JACC: CARDIOVASCULAR IMAGING VOL. 11, NO. 8, 2018

Cardiovascular Magnetic Resonance in the Oncology Patient

Jennifer H. Jordan, PhD, MS, Ryan M. Todd, BS, Sujethra Vasu, MBBS, W. Gregory Hundley, MD

ABSTRACT

Patients with or receiving potentially cardiotoxic treatment for cancer are susceptible to developing decrements in left ventricular mass, diastolic function, or systolic function. They may also experience valvular heart disease, pericardial disease, or intracardiac masses. Cardiovascular magnetic resonance may be used to assess cardiac anatomy, structure, and function and to characterize myocardial tissue. This combination of features facilitates the diagnosis and management of disease processes in patients with or those who have survived cancer. This report outlines and describes prior research involving cardiovascular magnetic resonance for assessing cardiovascular disease in patients with or previously having received treatment for cancer. (J Am Coll Cardiol Img 2018;11:1150–72) © 2018 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

The emerging field of cardio-oncology involves assessment of cardiovascular disease specific to patients with or surviving cancer (1). Cancer survivors experience a 5-fold increase in the risk for developing heart failure, myocardial infarction, pericardial disease, or valvular abnormalities compared with their siblings without cancer (2). Each disease process may be noninvasively assessed with cardiovascular magnetic resonance (CMR) to establish a diagnosis or to guide therapy to address cardiovascular disease (**Central Illustration**) (3–5). In this report, we review the use of CMR for assessing the heart and surrounding structures in patients with or surviving cancer suspected of having cardiac abnormalities.

THE ROLE OF CMR IN PATIENTS WITH MALIGNANCIES

Several cardiac abnormalities may result from cancer or its treatment that promote a CMR evaluation (**Figure 1**). Preserving left ventricular (LV) function is often critical to enable delivery of one of several cancer therapeutic options designed to improve overall survival in patients with cancer. Thus, measurement of ventricular volumes, left ventricular ejection fraction (LVEF), and mass is a frequent consideration for patients receiving cancer treatment. Even though transthoracic echocardiography (TTE) and radionuclide scintigraphy are often used to measure LVEF in patients receiving potentially cardiotoxic chemotherapy (**Central Illustration**), CMR is useful when one needs to characterize the LV myocardium to determine the etiology of a reduced LVEF. Myocardial inflammatory or infiltrative processes (e.g., myocarditis, amyloid, or iron deposition) serve as examples for which serial CMR LVEF and tissue characterization measures may be beneficial (6–9). In addition, CMR may differentiate the etiology of a newly identified abnormal myocardial mass, evaluate a pericardial disease process, or determine the cause of a valve leaflet abnormality during the same examination when LVEF is measured.

PERFORMANCE OF CMR

Descriptions of CMR imaging techniques, acquisition parameters, and analysis methods are provided in one of several publications authored by the Society of Cardiovascular Magnetic Resonance, the American College of Cardiology, and the American Heart Association (7,8,10). As of 2018, suggested revisions to imaging protocols, analysis methods, and reporting structures are currently under development with the Society for Cardiovascular Magnetic Resonance, with expected release in late 2018 or

From the Department of Internal Medicine, Section on Cardiovascular Medicine at the Wake Forest School of Medicine, Winston-Salem, North Carolina. This research was supported in part by grants from the National Institute of Health (R01CA199167, R01CA167821, and R01HL118740) and a THRIVE Initiative research grant from the ILSI Health and Environmental Sciences Institute. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received January 30, 2018; revised manuscript received June 5, 2018, accepted June 14, 2018.

ISSN 1936-878X https://doi.org/10.1016/j.jcmg.2018.06.004

early 2019. **Table 1** categorizes existing magnetic resonance methods into those that provide anatomic, functional, and tissue characterization information that is useful for diagnosing the conditions described within this review. Throughout the paper, tables are provided that highlight key CMR imaging methods and features.

