75:620–628.
5. Xia Y, Jin R, Zhao J, Li W, Shen H. Risk of COVID-19 for patients with cancer. *Lancet Oncol*. 2020;21:e180.
6. Yu J, Ouyang W, Chua MLK, Xie C. SARS-CoV-2 transmission in patients with cancer at a tertiary care hospital in Wuhan, China. *JAMA Oncol*. 2020;6:1109–1110.
7. Zhang L, Zhu F, Xie L, Wang C, Wang J, Chen R, Jia P, Guan HQ, Peng L, Chen Y, et al. Clinical characteristics of COVID-19-infected cancer patients: a retrospective case study in three hospitals within Wuhan, China. *Ann Oncol*. 2020;31:894–901.
8. Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, Wang H, Wan J, Wang X, Lu Z. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). *JAMA Cardiol*. 2020;5:1–8.
9. Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, Gong W, Liu X, Liang J, Zhao Q, et al. Association of cardiac injury with mortality in hospitalized patients With COVID-19 in Wuhan, China. *JAMA Cardiol*. 2020;5:802–810.
10. Taplitz RA, Kennedy EB, Bow EJ, Crews J, Gleason C, Hawley DK, Langston AA, Nastoupil LJ, Rajotte M, Rolston KV, et al. Antimicrobial prophylaxis for adult patients with cancer-related immunosuppression: ASCO and IDSA clinical practice guideline update. *J Clin Oncol*. 2018;36:3043–3054.
11. Rolston KV. Infections in cancer patients with solid tumors: a review. *Infect Dis Ther*. 2017;6:69–83.
12. Kwong JC, Schwartz KL, Campitelli MA, Chung H, Crowcroft NS, Karnauchow T, Katz K, Ko DT, McGeer AJ, McNally D, et al. Acute myocardial infarction after laboratory-confirmed influenza infection. *N Engl J Med*. 2018;378:345–353.
13. Kytomaa S, Hegde S, Claggett B, Udell JA, Rosamond W, Temte J, Nichol K, Wright JD, Solomon SD, Vardeny O. Association of influenza-like illness activity with hospitalizations for heart failure: the Atherosclerosis Risk in Communities Study. *JAMA Cardiol*. 2019;4:363–369.
14. Zheng YY, Ma YT, Zhang JY, Xie X. COVID-19 and the cardiovascular system. *Nat Rev Cardiol*. 2020;17:259–260.
15. National Health Services, United Kingdom. Who's at higher risk from coronavirus. Date published 20 June 2020. Available at: https://www.nhs.uk/conditions/coronavirus-covid-19/people-at-higher-risk/whos-at-higher-risk-from-coronavirus/. Accessed June 28, 2020.
16. Centers for Disease Control and Prevention. Coronavirus disease 2019: people who are at higher risk for severe illness. Date published: 14 May 2020. Available at: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-at-higher-risk.html. Accessed June 28, 2020.
17. Ministry of Health, New Zealand. COVID-19: advice for higher risk people. Date published: 11 June 2020. Available at: https://www.health.govt.nz/our-work/diseases-and-conditions/covid-19-novel-coronavirus/covid-19-information-specific-audiences/covid-19-advice-higher-risk-people. Accessed June 28, 2020.
18. Government of Canada. People who are at high risk for severe illness from COVID-19. Date published: 19 June 2020. Available at: https://www.canada.ca/en/public-health/services/publications/diseases-conditions/people-high-risk-for-severe-illness-covid-19.html. Accessed June 28, 2020.
19. Liang W, Guan W, Chen R, Wang W, Li J, Xu K, Li C, Ai Q, Lu W, Liang H, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *Lancet Oncol*. 2020;21:335–337.
20. Deng G, Yin M, Chen X, Zeng F. Clinical determinants for fatality of 44,672 patients with COVID-19. *Crit Care*. 2020;24:179.
21. Desai A, Sachdeva S, Parekh T, Desai R. COVID-19 and cancer: lessons from a pooled meta-analysis. *JCO Glob Oncol*. 2020;6:557–559.

22. Wang B, Li R, Lu Z, Huang Y. Does comorbidity increase the risk of patients with COVID-19: evidence from meta-analysis. *Aging*. 2020;12:6049–6057.
23. Miyashita H, Mikami T, Chopra N, Yamada T, Chernyavsky S, Rizk D, Cruz C. Do patients with cancer have a poorer prognosis of COVID-19? An experience in New York City. *Ann Oncol*. 2020;31:1088–1089.
