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ORIGINAL RESEARCH

Global Longitudinal Strain Is a Superior Predictor of All-Cause Mortality in Heart Failure With Reduced Ejection Fraction

Morten Sengeløv, MB,* Peter Godsk Jørgensen, MD,*† Jan Skov Jensen, MD, PhD, DMSc,*† Niels Eske Bruun, MD, DMSc,*‡ Flemming Javier Olsen, MB,* Thomas Fritz-Hansen, MD,* Kotaro Nochioka, MD, PhD,§ Tor Biering-Sørensen, MD, PhD*†§

ABSTRACT

OBJECTIVES The purpose of this study was to investigate the prognostic value of global longitudinal strain (GLS) in heart failure with reduced ejection fraction (HFrEF) patients in relation to all-cause mortality.

BACKGROUND Measurement of myocardial deformation by 2-dimensional speckle tracking echocardiography, specifically GLS, may be superior to conventional echocardiographic parameters, including left ventricular ejection fraction, in predicting all-cause mortality in HFrEF patients.

METHODS Transthoracic echocardiographic examinations were retrieved for 1,065 HFrEF patients admitted to a heart failure clinic. The echocardiographic images were analyzed, and conventional and novel echocardiographic parameters were obtained.

RESULTS Many of the conventional echocardiographic parameters proved to be predictors of mortality. However, GLS remained an independent predictor of mortality in the multivariable model after adjusting for age, sex, body mass index, total cholesterol, mean arterial pressure, heart rate, ischemic cardiomyopathy, percutaneous transluminal coronary angioplasty, coronary artery bypass graft surgery, noninsulin dependent diabetes mellitus, and conventional echocardiographic parameters (hazard ratio [HR]: 1.15; 95% confidence interval [CI]: 1.04 to 1.27; $p = 0.008$, per 1% decrease). No other echocardiographic parameter remained an independent predictor after adjusting for these variables. Furthermore, GLS had the highest C-statistics of all the echocardiographic parameters and added incremental prognostic value with a significant increase in the net reclassification improvement ($p = 0.009$). Atrial fibrillation (AF) modified the relationship between GLS and mortality (p value for interaction = 0.036); HR: 1.08 (95% CI: 0.97 to 1.19), $p = 0.150$ and HR: 1.22 (95% CI: 1.15 to 1.29), $p < 0.001$, per 1% decrease in GLS for patients with and without AF, respectively. Sex also modified the relationship between GLS and mortality (p value for interaction = 0.047); HR: 1.23 (95% CI: 1.16 to 1.30), $p < 0.001$ and HR: 1.09 (95% CI: 0.99 to 1.20), $p = 0.083$, per 1% decrease in GLS for men and women, respectively.

CONCLUSIONS GLS is an independent predictor of all-cause mortality in HFrEF patients, especially in male patients without AF. Furthermore, GLS was a superior prognosticator compared with all other echocardiographic parameters. (J Am Coll Cardiol Img 2015;8:1351–9) © 2015 by the American College of Cardiology Foundation.

From the *Department of Cardiology, Gentofte Hospital, University of Copenhagen, Copenhagen, Denmark; †Institute of Clinical Medicine, Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark; ‡Clinical Institute, Aalborg University, Aalborg, Denmark; and the §Cardiovascular Medicine Division, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts. This study was financially supported by the Danish Council for Independent Research. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

