

EDITORIAL

Multimodality Imaging for Cardiomyopathies in the Era of Precision Medicine

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A clinical approach to new cardiomyopathy entails defining patient phenotype and disease pathophysiology. After echocardiography, invasive assessments to define hemodynamics and coronary anatomy are usually pursued. In selected non-ischemic cases, endomyocardial biopsies are performed in search for an etiology. Fortunately, advances in cardiac imaging allow for a multifaceted cardiac evaluation in a single study, reducing cost, lead time to diagnosis, and procedural adverse events while still providing supreme accuracy. As the stream of science and clinical practice worldwide emphasizes personalized and high-value care, noninvasive imaging has emerged as a new standard to prevent, diagnose, and guide the treatment of cardiac disease, reserving invasive procedures to cases where an intervention is required. Given their versatility and precision compared to nuclear imaging and echocardiography, we elected to focus on computed tomography (CT) and cardiac magnetic resonance (CMR) in this monograph. Given the many etiologies and phenotypes of heart disease, the most useful diagnostic modalities for cardiomyopathies are those which provide a precise and multidimensional evaluation of the heart.

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Coronary assessment. Distinguishing ischemic from nonischemic cardiomyopathies is often pivotal in heart disease management. Modern coronary computed tomography angiography (CCTA) has excellent sensitivity (about 95%) and modest specificity (about 83%) for the identification of significant coronary lesions [1]. Ultra-high-resolution CT is now commercially available and can generate thinner slices allowing for plaque characterization to infer plaque stability, risk of future events, and even interventional procedural planning [2]. CT myocardial perfusion imaging (CT-MPI) and CT fractional flow reserve (CT-FFR) are commercially available to assess the functional limitations of coronary lesions [3]. A recent meta-analysis indicates that CT-FFR performs similarly to invasive fractional flow reserve (FFR) when considering the significance of coronary stenotic lesions [4]. CCTA is particularly useful in congenital defects such as anomalous coronaries or aortic coarctation and when coronary physiology is altered, such as post-heart transplantation or during mechanical circulatory support.

Compared to CT, CMR spatial resolution is usually 2–5 mm, no match to CCTA with a resolution of 0.25–0.5 mm. This explains the limited utility of CMR coronary angiography to ruling out anomalous coronary course. However, CMR shines in temporal resolution with 25–30 frames per R-R interval, compared to 10–15 frames per R-R for CCTA. CMR versatility is augmented by combining

coronary perfusion and functional assessment with Regadenoson, dobutamine, or exercise stress testing. A stress CMR study provides ECG stress data, functional capacity data, rest/stress perfusion, and inducible functional anomalies such as heart failure with preserved ejection fraction [5]. While performing in par with perfusion positron emission tomography (PET) in assessing ischemia, the combination of spatial and temporal resolution combination with CMR far supersedes that of CCTA, echocardiography, and nuclear imaging [6]. CMR can quantitatively measure the amount of blood flow per gram of tissue, which is useful for assessing microvascular dysfunction that challenges CCTA and balanced ischemia that challenge nuclear imaging [7]. Oxygen-sensitive imaging and phosphorus spectroscopy CMR remain in the research realm, with unclear feasibility for translation into bedside practice.

Tissue characterization. CMR dominates the realm of tissue characterization. Its advent has changed the disease course of cardiac hemosiderosis, amyloidosis, and cardiac sarcoidosis. Routine CMR cardiomyopathy protocols include injury assessment via late gadolinium enhancement and T1 relaxation mapping, edema assessment via T2 weighted imaging or T2 relaxation mapping, and infiltration assessment by calculating extracellular volume. These quantitative sequences allow precision in diagnosis, follow up, and translational research. CMR has several advantages over endomyocardial biopsy. CMR is safer, more cost-effective, more accessible, and is not affected by sampling error in the case of regional myocardial disease. Tissue characterization by CMR can be performed even without gadolinium-based contrast. It is not limited by acoustic windows of echocardiography, vascular access limitations of endomyocardial biopsy, or dietary restriction requirements of fluorodeoxyglucose (FDG)-PET. Tissue characterization via CCTA is also possible, with current applications centered primarily on identifying myocardial fibrosis and edema [8–10]. However, lower contrast resolution limits more thorough assessment of the myocardium. Other methods are under investigation, such as photon-counting detector CT which may lead to images with higher specificity, reduced radiation, and fewer artifacts [11].

Most clinical studies comparing invasive versus noninvasive testing of patients with cardiomyopathies compare one aspect, such as detecting severe CAD or active sarcoidosis. However, the practical value of a test lies in the collective information provided by the single study. For example, stress CMR in a 65-year-old man can provide cardiac anatomy, ventricular function, ECG stress data, rest and stress perfusion, active injury presence, the injury's chronicity, predictors of viability, and cardiac output. Similarly, a CT can assess cardiac structure, function, stroke volume, coronary anatomy, detailed plaque analysis, vascular pathology, valve function, thrombus presence, and can rule out vascular anomalies. Furthermore, CMR and CT provide a wealth of data on noncardiac structures such as core muscles, lungs, major vessels, and thrombi that can be utilized along the clinical care course, especially in severe cases when heart transplantation or mechanical circulatory support is required or specialized interventions such as immunosuppression is needed. Lastly, the multidimensionality of CMR and CT results in excellent prognostic power for arrhythmia, heart failure events, coronary events, and all-cause mortality [12].

The OUTSMART-HF trial is one of the few published randomized trials investigating the role of CMR in routine cardiac care for patients with nonischemic cardiomyopathies. In this trial, there was no statistically significant difference in the diagnosis of specific heart failure causes or in 12-month survival when comparing a population of patients that received routine CMR versus selective CMR. However, it is important to note that almost 25% of patients in the selective group had CMR performed [13]. When comparing CMR and CCTA in patients with chest pain and previously revascularized disease, CMR was more cost-effective and had lower rates of major adverse cardiac events. The EXACT-COST trial randomized patients to exercise CMR versus treadmill exercise single-photon emission computed tomography (SPECT). Over a 12 month follow-up period there was no difference in outcomes, however, the CMR group had 38% less medical cost and 62% less work hours lost [14]. Similarly, in patients with a low pretest probability for coronary disease, CCTA is more cost-effective [15].

Multimodality cardiac imaging allows for rapid, accurate, reproducible assessments of cardiac anatomy, physiology, and tissue characterization while avoiding the risks associated with traditional invasive techniques. Between CMR with or without gadolinium and CCTA the vast majority of patients with cardiomyopathies would be able to receive an anatomic noninvasive test early to begin their evaluation. Performing CMR or CT early on every

patient as opposed to selectively may not alter the final diagnosis, but it does set the trajectory of their evaluation on the appropriate path (ischemic heart disease, infiltrative cardiomyopathy, genetic disease, myocarditis etc.) resulting in personalized care [13]. A heart team collaboration at the research and clinical levels will enhance accuracy, accessibility, and most importantly, develop a pragmatic implementation approach of these techniques.

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