The Prognostic Value of Global Circumferential Strain in Patients With Suspected Myocardial Disease*

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Measurements of cardiac output by indicator or thermodilution techniques were among the first methods developed to assess cardiac function (1). It is clear, however, that even when normalized for body size, cardiac output measured at rest is limited as a clinical measure because the heart is designed to support vast demand variations during daily life. Except for critical care situations in which cardiac output is useful as a clinical parameter, the most used index of cardiac performance is left ventricular ejection fraction (LVEF). LVEF has proved to be a reliable parameter to the clinician contemplating the prognosis and management of patients with heart disease (e.g., in selecting patients for implantable cardioverter-defibrillators). Over the past several decades, it has become established that performance measurements at different loading conditions or oxygen demand are preferable to those obtained at rest (2). However, the simplicity of parameters such as LVEF have proved to be sufficient for most clinical needs.

As part of the efforts to quantify cardiac function, several techniques to assess regional myocardial deformation have been developed, based primarily on the measurement of myocardial strain along different orientations. Over the past 2 decades, myocardial tagging (3,4) substituted invasive methods of measuring myocardial deformation and ushered in an era of unprecedented progress in our understanding of myocardial function (5,6). Tissue Doppler and speckle tracking techniques have extended the ability to assess myocardial segmental deformation in systole and diastole on ultrasound (7), creating the possibility of even wider clinical utilization. Although LVEF is load dependent, such dependence appears to be less for shortening measured along normal orientations such as circumferential and longitudinal. However, although cardiac magnetic resonance (CMR) tagging has been used as a clinical research tool and in population studies, its prognostic potential in clinical settings has not been established.

In this issue of iJACC, Mordi et al. (8) present data supporting the application of circumferential shortening measured by CMR tagging to assess prognosis in 539 patients with suspected heart disease referred for CMR. A comprehensive assessment of cardiac global structure and function, myocardial global circumferential strain (GCS), and myocardial fibrosis by late gadolinium enhancement (LGE) were performed. The authors examined whether such parameters improved the power of detecting the primary endpoint, the prevalence of major adverse cardiovascular events, which included a combination of all-cause mortality, heart failure–related hospitalization, and aborted sudden cardiac death. Two-thirds of the patients were male, and the cohort was relatively young (mean age 48.1 years). Indications for CMR included assessment of nonischemic (36.9%) or ischemic (19.9%) cardiomyopathy, ventricular arrhythmia (13.9%), suspected myocarditis (11.9%), or LV hypertrophy (10.9%). Overall, 11.5% (62 of 539) of the enrolled patients developed the primary endpoint over a mean duration of follow-up of 2.2 years. On multivariate analysis, ischemic heart disease, LVEF <35%, and the presence of myocardial fibrosis by LGE were predictors of untoward outcomes. Reduced GCS as measured was also a strong predictor of an
unfavorable prognosis. The combination of fibrosis by LGE with reduced GCS in patients with LVEF $\geq 35\%$ was prognostically similar to that in patients with LVEF $<35\%$.

The authors performed CMR tagging using commercial software now available for all major CMR vendors and analyzed the data using harmonic phase imaging, a method developed and validated a decade ago (9) and that has been applied to clinical and large-scale population studies (10,11). This is the first study establishing the prognostic significance of reduced GCS in a large-scale cohort of patients being investigated for cardiac structural and functional impairment. GCS across the left ventricle can be easily analyzed by CMR. Large datasets with reference values (12) exist for this technique, including that in the present study (8). The results of the present study, as well as those from previous studies using CMR tagging (6) and echocardiography (7), suggest that regional function defined by strain may be more sensitive than ejection fraction in the detection of incipient myocardial dysfunction.

The authors utilized standard statistical methodology to assess the incremental prognostic value of distinct CMR parameters added to clinical indicators. They also used a combined model to evaluate the added value of specific CMR indices over and above other CMR parameters, as demonstrated in Table 6 (8). For that analysis, each parameter was classified as normal or abnormal as defined from cutoff points obtained from a receiver-operating characteristic curve. The areas under the curve were 0.834 for LVEF, 0.699 for LGE, and 0.820 for GCS. Some would want to see the additional power of indexes measured as increments to the areas under the curve of base models, which are more powerful than chi-square analysis and are a higher benchmark for incremental prognostic power (13). Others would want to see the power to reclassify patients using net reclassification index or integrated discrimination improvement as further evidence of the utility of this marker.

In a subgroup analysis, the authors demonstrate that the presence of myocardial fibrosis by LGE and/or myocardial dysfunction by reduced circumferential strain identified patients who were at higher risk for adverse outcomes despite having LVEF $\geq 35\%$. It is suggested that LGE and reduced circumferential strain may be particularly significant for detecting higher risk for malignant arrhythmias because 11 of 35 patients with the primary outcome in that group died and an additional 10 patients had aborted sudden cardiac death. Since the first study reporting on the prognostic power of myocardial fibrosis detected as delayed enhancement in post-infarct patients, several studies have established that association in different patient groups (14-16). The present study is unique for its assessment of this association in a large-scale cohort of patients with LVEF $\geq 35\%$ (n = 474). Yet, it would be important to assess the prognostic value of GCS and LGE in different subgroups (including those with ischemic heart disease, dilated cardiomypathy, or amyloidosis). The only subgroup that was tested was that with nonischemic cardiomyopathy.

Finally, it is worth mentioning that data accumulated from other studies, in particular the Multi-Ethnic Study on Atherosclerosis, appear to support the authors’ hypothesis that alterations of GCS may reflect myocardial fibrosis. Established risk factors for diffuse myocardial fibrosis, such as aging (5), LV hypertrophy (11), and atherosclerosis (17), are associated with decreased regional and global circumferential strain. Similar to the findings described by Mordi et al. (8), among the participants in the Multi-Ethnic Study on Atherosclerosis who were healthy at study entry, strain deficits predicted prognosis over and above LVEF (6). The current study is a crucial step toward bringing such knowledge to application where it matters most, that is, patients with suspected heart disease.

**REFERENCES**


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