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Feature-Tracking Global Longitudinal Strain Predicts Death in a Multicenter Population of Patients with Ischemic and Nonischemic Dilated Cardiomyopathy Incremental to Ejection Fraction and Late Gadolinium Enhancement

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ABSTRACT

OBJECTIVES The aim of this study was to evaluate the prognostic value of cardiac magnetic resonance (CMR) feature-tracking–derived global longitudinal strain (GLS) in a large multicenter population of patients with ischemic and nonischemic dilated cardiomyopathy.

BACKGROUND Direct assessment of myocardial fiber deformation with GLS using echocardiography or CMR feature tracking has shown promise in providing prognostic information incremental to ejection fraction (EF) in single-center studies. Given the growing use of CMR for assessing persons with left ventricular (LV) dysfunction, we hypothesized that feature-tracking–derived GLS may provide independent prognostic information in a multicenter population of patients with ischemic and nonischemic dilated cardiomyopathy.

METHODS Consecutive patients at 4 U.S. medical centers undergoing CMR with EF <50% and ischemic or nonischemic dilated cardiomyopathy were included in this study. Feature-tracking GLS was calculated from 3 long-axis cine-views. The primary endpoint was all-cause death. Cox proportional hazards regression modeling was used to examine the association between GLS and death. Incremental prognostic value of GLS was assessed in nested models.

RESULTS Of the 1,012 patients in this study, 133 died during median follow-up of 4.4 years. By Kaplan-Meier analysis, the risk of death increased significantly with worsening GLS tertiles (log-rank $p < 0.0001$). Each 1% worsening in GLS was associated with an 89.1% increased risk of death after adjustment for clinical and imaging risk factors including EF and late gadolinium enhancement (LGE) (hazard ratio [HR]:1.891 per %; $p < 0.001$). Addition of GLS in this model resulted in significant improvement in the C-statistic (0.628 to 0.867; $p < 0.0001$). Continuous net reclassification improvement (NRI) was 1.148 (95% confidence interval: 0.996 to 1.318). GLS was independently associated with death after adjustment for clinical and imaging risk factors (including EF and late gadolinium enhancement) in both ischemic (HR: 1.942 per %; $p < 0.001$) and nonischemic dilated cardiomyopathy subgroups (HR: 2.101 per %; $p < 0.001$).

CONCLUSIONS CMR feature-tracking–derived GLS is a powerful independent predictor of mortality in a multicenter population of patients with ischemic or nonischemic dilated cardiomyopathy, incremental to common clinical and CMR risk factors including EF and LGE. (J Am Coll Cardiol Img 2018;■:■–■) © 2018 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance

EF = ejection fraction

GLS = global longitudinal strain

ICD = implantable cardioverter defibrillator

LGE = late gadolinium enhancement

LV = left ventricular

NRI = net reclassification improvement

Ejection fraction (EF) is the principal measure used in clinical practice to assess cardiac mechanics. It provides significant prognostic information and is used widely for many clinical and therapeutic decisions, particularly in patients with left ventricular (LV) dysfunction. More recently, direct assessment of myocardial fiber deformation with echocardiographic global longitudinal strain (GLS) imaging has shown promise in providing diagnostic and prognostic information that is incremental to EF (1,2).

Cardiac magnetic resonance (CMR) imaging has evolved into a major tool for assessment of patients with LV dysfunction, providing precise measurements of EF and tissue characterization with late gadolinium enhancement (LGE) (3). LGE can help establish the underlying cause of LV dysfunction and is a powerful predictor of adverse cardiovascular outcomes (3). Recent developments in CMR feature-tracking techniques now allow assessment of GLS from standard cine-CMR images (4).

We have recently reported the prognostic association of GLS with mortality in a small population of mixed cardiomyopathy patients from a single center (5). However, the prognostic value of GLS in patients with ischemic versus nonischemic cardiomyopathy is unknown. Moreover, the robustness of these associations, as well as the variability of feature-tracking GLS measurements in a multicenter setting, remains unclear. The aim of this study was to evaluate the prognostic value of CMR feature-tracking-derived GLS in a large multicenter population of patients with ischemic and nonischemic cardiomyopathy undergoing CMR at several centers in the United States.

METHODS

STUDY DESIGN. Four geographically diverse medical centers in the United States participated in this observational multicenter study. The University of Illinois in Chicago served as the data-coordinating center, using a cloud-based database (CloudCMR, HeartIT, Durham, North Carolina) containing de-identified searchable data from consecutive patients with full DICOM datasets from the participating centers. Institutional review board approval was obtained at each center.

STUDY POPULATION. Consecutive patients (n = 1,047) with EFs <50% and ischemic or nonischemic dilated cardiomyopathy who had undergone clinical CMR in 2011 with both cine- and LGE imaging formed the study population. A subgroup of patients from a single center in this study was used in a previous report (5). Patients with uninterpretable image quality for GLS assessment (n = 35) were excluded, leaving 1,012 patients, which formed the study population. Baseline demographics were obtained by local site investigators at the time of the clinical study.

CMR ACQUISITION. Images were acquired with phased-array receiver coils, according to the routine scan protocol at each site, using a variety of scanners from all 3 major vendors (Siemens, Philips, and General Electric) at both 1.5- and 3-T. A typical protocol included steady-state free-precession cine-images acquired in multiple short-axis and 3 long-axis views with short-axis views obtained every 1 cm to cover the entire left ventricle. Typical temporal resolution of cine-images was <45 ms. LGE imaging was performed 10 to 15 min after administration of gadolinium contrast material (0.15 mmol/kg), using a 2-dimensional (2D) segmented gradient echo inversion-recovery sequence in the same views used for cine-CMR. Inversion delay times were typically 280 to 360 ms.

CMR ANALYSIS AND GLS ASSESSMENT. The study-site investigators analyzed images on locally available workstations and were blinded to follow-up data. Delayed enhancement was assessed as described previously (6–9). In brief, LGE was scored visually on a 17-segment model with a 5-point scale for each segment (0 = no LGE, 1 = 1% to 25%, 2 = 26% to 50%, 3 = 51% to 75%, 4 = 76% to 100%). LGE extent as a percentage of LV myocardium was calculated by summing the regional scores, each weighted by the LGE range midpoint (i.e., 1 = 13%, 2 = 38%, 3 = 63%, 4 = 88%) and dividing by 17. LV volumes and mass were manually quantified at the data coordinating center from short-axis cine-images. At the data-coordinating center, endocardial LV contours were manually traced (by a single physician who was blinded to patient information and outcomes) in all 3 long-axis cine-views to derive GLS using the Q strain feature-tracking package (Medis Medical Imaging Systems, Leiden, the Netherlands) (**Figure 1**). In 100 randomly selected patients, a second blinded CMR physician measured GLS for assessment of interobserver variability. In another 100 randomly selected patients, the same physician remeasured GLS in a blinded fashion for assessment of intraobserver variability.

FOLLOW-UP. Patients were followed for the primary outcome of all-cause mortality using the United States Social Security Death Index. Time to event was calculated as the period between the CMR study and