CABG = coronary artery bypass graft

CART = classification and regression tree

DT = deceleration time

GCS = global circumferential strain

GLS = global longitudinal strain

HFrEF = heart failure with reduced ejection fraction

LAVI = left atrial volume index

LV = left ventricular

LVEF = left ventricular ejection fraction

LVMI = left ventricular mass index

MAP = mean arterial pressure

NIDDM = noninsulin dependent diabetes mellitus

NRI = net reclassification improvement

PTCA = percutaneous transluminal coronary angioplasty

TAPSE = tricuspid annular plane systolic excursion

Echocardiography is the principal cardiac imaging tool used when assessing left ventricular (LV) systolic function in patients with heart failure (HF). Patients with HF who have undergone an echocardiographic examination have a greater chance of survival because of intensified medical treatment and intervention (1), and quantifying LV systolic function is vital in predicting adverse outcomes in patients with HF (2). Two-dimensional echocardiography can be used for evaluating LV systolic function by obtaining left ventricular ejection fraction (LVEF) (3). This parameter is widely used in clinical practice (4) and has been established as a predictor of mortality in HF patients (5). However, a measurement of LVEF depends on factors such as image quality, tracing of the endocardium, and geometric assumptions. Two-dimensional speckle tracking echocardiography has in recent years emerged as a method for assessing LV systolic and diastolic function (6). The technique measures the displacement of speckles on the 2-dimensional echocardiographic image. Speckle tracking offers a directional independence of the ultrasound beam (7,8) and represents myocardial deformation rather than volumetric change as seen by the LVEF method. Global longitudinal strain (GLS), obtained by 2-dimensional speckle tracking echocardiography, is

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a measurement that has previously been demonstrated to be of prognostic value in patients having a wide array of cardiac diseases (9). There is also evidence supporting the prognostic value of GLS in HF patients (10–13). However, the previous studies on HF were either small or did not consider alternative echocardiographic predictors. Additionally, no other studies have investigated echocardiographic risk stratification models obtained by classification and regression tree (CART) analysis and net reclassification improvement (NRI). The aim of this study was to investigate the predictive value of GLS compared with conventional echocardiographic parameters in predicting mortality in a large cohort of patients with HF with reduced LVEF (HFrEF). In addition, we sought to identify the optimal echocardiographic risk stratification model in this patient population.

METHODS

STUDY POPULATION. In this large-scale retrospective study, we identified 1,102 nonacute consecutive patients referred to Gentofte Hospital's HFrEF clinic in the period from 2005 to 2013. Patients had an LVEF of 45% or lower at referral. The baseline clinical data for the patients was retrieved from the HFrEF clinic's database, which was registered at the patient's first visit and includes history of diseases and previous procedures performed. All patients had a diagnosis of HFrEF by an experienced clinician and a history of angiography to evaluate coronary artery status. The 1,102 patients were cross-referenced with the hospital's echocardiographic database, in which an echocardiographic examination was retrieved for every patient. We included patients with an echocardiographic examination performed at a maximum of 1 year from the first admittance (median 30 days before admittance; interquartile range [IQR]: 6 to 56 days before admittance). Twenty-two patients did not have an echocardiographic examination within 1 year of admittance and were therefore excluded. Furthermore, 15 patients were excluded due to a poor or inadequate echocardiographic examination. In the end, 1,065 patients had echocardiographic images eligible for analysis. All clinical baseline data were obtained on admission to the HFrEF clinic and registered by an experienced clinician. The relevant status of medication initiated at admission date was retrieved from the database as well. Information on mortality status was retrieved from the Danish National Registry of Mortality, and follow-up was 100%. Ischemic cardiomyopathy was defined as patients who had a history of myocardial infarction and/or having undergone percutaneous transluminal coronary angioplasty (PTCA) and/or coronary artery bypass graft (CABG) surgery.

ECHOCARDIOGRAPHY. All the echocardiograms were obtained using either Vivid 7 or 9 echocardiographic machines (GE Healthcare, Little Chalfont, United Kingdom). The images were stored in a GE Healthcare image vault. The echocardiograms were subsequently analyzed offline in Echopac version 12 (GE Healthcare) by a single investigator blinded to all baseline patient data.

Conventional echocardiography. LVEF was obtained using the modified Simpson rule (4). LV end-diastolic dimensions were measured in the parasternal long-axis view at the tip of the mitral valve leaflets. These include interventricular septum thickness, LV posterior wall dimension, and LV internal dimension (4).

The anatomic LV mass was estimated by the Devereux formula (14). LV mass was then divided by the body surface area to obtain the left ventricular mass index (LVMI). Body surface area (m^2) was