

VIEWPOINT

Modified Routine Cardiac Imaging Surveillance of Adult Cancer Patients and Survivors During the COVID-19 Pandemic



Oscar Calvillo-Argüelles, MD,^a Husam Abdel-Qadir, MD, PhD,^{a,b} Bonnie Ky, MD, MSCE,^{c,d} Jennifer E. Liu, MD,^e Juan C. Lopez-Mattei, MD,^f Eitan Amir, MD, PhD,^g Paaladinesh Thavendiranathan, MD, SM^a

The coronavirus disease-2019 (COVID-19) pandemic has overwhelmed health care systems internationally, prompting difficult decisions and ethical dilemmas over resource allocation (1). In-person health care encounters have been restricted to reduce exposures to patients and providers. These restrictions are particularly relevant to patients with cancer and/or cardiovascular disease (CVD) who have a greater risk of infection and worse

outcomes with COVID-19 (2). We must therefore reconsider which in-person encounters, including imaging tests, are essential; that is, where the risk of undetected CVD outweighs the risk of potential infection.

The goal of this viewpoint was to provide general guidance, based on available evidence, regarding the role of routine cardiac surveillance during this pandemic (1). These are not societal guidelines, and recommendations may change as the pandemic evolves.

OVERARCHING PRINCIPLES WITH CARDIAC SURVEILLANCE DURING COVID-19

Although cardiac imaging surveillance through cancer treatment is a pillar of cardio-oncology practice, it is important to recognize that most recommendations are based on expert consensus. Many routine tests have relatively low yield for detecting abnormal findings or modifying clinical care in asymptomatic patients (3). Thus, it may be possible to adopt temporary measures during this pandemic that strike a balance between the early detection and prevention of cancer therapy-related cardiac dysfunction (CTRCD) and risk of COVID-19 transmission. This requires individualizing imaging approaches to prioritize patients at the highest risk of CTRCD while deferring testing among lower risk individuals.

Importantly, we do not advocate completely omitting testing that would otherwise be clinically indicated. Rather, we attempt to prioritize cardiovascular imaging tests that should ideally be conducted without delay. For other patients, we should consider deferring tests to a later time point after the pandemic resolves, when routine practices are more feasible. Importantly, despite reduced surveillance,

From the ^aTed Rogers Program in Cardiotoxicity Prevention, Peter Munk Cardiac Center, Toronto General Hospital, University Health Network, University of Toronto, Toronto, Ontario, Canada; ^bDepartment of Medicine, Women's College Hospital, Toronto, Ontario, Canada; ^cPenn Cardiovascular Institute, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, USA; ^dCenter for Epidemiology and Biostatistics, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, USA; ^eMemorial Sloan-Kettering Cancer Center, Department of Medicine/Cardiology Service, New York, New York, USA; ^fThe University of Texas MD Anderson Cancer Center, Department of Cardiology, Houston, Texas, USA; and the ^gPrincess Margaret Cancer Center, Division of Medical Oncology, University Health Network, University of Toronto, Toronto, Ontario, Canada. Dr. Calvillo-Argüelles is supported by the Hold'em for Life Oncology Clinician Scientist Award at the University of Toronto's Faculty of Medicine. Dr. Abdel-Qadir has served as a consultant for Amgen; and is a member of endpoint adjudication committee for the THEMIS trial funded by AstraZeneca. Dr. Ky is supported by the National Institutes of Health (R21HL141802, R34HL146927, and R01HL118018) and an American Heart Association Transformational Project Award (TPA34910059). Dr. Liu is a consultant for Bay Labs; and an advisory board member for Pfizer. Dr. Amir has provided expert testimony Genentech/Roche; and consulting for Sanofi and ApobioRx. Dr. Thavendiranathan (147814) is supported by the Canadian Institutes of Health Research New Investigator Award. Dr. Lopez-Mattei has reported that he has no relationships relevant to the contents of this paper to disclose.

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careful monitoring of symptoms, cardiovascular risk factor modification, and disease management should continue in all patients.

