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Precision Phenotyping in Heart Failure and Pattern Clustering of Ultrasound Data for the Assessment of Diastolic Dysfunction

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ABSTRACT

OBJECTIVES The aim of this study was to investigate whether cluster analysis of left atrial and left ventricular (LV) mechanical deformation parameters provide sufficient information for Doppler-independent assessment of LV diastolic function.

BACKGROUND Medical imaging produces substantial phenotyping data, and superior computational analyses could allow automated classification of repetitive patterns into patient groups with similar behavior.

METHODS The authors performed a cluster analysis and developed a model of LV diastolic function from an initial exploratory cohort of 130 patients that was subsequently tested in a prospective cohort of 44 patients undergoing cardiac catheterization. Patients in both study groups had standard echocardiographic examination with Doppler-derived assessment of diastolic function. Both the left ventricle and the left atrium were tracked simultaneously using speckle-tracking echocardiography (STE) for measuring simultaneous changes in left atrial and ventricular volumes, volume rates, longitudinal strains, and strain rates. Patients in the validation group also underwent invasive measurements of pulmonary capillary wedge pressure and LV end diastolic pressure immediately after echocardiography. The similarity between STE and conventional 2-dimensional and Doppler methods of diastolic function was investigated in both the exploratory and validation cohorts.

RESULTS STE demonstrated strong correlations with the conventional indices and independently clustered the patients into 3 groups with conventional measurements verifying increasing severity of diastolic dysfunction and LV filling pressures. A multivariable linear regression model also allowed estimation of E/e′ and pulmonary capillary wedge pressure by STE in the validation cohort.

CONCLUSIONS Tracking deformation of the left-sided cardiac chambers from routine cardiac ultrasound images provides accurate information for Doppler-independent phenotypic characterization of LV diastolic function and noninvasive assessment of LV filling pressures. (J Am Coll Cardiol Img 2017;■:■–■) © 2017 by the American College of Cardiology Foundation.

Heart failure (HF) is a major public health problem in the United States. It is estimated that, by 2030, HF prevalence will grow by 25% and annual costs of care will increase from $21 to $53 billion (1). All efforts must be invested for investigating clinical, laboratory, and imaging data for better phenotypic characterization of HF (2,3) and designing cost-effective strategies for a reliable identification of high-risk populations at early stages. Amongst various cardiac imaging modalities, 2-dimensional (2D) and Doppler echocardiography techniques are most widely used in patients with HF

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ABBREVIATIONS AND ACRONYMS

AV = single beat simultaneous atrioventricular measurement

AV-S = atrio-ventricular longitudinal strain at peak left ventricular systole

LA = left atrium

LV = left ventricle

SRA = peak longitudinal strain rate during left atrial contraction

SRE = peak longitudinal strain rate during early left ventricular diastole

SRS = peak longitudinal strain rate during left ventricular systole

VRA = peak volume expansion rate during left atrial contraction

VRE = peak volume expansion rate during early left ventricular diastole

VRS = peak volume expansion rate during left ventricular systole

for the assessment of left ventricular (LV) structural and functional abnormalities (4). The newer approaches in tracking natural myocardial markers, or speckles, in 2D cardiac ultrasound images for computing myocardial deformation provide incremental characterization of myocardial functional abnormalities beyond ejection fraction (EF) (5). Recent multicenter studies and global scientific consortia have therefore endorsed standardization and automation of speckle tracking echocardiography (STE) for routine clinical application (6–8).

STE provides large sets of spatial and temporal measurements; therefore, novel big data analytic approaches may be well-suited for STE databases for pattern recognition and superior staging of cardiac muscle dysfunction (9). In this investigation, we hypothesized that the cumulative information obtained from STE-based measurements is similar to that obtained from the conventional 2D echocardiograms and Doppler measurements for characterizing LV diastolic function and LV filling pressures. Therefore, we measured the STE-derived parameters in an exploratory subset of patients with HF for understanding the relationships between STE and conventional variables. In a separate validation group of patients with invasive pressure measurements, we subsequently tested the accuracy of the multivariable models derived from the exploratory set for the assessment of Doppler-independent phenotypic characterization of the LV diastolic dysfunction and noninvasive assessment of LV filling pressures.

METHODS

STUDY POPULATION. Patients for exploratory and validation cohorts (Figure 1) were recruited from 2 centers; the Ain Shams University Hospital, Cairo, Egypt (CAI) and the Icahn School of Medicine at Mount Sinai, New York, New York (NY). The local ethics committees of both institutions approved the study. A single specialist analyzed echocardiographic studies from both institutions (Mount Sinai Core Laboratory).

Exploratory group. A convenience sample was developed from data retrieved from 2 centers (CAI and NY). The CAI cohort was obtained prospectively and included 108 consecutive patients with HF symptoms referred between June 2013 and March 2014 to a single operator (Dr. Abdel Rahman) who performed all of the echocardiograms. Patients were excluded if they had poor echocardiographic images, inadequate visualization of LV and left atrial (LA) biplane views, inadequate data for assessing LV diastolic function and filling pressures, systemic comorbidities (e.g., malignancies, terminal hepatic failure, end-stage chronic renal disease on dialysis), more than a mild degree of valve disease, and pericardial diseases. As such, 25 patients were excluded from subsequent study analyses because of significant mitral regurgitation (19 patients) and insufficient echocardiographic quality (6 patients). We further enriched this sample with 79 retrospectively identified patients from NY with HF symptoms who had undergone echocardiograms in the same period with a single physician (Dr. Sengupta). After applying the same exclusion criteria as used in CAI, 47 patients were selected, with 32 excluded because of significant mitral valve disease (22 patients) and insufficient image quality (10 patients). In summary, the exploratory group comprised 130 patients with HF symptoms (83 patients from CAI, and 47 patients from NY).

Validation group. We prospectively identified 44 consecutive patients with HF symptoms who were undergoing left and right heart catheterizations. The exclusion criteria used in the exploratory cohort were also observed for the validation group. Echocardiographic examinations were performed by an investigator blinded to the exploratory group analyses (Dr. Omar) and were acquired using the same standardized protocol. Echocardiographic examinations were performed just before right heart and left heart catheterization studies. Pulmonary capillary wedge pressure (PCWP) and left ventricular end-diastolic pressure (LVEDP), were measured by an investigator (Dr. Rifaie) blinded to echocardiographic data (4).

ECHOCARDIOGRAPHIC EXAMINATION. Two-dimensional echocardiography. All echocardiographic studies were performed with a commercially available echocardiography system equipped with a 2.5-MHz multifrequency phased array transducer (Vivid 7 or E9, GE-Vingmed, Horton, Norway). Digital, routine grayscale 2D loops from apical 2- and 4-chamber views with 3 consecutive beats were obtained with both the left ventricle and left atrium clearly and completely visualized. LV end-diastolic volume, end-systolic volume, and EF were calculated using the biplane Simpson method of discs and left atrial maximum volume (LAVmax) and minimum volume (LAVmin) were calculated using the biplane area-length method. All measurements were made in ≥3 consecutive cardiac cycles, and average values were used for the final analyses.