24. Mehta V, Goel S, Kabarriti R, Cole D, Goldfinger M, Acuna-Villaorduna A, Pradhan K, Thota R, Reissman S, Sparano JA, et al. Case fatality rate of cancer patients with COVID-19 in a New York hospital system. *Cancer Discov*. 2020;7:935–941.
25. Dai M, Liu D, Liu M, Zhou F, Li G, Chen Z, Zhang Z, You H, Wu M, Zheng Q, et al. Patients with cancer appear more vulnerable to SARS-COV-2: a multi-center study during the COVID-19 outbreak. *Cancer Discov*. 2020;10:783–791.
26. Robilotti EV, Babady NE, Mead PA, Rolling T, Perez-Johnston R, Bernardes M, Bogler Y, Caldararo M, Figueroa CJ, Glickman MS, et al. Determinants of COVID-19 disease severity in patients with cancer. *Nat Med*. 2020. Jun 24. [epub ahead of print]. DOI: 10.1038/s41591-020-0979-0.
27. Montopoli M, Zumerle S, Vettor R, Rugge M, Zorzi M, Catapano CV, Carbone GM, Cavalli A, Pagano F, Ragazzi E, et al. Androgen-deprivation therapies for prostate cancer and risk of infection by SARS-CoV-2: a population-based study (n=4532). *Ann Oncol*. 2020;31:1040–1045.
28. Zheng Z, Peng F, Xu B, Zhao J, Liu H, Peng J, Li Q, Jiang C, Zhou Y, Liu S, et al. Risk factors of critical & mortal COVID-19 cases: a systematic literature review and meta-analysis. *J Infect*. 2020;81:e16–e25.
29. Li B, Yang J, Zhao F, Zhi L, Wang X, Liu L, Bi Z, Zhao Y. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. *Clin Res Cardiol*. 2020;109:531–538.
30. Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, Ma K, Xu D, Yu H, Wang H, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. *BMJ*. 2020;368:m1091.
31. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. *JAMA*. 2020;323:1239. [epub ahead of print].
32. Li W, Moore MJ, Vasilieva N, Sui J, Wong SK, Berne MA, Somasundaran M, Sullivan JL, Luzuriaga K, Greenough TC, et al. Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus. *Nature*. 2003;426:450–454.
33. Vaduganathan M, Vardeny O, Michel T, McMurray JJV, Pfeffer MA, Solomon SD. Renin-angiotensin-aldosterone system inhibitors in patients with Covid-19. *N Engl J Med*. 2020;382:1653–1659.
34. Bavishi C, Maddox TM, Messerli FH. Coronavirus disease 2019 (COVID-19) infection and renin angiotensin system blockers. *JAMA Cardiol*. 2020;5:745. [epub ahead of print].
35. Zhang P, Zhu L, Cai J, Lei F, Qin J-J, Xie J, Liu Y-M, Zhao Y-C, Huang X, Lin L, et al. Association of inpatient use of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers with mortality among patients with hypertension hospitalized with COVID-19. *Circ Res*. 2020;126:1671–1681.
36. Mehta N, Kalra A, Nowacki AS, Anjewierden S, Han Z, Bhat P, Carmona-Rubio AE, Jacob M, Procop GW, Harrington S, et al. Association of use of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers with testing positive for coronavirus disease 2019 (COVID-19). *JAMA Cardiol*. 2020:e201855. [epub ahead of print]. DOI: 10.1001/jamacardio.2020.1855.
37. Reynolds HR, Adhikari S, Pulgarin C, Troxel AB, Iturrate E, Johnson SB, Hausvater A, Newman JD, Berger JS, Bangalore S, et al. Renin-angiotensin-aldosterone system inhibitors and risk of Covid-19. *N Engl J Med*. 2020;382:2441–2448.
38. Wise J. Covid-19: cancer mortality could rise at least 20% because of pandemic, study finds. *BMJ*. 2020;369:m1735.
39. Garcia S, Albaghdadi MS, Meraj PM, Schmidt C, Garberich R, Jaffer FA, Dixon S, Rade JJ, Tannenbaum M, Chambers J, et al. Reduction in ST-segment elevation cardiac catheterization laboratory activations in the United States during COVID-19 pandemic. *J Am Coll Cardiol*. 2020;75:2871–2872.
40. Solomon MD, McNulty EJ, Rana JS, Leong TK, Lee C, Sung S-H, Ambrosy AP, Sidney S, Go AS. The Covid-19 pandemic and the incidence of acute myocardial infarction. *N Engl J Med*. 2020. May 19 [epub ahead of print]. DOI: 10.1056/NEJMc2015630.