This Viewpoint focuses on surveillance for patients receiving anthracyclines and trastuzumab. There are no standard guidelines for routine imaging with other cardiotoxic therapies (e.g., vascular endothelial growth factor inhibitor, immune checkpoint inhibitors); these imaging practices should remain unchanged.

PRETREATMENT RISK ASSESSMENT

The American Society of Clinical Oncology guidelines recommend baseline cardiac imaging for individuals receiving potentially cardiotoxic therapies such as anthracyclines and/or trastuzumab (4). An implicit objective to these guidelines is the avoidance of longer-term cardiovascular risk rather than short-term cardiovascular risk. These guidelines define increased risk of CTRCD based on the planned treatment regimen and individual cardiovascular risk factors/comorbidities. Although baseline imaging can help identify patients at risk of CTRCD, it may be prudent to limit baseline testing during the pandemic to patients who are more likely to have abnormal test results or are at higher risk for CTRCD in the near or medium term, particularly if it may result in the initiation of cardioprotective medications or affect chemotherapy delivery (Table 1).

Thus, with anthracycline initiation, regardless of dose, it may be reasonable to prioritize baseline cardiac imaging for patients with: 1) established or suspected CVD based on medical history (e.g., myocardial infarction, cardiomyopathy, arrhythmia, moderate or greater valvular disease); 2) signs or symptoms of cardiac dysfunction; and 3) 2 or more risk factors for CTRCD, including age ≥ 60 years, hypertension, diabetes, dyslipidemia, smoking, or obesity. Prior research indicates that overt CTRCD is unlikely in the near term in young patients without risk factors (5). For other asymptomatic patients, we recommend optimizing risk factors before chemotherapy and deferring imaging until after COVID-19-associated restrictions end.

When considering anthracycline dose as a risk factor for CTRCD, although we recognize that there is no safe dose, the risk rises substantially beyond 250 mg/m² of doxorubicin-equivalent dose with even greater risk at >400 mg/m² (4). However, for adult patients whose only risk factor is a high cumulative anthracycline dose, it may be reasonable to defer imaging until this high-risk dose is reached or at the completion of anthracycline treatment. Because

cardiac dysfunction rarely becomes clinically manifest at lower doses or before 3 to 6 months of treatment completion, this approach may allow identification and timely management of patients with CTRCD without baseline measurements (6,7).

Baseline imaging is also commonly performed before trastuzumab initiation. Despite the high rates of trastuzumab-associated CTRCD, these patients often have a favorable clinical course (8). Trastuzumab-associated CTRCD is less common without previous anthracycline exposure (9). Baseline imaging before trastuzumab can be considered for women with: 1) pre-existing CVD; 2) signs or symptoms of cardiac dysfunction; 3) ≥ 2 risk factors for CTRCD, including age ≥ 60 years, hypertension, diabetes, dyslipidemia, smoking, and obesity; and 4) exposure to anthracyclines as part of a previous or current treatment regimen. However, if imaging in the past 6 months shows normal cardiac function (left ventricular ejection fraction [LVEF] $\geq 55\%$) and the absence of significant valvular disease, additional baseline testing can likely be deferred.

SURVEILLANCE DURING CANCER TREATMENT

The optimal surveillance regimen during anthracycline chemotherapy remains incompletely defined. Although the American Society of Clinical Oncology guidelines recommend that surveillance frequency be based on cardiovascular and treatment-related risk factors and clinical judgment, the European Society for Medical Oncology guidelines advocate for additional imaging after every 100 mg/m² of doxorubicin-equivalent anthracycline exposure beyond 250 mg/m² (4,10). A recent multicenter study of 865 patients receiving high-risk cancer treatment regimens (84.5% anthracyclines) with rigorous monitoring showed a high cumulative incidence of CTRCD (37.5%) (11). However, the majority were mild (31.6%) CTRCD; moderate (LVEF 40% to 49%) and severe (LVEF <40% or symptomatic heart failure [HF]) CTRCD occurred in only 2.8% and 3.1% of patients, respectively. Mortality was associated with the development of severe rather than mild or moderate CTRCD. It may thus be reasonable to temporarily delay early, routine imaging during anthracycline therapy unless there is a potential immediate impact on clinical decisions. Potential scenarios include signs or symptoms of HF; anthracycline dosages ≥ 400 mg/m² with need for additional anthracycline therapy; and patients with baseline CVD or high burden of cardiovascular risk factors who received anthracycline dosages ≥ 250 mg/m² with continued need for

