Left ventricular systolic dysfunction without overt symptoms of heart failure is a common problem, with a prevalence of ranging from 0.9% to 20.8% in the general population depending on the definition of left ventricular systolic dysfunction and age group studied. The morbidity and mortality of this condition remain significant. In the SOLVD (Studies Of Left Ventricular Dysfunction) prevention trial, 30% of untreated participants progressed to clinical heart failure and experienced a high mortality rate. Although medical treatment reduces mortality, heart failure hospitalizations, and improves adverse remodeling, strategies for monitoring and guiding treatment are necessary. The need for more effective methods of risk stratification is heightened by the observation that the natural history of nonischemic dilated cardiomyopathy (NIDCM) is highly variable. Methods to identify subgroups of patients with NIDCM who are at higher risk of adverse outcomes, especially sudden cardiac death and heart failure hospitalization, may help allocate potentially costly therapy to those who would benefit the most or to target yet unproven therapies to those most likely to benefit. Beyond medical treatments, evidence on the appropriate use of invasive strategies such as novel instruments to monitor hemodynamic status in this patient population is limited. Detection of fibrosis by late gadolinium enhancement (LGE) imaging by cardiac magnetic resonance (CMR) is a promising tool for the risk stratification in this patient population. Fibrosis reduces left ventricular compliance, affects adverse remodeling, and creates a substrate for re-entry ventricular tachycardia. Therefore, the presence of myocardial LGE would provide a logical risk marker for future adverse events relating to either mechanical pump function impairment or ventricular dysrhythmias.

In this issue of Circulation: Heart Failure, Masci et al report the prognostic value of late gadolinium myocardial enhancement by CMR imaging in 228 patients with nonischemic dilated cardiomyopathy presenting for the first time and without symptoms or signs of overt decompensation. Coronary artery disease as the cause of left ventricular dysfunction was ruled out by either coronary angiography or coronary computed tomographic angiography. The study cohort was enrolled from 3 centers and was prospectively followed for clinical events for a median of 23 months. The typical pattern of midwall LGE (also the lack of LGE) has been well described from prior studies of patients with nonischemic dilated cardiomyopathy, and it offers a clinically relevant determination of the pathogenesis of heart failure. With the advent of technical improvements, LGE imaging of myocardial fibrosis can be acquired using standardized protocol even in patients who are not capable of repeated breath holding. The authors report that LGE presence in this cohort was associated with a 4-fold increased risk of reaching the primary end point of cardiovascular death, clinical heart failure, or aborted sudden death. This risk association was incremental to the risk profiles offered by clinical risk factors, left ventricular ejection fraction, and left ventricular volumes. LGE was particularly robust at predicting progression to symptomatic heart failure and aborted sudden cardiac death with a hazard ratio of 5.2 and 8.3 for both of these outcomes, respectively. In patients who did not experience clinical events, LGE correctly reclassified 21% to low risk while incorrectly upgrading 3% to high risk. In patients who experienced clinical events, LGE reclassified 12% to high risk and, importantly, did not incorrectly reclassify those already in the high-risk category to low risk.

This study adds to the existing and growing body of literature demonstrating the prognostic value of LGE in patients with NIDCM at various stages of heart failure. The authors aimed to study a unique and inadequately studied patient population: those patients without a prior history of overt cardiac decompensation. However, as the authors point out, there was an inherent referral bias owing to local practice of CMR use and tertiary referral environment. Therefore, the study population may represent a slightly higher risk subgroup than subjects who would otherwise not be referred to CMR, and the results may not be generalizable to all patients with left ventricular systolic dysfunction detected incidentally or through screening programs. Because 66% (151 of 228) of patients were referred for symptoms including chest pain, palpitations, and syncope/presyncope, the true New York Heart Association functional status of these patients was not clearly defined, and the presence of symptoms were not included in the multivariate model. The reported robust prognostic value of LGE imaging could, therefore, have been inflated by not accounting for the effects of simple and routine bedside tools such as patients’ functional class.