At present, several CMR imaging techniques incorporate the administration of gadolinium-based contrast agents (GBCAs). It should be noted that the administration of GBCAs can be associated with 3 untoward conditions: 1) allergic reactions to the agents themselves (dependent on GBCA type) with an incidence of 1:10,000 to 1:40,000 in the general population; 2) a serious but rare risk for nephrogenic systemic fibrosis in those with renal insufficiency; and 3) recent findings related to the unknown clinical significance of the potential accumulation of gadolinium in the brain stem after repetitive administration of these agents (11–13). These risks should be considered when evaluating any patient undergoing a CMR examination, but particularly in patients with cancer who, like other populations, may receive repetitive GBCAs to assess the extent of their malignancies. Gadolinium-enhanced contrast studies may provide clarity for questions related to tissue characterization.

LV DYSFUNCTION

To date, LVEF is the most widely used measure for identifying LV dysfunction resulting from the administration of cancer therapeutics (14,15). Early cardio-oncology studies identified that declines in LVEF after anthracycline administration are associated with development of congestive heart failure (16). Noninvasively, LVEF may be measured using radionuclide multiple-gated acquisition, 2-dimensional (2D) and 3-dimensional (3D) TTE, cardiac computed tomography, and CMR (5,17–21).

Reductions in LVEF after anthracycline treatment were first observed with radionuclide multiple-gated acquisition scans in the 1970s (16,22). Because radionuclide multiple-gated acquisition and cardiac computed tomography incorporate ionizing radiation, a limitation in patients who may be exposed to ionizing radiation exposure for treatment of their cancer, the use of TTE and CMR is increasingly preferred for performing serial measurements of LVEF during receipt of potentially cardiotoxic chemotherapy (23).

CMR measures of LVEF are most frequently quantified from a contiguous short-axis series of slices spanning the cardiac apex to its base using a steady-state free precession cine white-blood imaging technique (**Table 2**). The LV endocardial border contours from the end-diastolic and end-systolic frames in the cine sequence are used to provide LV cavity areas for each slice. By multiplying the area from the corresponding end-diastolic or end-systolic frame by the slice thickness, a volume for each slice of the cine sequence is obtained. By summing the volumes of all the slices and accounting for the interslice gaps, one can derive left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volume (LVESV) using the modified Simpson rule (10). The LVEF is then calculated by subtracting LVESV from LVEDV and dividing this value (LV stroke volume) by LVEDV (10).

Serial CMR imaging studies of women treated for breast cancer after receipt of anthracycline-based chemotherapy have demonstrated declines in LVEF both during and 12 to 24 months after initiating therapy (**Table 3**). Importantly, some studies have indicated early declines in LVEF 1 month into therapy, which translates into receipt of only 1 or 2 doses of an anthracycline agent. The prognostic implications of these acute changes are not yet known.

Several primarily echocardiography based algorithms have been proposed for monitoring cardiotoxicity (defined as LVEF decline >10% to <53%) in the setting of trastuzumab and other targeted therapies (14,24,25). Recent consensus statements recommend baseline evaluation of LVEF with 2D or 3D echocardiography. If the LVEF is <53% by echocardiography or if poor image quality prohibits measurement of LVEF, CMR is recommended (14). Similar algorithms are proposed for surveillance of patients with cancer and survivors (14).

CMR is of particular advantage in this population because of its high spatial and temporal resolution, reproducibility, and accuracy for LVEF quantification to detect subclinical declines in LVEF, which may occur as early as 1 month after the receipt of cardiotoxic therapies (26,27). In the St. Jude Lifetime Cohort of adult survivors of pediatric cancers, Armstrong et al. (28) performed a head-to-head comparison of 2D and 3D echocardiographic measures with CMR measures of LVEF. The results of this study indicated that LVEF values derived from 2D echocardiography overestimated the mean LVEF by

ABBREVIATIONS AND ACRONYMS

2D = 2-dimensional

3D = 3-dimensional

CMR = cardiovascular magnetic resonance

ECV = extracellular volume

GBCA = gadolinium-based contrast agent

GLS = global longitudinal strain

HER2 = human epidermal growth factor receptor 2

LGE = late gadolinium enhancement

LV = left ventricular

LVEDV = left ventricular end-diastolic volume

LVEF = left ventricular ejection fraction

LVESV = left ventricular end-systolic volume

RV = right ventricular

RVEF = right ventricular ejection fraction

TLVDS = transient left ventricular dysfunction syndrome

TTE = transthoracic echocardiography