TABLE 1 Suggested Temporary Modifications to Routine Imaging Recommendations in Patients Receiving Cancer Therapy During the COVID-19 Pandemic

Routine Practice Recommendations	Potential Modifications During COVID-19
<p>Pretreatment: anthracyclines</p> <p>Baseline imaging before treatment with potentially cardiotoxic therapies (4,10)</p>	<p>Baseline imaging if:</p> <ol style="list-style-type: none"> 1. History of significant CVD (e.g., MI, cardiomyopathy, arrhythmia, moderate or greater valvular disease) 2. Signs and symptoms of cardiac dysfunction 3. 2 or more risk CV factors for CTRCD* 4. High anthracycline dose (e.g., doxorubicin-equivalent ≥ 250 mg/m²) †
<p>Pretreatment: trastuzumab</p> <p>Baseline imaging before treatment with potentially cardiotoxic therapies (4,10)</p>	<p>Baseline imaging if:</p> <ol style="list-style-type: none"> 1. History of CVD (e.g., MI, cardiomyopathy, arrhythmia, moderate or greater valvular disease) 2. Signs and symptoms of cardiac dysfunction 3. Two or more risk CV factors for CTRCD* 4. Exposure to anthracycline as part of current or previous treatment ‡
<p>During treatment: anthracyclines</p> <p>ASCO: Routine imaging surveillance may be considered in asymptomatic patients considered at increased risk of cardiac dysfunction with frequency determined by health care provider based on clinical judgment (4)</p> <p>ESMO: after each additional 100 mg/m² beyond 250 mg/m², as discussed elsewhere (10)</p> <p>Repeat imaging early upon diagnosis of CTRCD to guide re-initiation of cancer therapy or titrate cardiac medications</p>	<ol style="list-style-type: none"> 1. No routine screening in asymptomatic individuals during pandemic but return to institution-specific protocols post-pandemic 2. Consider in those with HF signs/symptoms, high doses of doxorubicin-equivalent (e.g. ≥ 400 mg/m²), or those reaching 250 mg/m² with prior CVD or multiple CV risk factors* with a continued need for anthracycline treatment 3. Early repeated imaging upon diagnosis of CTRCD should be performed as per institutional practices
<p>During treatment: trastuzumab</p> <p>Variability in practice, FDA package insert recommends baseline imaging and every 3 months during duration of trastuzumab therapy</p> <p>Repeat imaging early upon diagnosis of CTRCD to guide re-initiation of cancer therapy or titration of cardiac medications (10)</p>	<ol style="list-style-type: none"> 1. No prior anthracycline or CVD risk factors,* consider imaging at 6 and 12 months into trastuzumab therapy only § 2. Prior anthracycline exposure, CV risk factors,* with prior normal LVEF, consider follow-up imaging at 3, 6, and 12 months into trastuzumab therapy 3. Continue every 3 months imaging if known CVD, HF signs or symptoms, or low normal or reduced LVEF on previous testing 4. Metastatic setting: First year: repeat imaging every 6 months. Beyond first year: defer any further imaging if asymptomatic and results of previous studies normal 5. In patients who develop CTRCD, repeat imaging to guide ongoing cancer therapy or titration of cardiac medications
<p>Post-treatment: adult survivors of childhood and adolescent cancers</p> <ol style="list-style-type: none"> 1. Imaging in childhood cancer survivors: no later than 2 yrs after completion of treatment, at 5 yrs after diagnosis, and every 5 yrs (14) 2. Imaging in adolescent and young adult cancer survivors: every 1-2 yrs in high-risk patients (15) 	<p>Avoid screening studies in all survivors until end of pandemic unless there are HF symptoms or a change in cardiovascular status</p>
<p>Post-treatment: adult cancer survivors</p> <ol style="list-style-type: none"> 1. Imaging in high risk asymptomatic patients at 6-12 months post-treatment (4) and 2 yrs after treatment/periodically (10) 2. Imaging in symptomatic survivors (4) 	<p>Temporarily defer routine follow-up imaging in all patients unless there are HF symptoms or a change in cardiovascular status</p>