41. De Rosa S, Spaccarotella C, Basso C, Calabrò MP, Curcio A, Filardi PP, Mancone M, Mercuro G, Muscoli S, Nodari S, et al. Reduction of hospitalizations for myocardial infarction in Italy in the COVID-19 era. *Eur Heart J*. 2020;41:2083–2088.
42. Gupta AK, Jneid H, Addison D, Ardehali H, Boehme AK, Borgaonkar S, Boulestreau R, Clerkin K, Delarche N, DeVon HA, et al. Current perspectives on Coronavirus 2019 (COVID-19) and cardiovascular disease: a white paper by the JAHA editors. *J Am Heart Assoc*. 2020;9:e017013. DOI: 10.1161/JAHA.120.017013.
43. Akhmerov A, Marbán E. COVID-19 and the heart. *Circ Res*. 2020;126:1443–1455.
44. Ganatra S, Hammond SP, Nohria A. The novel coronavirus disease (COVID-19) threat for patients with cardiovascular disease and cancer. *JACC CardioOncol*. 2020;2:350–355.
45. American Society of Clinical Oncology. ASCO special report: a guide to cancer care delivery during the COVID-19 pandemic. Date published 19 May 2020. Available at: https://www.asco.org/sites/new-www.asco.org/files/content-files/2020-ASCO-Guide-Cancer-COVID19.pdf. Accessed June 28, 2020.
46. Ueda M, Martins R, Hendrie PC, McDonnell T, Crews JR, Wong TL, McCreery B, Jagels B, Crane A, Byrd DR, et al. Managing cancer care during the COVID-19 pandemic: agility and collaboration toward a common goal. *J Natl Compr Canc Netw*. 2020;18:1–4.
47. Parikh A, Kumar AA, Jahangir E. Cardio-oncology care in the time of COVID-19 and the role of telehealth. *JACC CardioOncol*. 2020;2:356–358.
48. Society of Cardiovascular Magnetic Resonance. SCMR's COVID-19 Preparedness Toolkit. Date published. 25 March 2020. Available at: https://scmr.org/page/COVID19. Accessed June 28, 2020.
49. European Society of Cardiology. Routine cardiotoxicity echo screening for chemotherapy patients during COVID-19. Date published: 15 April 2020. Available at: https://www.escardio.org/Councils/council-of-cardio-oncology/News/routine-cardiotoxicity-echo-screening-for-chemotherapy-patients-during-covid-19. Accessed June 28, 2020.
50. Choi AD, Abbara S, Branch KR, Feuchtner GM, Ghoshhajra B, Nieman K, Pontone G, Villines TC, Williams MC, Blankstein R. Society of Cardiovascular Computed Tomography guidance for use of cardiac computed tomography amidst the COVID-19 pandemic Endorsed by the American College of Cardiology. *J Cardiovasc Comput Tomogr*. 2020;14:101–104.
51. American Society of Echocardiography. ASE Statement on COVID-19. Date published 1 April 2020. Available at: https://www.asecho.org/ase-statement-covid-19. Accessed June 28, 2020.
52. Calvillo-Argüelles O, Abdel-Qadir H, Ky B, Liu JE, Lopez-Mattei JC, Amir E, Thavendiranathan P. Modified routine cardiac imaging surveillance of adult cancer patients and survivors during the COVID-19 pandemic. *JACC CardioOncol*. 2020;2:345–349.
53. Biersmith MA, Tong MS, Guha A, Simonetti OP, Addison D. Multimodality cardiac imaging in the era of emerging cancer therapies. *J Am Heart Assoc*. 2020;9:e013755. DOI: 10.1161/JAHA.119.013755.
54. Johri AM, Galen B, Kirkpatrick JN, Lanspa M, Mulvagh S, Thamman R. ASE statement on point-of-care ultrasound during the 2019 novel coronavirus pandemic. *J Am Soc Echocardiogr*. 2020;33:670–673.
55. Wiczer TE, Levine LB, Brumbaugh J, Coggins J, Zhao Q, Ruppert AS, Rogers K, McCoy A, Mousa L, Guha A, et al. Cumulative incidence, risk factors, and management of atrial fibrillation in patients receiving ibrutinib. *Blood Adv*. 2017;1:1739–1748.
56. Herrmann J. Adverse cardiac effects of cancer therapies: cardiotoxicity and arrhythmia. *Nat Rev Cardiol*. 2020;17:474–502.
57. Lopez-Jimenez F, Attia Z, Arruda-Olson AM, Carter R, Chareonthaitawee P, Jouni H, Kapa S, Lerman A, Luong C, Medina-Inojosa JR, et al. Artificial intelligence in cardiology: present and future. *Mayo Clin Proc*. 2020;95:1015–1039.