Identification of techniques to risk stratify patients in the preclinical stages of disease is crucial because of the enormous resource utilization implications of progression to symptomatic
heart failure. Assuming persistence of current practice patterns, the direct medical costs of heart failure are projected to increase from $21 billion in 2012 to $53 billion in 2030.\textsuperscript{15} Even with institution of guideline-based therapy, progression to symptomatic heart failure in this patient population remains high.\textsuperscript{5} Therefore, major societies are calling for a shift in care model toward prevention at stage A and stage B phases of heart failure.\textsuperscript{16} Implementation of cost effective strategies to curb progression to clinical heart failure and heart failure hospitalization in this patient population remains daunting, however, because the number of patients who have stage B heart failure is estimated to be 3× to 4× the number of patients with stage C and D.\textsuperscript{16} Based on the existing body of literature and the results of the current study, CMR may be the strategic choice to improve study design and execution by identifying phenotypes and pathophysiology most likely to benefit from potentially costly treatments. Specifically, the presence of LGE could serve as a branch point to select patients most likely to benefit from interventions aimed at mitigating progression to symptomatic heart failure. Several strategies for heart failure prevention can be tested using this LGE-guided approach. First, a CMR-guided strategy may the ideal way in which to identify patients who would benefit most from disease management programs that incorporate novel implantable haemodynamic monitoring systems.\textsuperscript{17} This is based on the hypothesis that, because myocardial fibrosis as assessed by LGE is associated with greater ventricular stiffness, LGE could identify a subgroup of patients with a propensity to higher filling pressures. Second, because heart failure with systolic dysfunction results in a maladaptive activation of mineralocorticoid receptors by aldosterone thereby promoting myocardial fibrosis and ventricular arrhythmias,\textsuperscript{18} an LGE-guided approach to instituting aldosterone receptor antagonist therapy could form the basis of trials testing the ability of aldosterone receptor antagonists such as spironolactone to change heart failure outcomes in patients without overt congestive heart failure. Finally, LGE in this population seems to be the ideal imaging technique in identifying arrhythmogenic substrates in patients who may benefit from implantable cardioverter defibrillator therapy. The role of implantable cardioverter defibrillator in the nonischemic dilated population remains ill-defined. With the exception of the DEFINITE (Defibrillators in Nonischemic Cardiomyopathy Treatment Evaluation) trial, implantable cardioverter defibrillator therapy in primary prophylaxis of dilated cardiomyopathy has not generally included asymptomatic patients in New York Heart Association functional class I. As such, contemporary guidelines give a class Iib recommendation for implantable cardioverter defibrillator implantation in patients with NIDCM who are New York Heart Association I.\textsuperscript{19} This is despite the fact that sudden cardiac death may be the first manifestation of NIDCM in a sizable proportion of patients.\textsuperscript{5} Other novel CMR techniques will almost certainly be expected to gain invaluable pathophysiologic insights of this disease at a preclinical stage. T1 mapping by CMR can quantify expansion of the myocardial extracellular volume fraction because of fibrotic burden of the disease not captured by LGE. Magnetic resonance spectroscopy assesses myocardial energetic states of NIDCM by determining the phosphocreatine/ATP ratios.\textsuperscript{20} CMR scar imaging combined with 3-dimensional imaging of myocardial tissue strains may shed new insights on how we can use cardiac resynchronization therapy in patients with NIDCM.\textsuperscript{21} In conclusion, from a patient management standpoint, the evidence provided by the current article in addition to the existing literature is encouraging. However, substantial prospective evidence in adopting CMR as a strategic tool in improving the appropriate use of medical or interventional therapies with the goals of reducing hospitalizations, patient morbidity, and the greater economic burden of heart failure management remains to be established. Given the burden of heart failure to society, the need to strategically evaluate the additional value of CMR onto current practice, is not just sensible but pressing.

Disclosures

None.

References


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It's Time to Study Cardiac Magnetic Resonance Imaging as a Strategic Tool in Nonischemic Cardiomyopathy

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