*Age ≥ 60 years, hypertension, diabetes, dyslipidemia, smoking, obesity. †If the only risk factor is high anthracycline dose (e.g., doxorubicin-equivalent ≥ 250 mg/m²), it is reasonable to consider imaging only once the high anthracycline dose threshold is met or after completion of cancer therapy. ‡If imaging in the previous 6 months shows normal cardiac function (left ventricular ejection fraction [LVEF] $\geq 55\%$) and the absence of significant valvular disease, additional baseline testing can be deferred. §Screening at 6 months should likely identify most patients with cancer therapy-related cardiac dysfunction (CTRCD) (7).

ASCO = American Society of Clinical Oncology; COVID-19 = coronavirus disease-2019; CV = cardiovascular; CVD = cardiovascular disease; ESMO = European Society of Medical Oncology; FDA = U.S. Food and Drug Administration; HF = heart failure; MI = myocardial infarction.

anthracyclines. This may allow for less frequent testing during the pandemic while still imaging patients before the occurrence of CTRCD, allowing timely cardioprotective therapy (6,7).

The most common scenario mandating repeated cardiac surveillance during treatment is for patients receiving trastuzumab therapy. European Society for Medical Oncology guidelines and the U.S. Food and Administration package insert recommend surveillance imaging every 3 months during trastuzumab treatment (10). However, most routine cardiac

surveillance tests during trastuzumab treatment may not result in changes in clinical care (3). Hence, during the COVID-19 pandemic, in women without cardiovascular risk factors treated with non-anthracycline regimens, it may be appropriate to only perform imaging at 6 and 12 months. In patients with risk factors for CTRCD such as previous anthracycline exposure, age ≥ 60 years, hypertension, diabetes, dyslipidemia, smoking, and obesity with a prior normal LVEF, it may be reasonable to consider imaging at 3, 6, and 12 months into trastuzumab

Precautions to Consider	Rationale
Dedicated rooms (e.g., in COVID-19-free zones) for immunosuppressed patients	To avoid using potentially contaminated equipment in immunocompromised patients
Use of "off-site" scanning locations	For cancer centers that do not have their own echocardiography laboratories, consider using an off-site location where the concentration of COVID-19 exposure may be less or moving a dedicated ultrasound machine to the cancer center
"Low exposure risk" sonographers to scan patients	Having sonographers un-exposed to COVID-19-positive patients and low risk of being asymptomatic carriers (e.g., no travel in past 14 days) may reduce potential risk of transmission
Using point-of-care ultrasound whenever possible with capacity to store images	Equipment easier to clean and assessment of LVEF assessment, masses, and pericardial effusions are the priority and can be assessed with these devices
Avoid ECG leads	ECG cables are challenging to clean between patients and may become a source of transmission
Use ultrasound transducer sleeves and single-use ultrasound gel packets	Use of disposable protective probe sleeves and gel can minimize transmission
Perform focused studies	Because the primary question in these patients is left ventricular function, short protocols to assess left ventricular function with focus on two-dimensional imaging may be sufficient
Use PPE as per hospital guidelines and specific barriers developed at the institution to protect sonographers and patients	Consider all patients to be asymptomatic carriers and take appropriate precautions. Consider requesting patients to wear masks/gloves if PPE available
Perform analysis after patient encounter	All post-processing should be done outside the clinical room setting to minimize exposure to patient
Reconsider low-yield tests	Sonographers and imaging laboratories should actively assess requests for screening tests in cancer survivors and consider in consultation with oncologist/cardio-oncologist if these tests could be safely postponed
Use of imaging-enhancing agents in nondiagnostic echo studies only	Limit use of an imaging enhancement agent to nondiagnostic echocardiogram studies to minimize examination length
Consider alternative imaging modalities (e.g., MUGA)	Alternate imaging modalities (e.g., MUGA scans) which can be performed rapidly while minimizing patient/ technologist exposure (https://zenodo.org/record/3738020#.XoXsHihKiUk)