58. Hoeger CW, Hayek SS. Role of cardiovascular biomarkers in the risk stratification, monitoring, and management of patients with cancer. *Cardiol Clin*. 2019;37:505–523.
59. Demissei BG, Freedman G, Feigenberg SJ, Plastaras JP, Maity A, Smith AM, McDonald C, Sheline K, Simone CB II, Lin LL, et al. Early changes in cardiovascular biomarkers with contemporary thoracic radiation therapy for breast cancer, lung cancer, and lymphoma. *Int J Radiat Oncol Biol Phys*. 2019;103:851–860.
60. Demissei BG, Hubbard RA, Zhang L, Smith AM, Sheline K, McDonald C, Narayan V, Domchek SM, DeMichele A, Shah P, et al. Changes in cardiovascular biomarkers with breast cancer therapy and associations

with cardiac dysfunction. *J Am Heart Assoc*. 2020;9:e014708. DOI: 10.1161/JAHA.119.014708.
61. Crimm HA, Taylor JR, Fogarty BT, Villines TC. Prone patient positioning to exclude left atrial appendage thrombus using cardiac CT. *J Cardiovasc Comput Tomogr*. 2018;12:176–178.
62. Lazoura O, Ismail TF, Pavitt C, Lindsay A, Sriharan M, Rubens M, Padley S, Duncan A, Wong T, Nicol E. A low-dose, dual-phase cardiovascular CT protocol to assess left atrial appendage anatomy and exclude thrombus prior to left atrial intervention. *Int J Cardiovasc Imaging*. 2016;32:347–354.
63. Balanescu DV, Donisan T, Deswal A, Palaskas N, Song J, Lopez-Mattei J, Kim PY, Durand JB, Doundoua D, Marmagkiolis K, et al. Acute myocardial infarction in a high-risk cancer population: outcomes following conservative versus invasive management. *Int J Cardiol*. 2020;31:1–8.
64. Mahmud E, Dauerman HL, Welt FG, Messenger JC, Rao SV, Grines C, Mattu A, Kirtane AJ, Jauhar R, Meraj P, et al. Management of acute myocardial infarction during the COVID-19 pandemic. *J Am Coll Cardiol*. 2020. [epub ahead of print]. DOI: 10.1016/j.jacc.2020.04.039.
65. Guha A, Dey AK, Arora S, Cavender MA, Vavalle JP, Sabik JF III, Jimenez E, Jneid H, Addison D. Contemporary trends and outcomes of percutaneous and surgical aortic valve replacement in patients with cancer. *J Am Heart Assoc*. 2020;9:e014248. DOI: 10.1161/JAHA.119.014248.
66. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet*. 2020;395:1033–1034.
67. Coleman CM, Sisk JM, Mingo RM, Nelson EA, White JM, Frieman MB. Abelson kinase inhibitors are potent inhibitors of severe acute respiratory syndrome coronavirus and Middle East respiratory syndrome coronavirus fusion. *J Virol*. 2016;90:8924–8933.
68. Xu X, Han M, Li T, Sun W, Wang D, Fu B, Zhou Y, Zheng X, Yang Y, Li X, et al. Effective treatment of severe COVID-19 patients with tocilizumab. *Proc Natl Acad Sci USA*. 2020;117:10970–10975.
69. Treon SP, Castillo JJ, Skarbnik AP, Soumerai JD, Ghobrial IM, Guerrera ML, Meid K, Yang G. The BTK inhibitor ibrutinib may protect against pulmonary injury in COVID-19–infected patients. *Blood*. 2020;135:1912–1915.
70. Siddiqi HK, Neilan TG. COVID-19, immuno-oncology and cardiovascular disease: viewpoint from the intersection. *J Cardiovasc Transl Res*. 2020;12:347–348.
71. Neelapu SS, Locke FL, Bartlett NL, Lekakis LJ, Miklos DB, Jacobson CA, Braunschweig I, Oluwole OO, Siddiqi T, Lin Y, et al. Axicabtagene ciloleucel CAR T-cell therapy in refractory large B-cell lymphoma. *N Engl J Med*. 2017;377:2531–2544.
72. Schmid P, Adams S, Rugo HS, Schneeweiss A, Barrios CH, Iwata H, Diéras V, Hegg R, Im SA, Shaw Wright G, et al. Atezolizumab and nab-paclitaxel in advanced triple-negative breast cancer. *N Engl J Med*. 2018;379:2108–2121.
73. Ourradi K, Blythe T, Jarrett C, Barratt SL, Welsh GI, Millar AB. VEGF isoforms have differential effects on permeability of human pulmonary microvascular endothelial cells. *Respir Res*. 2017;18:116.