

MINI-FOCUS ISSUE: MYOCARDIAL AND PERICARDIAL INFLAMMATION

INTRODUCTION

Myocarditis in 2020

Advancements in Imaging and Clinical Management*



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Advances in cardiac imaging allow for greater sensitivity in the diagnosis of myocarditis. Although imaging informs clinical decision making, clinical management often still requires endomyocardial biopsy and remains individualized as to the cause of myocarditis.

Myocarditis is characterized by cardiac inflammation precipitated by various causes and can result in heart failure, cardiogenic shock, episodes of arrhythmia, sudden death, or dilated cardiomyopathy (1). At the start of the 19th century, there was a prevailing prejudice against the term myocarditis due to overuse in any cardiac condition without a murmur, often leading to missed cases of hypertensive or atherosclerotic heart disease (2). Since then, the pendulum has swung in the opposite direction with concerns that cases of true myocarditis are sometimes underdiagnosed due to a lack of clinical suspicion and insufficient imaging modalities (3).

SEE PAGES 180, 186, 191, 200, AND 203

The diagnostic classification of myocarditis has evolved over the years. For example, Fenoglio et al. (4) proposed a biopsy-based classification system in 1983, and Liberman et al. (5) added a clinicopathological classification in 1991. Since then, advancements in imaging, particularly cardiac magnetic resonance (CMR), have led to diagnostic criteria to help identify cases of myocarditis noninvasively. One set of criteria is the 2009 Lake Louise criteria that incorporated CMR findings of edema (T2-weighted imaging), hyperemia (early gadolinium enhancement), and signs of necrosis/fibrosis (late gadolinium enhancement) (6). A positive test result occurs when

2 criteria are met, yielding a sensitivity of 72.5% and a specificity of 96.2% (1,6). The Lake Louise criteria were revised in 2018 to incorporate novel CMR mapping techniques that involved quantifying T1 and T2 relaxation times (7). These revisions increased sensitivity to 87.5% and had similar specificity (1).

Advantages of CMR include the fact that it is noninvasive, it is able to visualize inflammation in areas not reached by biopsy due to sampling error, and it can help rule out acute coronary syndromes (8). Although CMR plays a central role in diagnosing myocarditis, it has limitations. Limited access in smaller centers and renal failure may make it challenging to acquire in a timely fashion (8). Furthermore, in critically ill patients with acute myocarditis, it is often not practical to transport the patient to the CMR imaging scanner (8). In cases with very diffuse or very subtle inflammation, false negatives can result due to minimal or no differences between signal intensities of diseased and healthy myocardium (1). Moreover, CMR alone cannot provide the cause of the myocarditis (8).

Although CMR is presently the best tool for initial assessment of myocarditis, there have been promising developments using fluorodeoxyglucose (FDG)-labeled positron emission tomography (PET) along with computed tomography (PET/CT) or PET/CMR (9). PET has the added ability to detect metabolic activity of myocardial inflammation by assessing FDG uptake in myocardial cells (9). This compliments findings using CMR (9). Small studies and observational data show that hybrid PET/CT and PET/CMR correlate with CMR results and may have higher sensitivity in detecting active myocarditis than CMR alone (9). This is especially useful in borderline cases of myocarditis or low-level chronic inflammation (9). Larger studies are needed to further corroborate these findings. In this issue of *JACC: Case Reports*, additional imaging techniques such as longitudinal strain patterns in cardiac inflammation are reported (10). This helps to characterize manifestations associated with myocarditis such as constrictive pericarditis.

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Myocarditis can be precipitated by various causes including infections, autoimmune diseases, and drugs such as immune checkpoint inhibitors (ICI)-associated myocarditis (11). In this issue of *JACC: Case Reports*, there is a focus on myocarditis associated with ICI (12-14). ICI-associated myocarditis is being increasingly recognized as ICI therapy becomes more widespread (15). For example, Mahmood et al. (15) identified 35 patients with ICI-associated myocarditis. That study reported that myocarditis occurred early after initiating ICI therapy, has a more fulminant course, and higher steroid doses were associated with fewer major adverse cardiac events. This diagnosis has serious implications for patients who may already be quite sick from their underlying malignancy. Prompt diagnosis and aggressive treatment are key to managing this grave side effect of ICI therapy (15).

Although noninvasive cardiac imaging plays an increasingly larger role in diagnosing myocarditis, there remains a pivotal role for endomyocardial biopsy (11). Although certain patterns of late gadolinium enhancement can be suggestive of a cause of myocarditis, CMR cannot distinguish between the major types of myocarditis (3). In those instances, endomyocardial biopsy can help confirm the diagnosis and guide ongoing management (11). Knowledge of the specific cause is particularly key in cases of steroid refractory myocarditis requiring escalation of immunosuppression. Although there are risks associated with endomyocardial biopsy, experienced operators have very low complication rates (11).

Cardiac imaging can also be very useful in those cases to guide the optimal biopsy approach.

Future directions in the field of myocarditis include answering such clinical questions as the emerging role of hybrid PET imaging, optimal long-term surveillance of myocarditis, and management for each cause of myocarditis. For example, recently, Acquaro et al. (16) investigated the prognostic value of serial CMR in patients with acute myocarditis. They found that late gadolinium enhancement on the 6-month CMR had worse prognosis, particularly in the absence of edema (16). This highlights the role of ongoing surveillance imaging to guide long-term medical management. Further studies are needed to characterize the optimal surveillance protocol.

In conclusion, this issue of *JACC: Case Reports* highlights developments in the multifaceted world of myocarditis. Advances in cardiac imaging are allowing for increased sensitivity in prompt diagnosis and further exciting developments are anticipated. The emergence of ICI-associated myocarditis is a cause for concern, bringing urgency to further research in finding risk factors and optimal management. The work of research teams around the world continues to advance this field beyond 2020.

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