ECG = electrocardiography; MUGAs = multigated acquisition scans; PPE = personal protective equipment; other abbreviations as in [Table 1](#).

therapy similar to clinical trial protocols (12). However, patients with a borderline LVEF (e.g., LVEF 50% to 55%), reduced LVEF on a previous study, pre-existing CVD, or any signs or symptoms of HF should continue to have imaging as per current clinical practice. Although exact risk with additional cardiotoxic exposures such as radiation and pertuzumab therapy are not well defined, a similar imaging protocol could be considered in these patients. If clinical concerns regarding the development of HF are raised during telemedicine visits or at the time of treatment, patients should undergo timely imaging (3). We reiterate the importance of cardiovascular risk factor modification, disease management, and monitoring of symptoms in these patients.

Patients with metastatic human epidermal growth factor receptor-2-positive breast cancer receiving prolonged human epidermal growth factor receptor-2-targeted treatment are at increased risk for CTRCD (13). The median time to CTRCD in this population is ~8 to 11 months. It is reasonable to conduct testing less frequently in this group during the COVID-19 pandemic. During the first year of therapy, it may be reasonable to repeat imaging every 6 months in asymptomatic patients. Beyond the first year, subsequent testing could potentially be deferred until after COVID-19 restrictions are removed for asymptomatic patients if results of all prior studies have been normal.

In patients who develop CTRCD and require cardiac treatments and/or withholding of cancer therapy, repeat imaging should continue as per institutional standards of care (10).

ROUTINE IMAGING OF CANCER SURVIVORS AFTER TREATMENT

Current guidelines recommend long-term surveillance of adult survivors of pediatric, adolescent, and young adult cancers at higher risk based on patient characteristics and treatment exposures (14,15). Because this is a longer-term concern, it may be reasonable to defer routine screening in asymptomatic survivors during this pandemic. Currently, there are no recommendations for routine surveillance in older adult cancer survivors; this should remain the standard unless patients develop HF symptoms.

CONSIDERATIONS FOR SAFE IMAGING DURING COVID-19

Many patients will still require timely cardiac imaging. These studies should be performed with precautions to minimize the exposures ([Table 2](#)), and the American Society of Echocardiography has developed guidance on how to practice echocardiography safely during this pandemic (16). Of note, there are

also alternative imaging modalities that can be considered.

CONCLUSIONS

Several modifications to routine cardiac imaging practices in cancer patients can be considered during the COVID-19 pandemic. Because there are no data specific to these circumstances, our suggestions are not intended to change long-term practice. Rather, these are temporary measures in which routine testing in asymptomatic patients may be deferred to minimize COVID-19 transmission. The suggestions are informed by existing literature in conjunction with our opinion, which is borne from clinical experience. We recognize that some CTRCD events may be undetected. However, this likely poses a small absolute risk in the short term. Any modifications to local practice patterns should not be enacted

unilaterally. They need to be discussed collaboratively among cardiologists and oncologists and carefully with patients, who also need to be educated and informed, with individualization of practices to institutional and patient-specific needs. We believe that such approaches to reduce cardiac imaging during the COVID-19 pandemic will allow the cardio-oncology community to help in “flattening the curve.”

ADDRESS FOR CORRESPONDENCE: Dr. Paaladinesh Thavendiranathan, Ted Rogers Program in Cardiotoxicity Prevention, Peter Munk Cardiac Center, Toronto General Hospital, University of Toronto, 585 University Avenue, Toronto, Ontario M5G2 2N2, Canada. E-mail: dinesh.thavendiranathan@uhn.ca. Twitter: [@oscaar84](https://twitter.com/oscaar84), [@husam247](https://twitter.com/husam247), [@pennmedicine](https://twitter.com/pennmedicine), [@Liu_MSKCardOnc](https://twitter.com/Liu_MSKCardOnc), [@onco_cardiology](https://twitter.com/onco_cardiology), [@dineshpmccl](https://twitter.com/dineshpmccl).

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