Myotonic dystrophy type 2 (DM2) is an autosomal recessive muscular dystrophy classically affecting skeletal muscle with a latency of 30 to 40 years before the expression of symptoms of skeletal muscle weakness and myalgias. Postmortem studies have identified histopathologic and clinical involvement of the heart, and cardiac arrhythmias and sudden death have been observed, including in patients without previous cardiac symptoms. Although investigations of other muscular dystrophies have used cardiac magnetic resonance (CMR) assessments of myocardial tissue structure and its relationship with cardiovascular outcomes, no large investigations of DM2 with comprehensive tissue-based structural phenotypes has been reported. In this issue of Circulation: Cardiovascular Imaging, Schmacht et al provide detailed CMR characterization of subclinical myocardial phenotypes analogous to peripheral skeletal abnormalities present in DM2.

See Article by Schmacht et al

In 27 individuals with genetically confirmed DM2, the investigators use a comprehensive, multifaceted CMR approach including parametric tissue $T_1/T_2$, mapping, spectroscopy, and late gadolinium enhancement to define different mechanistic axes. Their principal findings are impressive, even in this limited sample: late gadolinium enhancement and focal fat deposits (both spatially restricted) were detected in >20% of study participants, and both extracellular volume fraction and native $T_1$ time were abnormal relative to healthy volunteers (despite preserved left ventricular systolic function). In addition, Schmacht et al demonstrate a relationship between fibrosis and conduction abnormalities, providing an important clinical correlate of CMR tissue characterization. These results add to the growing evidence supporting the use of CMR imaging for subclinical disease identification and risk stratification in muscular dystrophies. In a recent report studying 63 men with Duchenne or Becker muscular dystrophy, Becker et al reported decreased left ventricular function in ≈50%, with late gadolinium enhancement present in >75%. Recent reports suggest that diffuse fibrosis and native $T_1$ times are also abnormal in Duchenne muscular dystrophy. Moreover, carriers of muscular dystrophy genes seem to harbor subclinical fibrosis, and both diffuse and focal fibroses by CMR seem to predict arrhythmic events across left ventricular function and may even predict loss of left ventricular function over time. Larger, prospective studies across muscular dystrophies will be required to provide definitive evidence; however, unique CMR indices of tissue structure in suspected and confirmed muscular dystrophies seem to stratify clinical risk.

Several outstanding questions and limitations surrounding the clinical translation of these findings remain. The authors recognize the limited size of their patient and control populations, raising the possibility of type 1 error in detection of multiple phenotypes. More important, however, is the possible therapeutic implication of these findings. Can the results of a CMR study applied early in the course of muscular dystrophies impact long-term prognosis to heart failure and requirement for transplantation? Data from a genetic murine model of Duchenne muscular dystrophy suggest that application of traditional therapies early in the course of cardiomyopathy (eg, angiotensin converting enzyme inhibition and β-blockade) may not be of clinical benefit. Nevertheless, large studies in patients with muscular dystrophy using CMR imaging of early phenotypes will be of interest to define disease-specific therapies that may forestall the progression to heart failure, particularly in those with high-risk CMR features. Furthermore, can CMR findings described by Schmacht et al be used to inform the use of more easily detected circulating biomarkers of cardiac fibrosis to identify DM2 patients with structural cardiac disease? Recent work suggests that circulating extracellular RNAs may have a role in this regard in muscular dystrophies, but confirmation in larger populations is required. Finally, can CMR features be used to identify DM2 patients at risk for ventricular arrhythmias and sudden cardiac death, enabling patients with these features to benefit from an implantable cardiac defibrillator?

Ultimately, the results from Schmacht et al are an important step in solidifying a role for advanced CMR techniques in identifying preclinical abnormalities in cardiac structure and function for improved risk stratification. Realizing the true benefit of CMR-based screening of individuals who carry or are afflicted with muscular dystrophy requires...
concerted, multidisciplinary efforts involving heart failure, genetics, and advanced imaging expertise in adequately powered clinical studies.

Disclosures
None.

References

Key Words: Editorials ▪ biomarkers ▪ cardiomyopathy ▪ heart failure ▪ myalgia
Targeting the Heart for Risk Assessment in Myotonic Dystrophy: An Application for Cardiac Magnetic Resonance
Ravi V. Shah and Marc J. Semigran

Circ Cardiovasc Imaging. 2016;9:
doi: 10.1161/CIRCIMAGING.116.005092
Circulation: Cardiovascular Imaging is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2016 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-9651. Online ISSN: 1942-0080

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circimaging.ahajournals.org/content/9/7/e005092

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Cardiovascular Imaging can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Cardiovascular Imaging is online at:
http://circimaging.ahajournals.org/subscriptions/