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What can three-dimensional speckle-tracking echocardiography contribute to evaluate global left ventricular systolic performance in patients with heart failure?

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ABSTRACT

Purpose: Three-dimensional speckle-tracking echocardiography (3D-STE) is a newly developed technique to evaluate left ventricular (LV) deformation by measuring the area strain (AS) of endocardial surface that combines information from both longitudinal (LS) and circumferential strain (CS). We performed a study to examine myocardial deformation in patients with heart failure (HF) using 3D-STE.
Method: A total of 149 subjects including 58 patients with HF and preserved ejection fraction (HFPEF), 45 patients with HF and reduced ejection fraction (HFREF), and 46 normal subjects were prospectively studied by 3D-STE.
Result: After adjusting for age, gender and BSA, global CS, LS, radial strain (RS) and AS derived from 3D-STE in patients with HFPEF were significantly higher than their counterparts in patients with HFREF (all $p < 0.001$), but lower than that in normal subjects (all $p < 0.05$). In addition, among all the strain parameters, global AS exhibited the highest correlation with LV ejection fraction ($y = 1.243x + 6.332$, $r = 0.982$, $p < 0.001$) and the best intra- (ICCs: 0.986, $p < 0.001$) and inter-observer variability (ICCs: 0.978, $p < 0.001$) than other parameters of 3D strain (CS: 0.981 and 0.974; LS: 0.908 and 0.841; RS: 0.946 and 0.915; all $p < 0.001$).
Conclusions: Measurement of endocardial surface AS based on 3D-STE technique is reproducible and proves to be accurate and comprehensive in assessing the global LV performance and multidirectional deformation of the LV myocardium in HF patients.

1. Introduction

Heart failure (HF) with preserved ejection fraction (HFPEF) comprises approximately half of patients presented with heart failure [1], with morbidity and mortality similar to that of patients with reduced ejection fraction (HFREF) [2], therefore, accurate assessment of left ventricular (LV) function in HFPEF plays an important role in routine clinical practice. Given its noninvasive nature and wide availability, echocardiography is the most useful imaging modality for evaluating heart failure and its response to treatment [3–6]. Conventional indices of regional and global left ventricular function, such as fractional shortening and ejection fraction (EF), are largely dependent on loading conditions and geometric assumptions [7,8]. Myocardial velocities determined by tissue Doppler imaging (TDI) do not rely on geometric assumptions but are inherently limited by angle dependency, noise artifacts and confounding of interpretation by tethering of adjacent myocardium and cardiac translational movements, and assessment being confined to myocardial segments that move along the direction of the ultrasound beam [9,10]. Recently, two-dimensional (2D) speckle-tracking echocardiography (2D-STE) has been introduced as a new method to quantify myocardial strain. This technique measures myocardial deformation in longitudinal, radial and circumferential directions by means of frame-by-frame tracking. Validation studies with tagged CMR imaging and sonomicrometry [11—14] have provided evidence that 2D-STE is reliable to determine ventricular myocardial function. However, 2D-STE analysis has some primary limitations, such as foreshortened views, geometric modeling, and out-of-plane motion of the speckles.

More recently, the advent of three-dimensional (3D) speckle-tracking echocardiography (3D-STE) that is capable to accurately assess myocardial deformation in all three spatial dimensions from 3D data sets [15–18], has the potential to overcome the limitations of Doppler-based strain or 2D-based speckle-tracking strain [16–24]. Area strain (AS), an innovative feature of 3D-STE, integrates both longitudinal (LS) and circumferential strain (CS) and reflects

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regional changes in endocardial surface area throughout the cardiac cycle, thus represents a faster and more comprehensive parameter in evaluation of myocardial function.

The aims of our study were to (1) examine the feasibility and reproducibility of LV 3D strain analysis by real-time (RT) 3D-STE in patients with HF and (2) to compare the strain results obtained using 2D-STE and 3D-STE techniques in clinical practice.

2. Methods

2.1. Study population and protocol

The study population consisted of 103 patients with HF recruited from our outpatient clinic, and 46 healthy volunteers (control group). All patients had experienced at least one episode of HF-related hospitalization within the past year. Of the 103 HF patients, 58 met the criteria of the Heart Failure and Echocardiography Associations of the European Society of Cardiology for HFPEF with LV ejection fraction (EF) ≥50%, and 45 had HFREF with LVEF <50% by echocardiography and with signs and symptoms of HF [25]. All patients were stabilized by medications and underwent standard echocardiography and 3D-STE at least 6 weeks after discharge.

The exclusion criteria were: 1) atrial fibrillation, sick sinus syndrome, second- or third-degree heart block with or without a pacemaker, 2) unstable conditions (acute coronary syndrome or cardiac shock), 3) significant congenital or valvular heart disease, 4) restrictive cardiomyopathy, 5) HF caused by primary renal disease, 6) systemic infection, 7) pregnancy and 8) suboptimal image quality unsuitable for strain measurements.

The control group recruited from the community had no history of cardiovascular or systemic diseases, and had a normal physical examination, electrocardiographic, and echocardiographic findings. Written informed consent was obtained from all subjects.

2.2. Speckle-tracking analysis by 2D echocardiography

Two-dimensional echocardiographic images performed with an Artida ultrasound system (Toshiba Medical Systems, Tokyo, Japan) with a PST-30SBT probe were used to obtain conventional 2D and Doppler parameters according to the American Society of Echocardiography guidelines [8]. 2D data acquisitions were also obtained, including parasternal long-axis and short-axis views and three standard apical views. The LV was divided according to the 16-segment model (6 basal, 6 mid-LV, and 4 apical) of the American Society of Echocardiography, and each segment was individually analyzed. Frame rates were set in 50 to 70 Hz in this study. The software automatically tracked the contour on subsequent frames after three endocardial markers were placed at end-diastolic frame. Adequate tracking could be verified in real time and adjusted by manual to ensure optimal tracking [26–29]. Short-axis images, obtained at the mitral valve, papillary muscle, and apical levels, were used to compute circumferential and radial strain (RS). Longitudinal strain was acquired in the apical 4-, 3-, and 2-chamber views, using similar methodology. The global strain was the mean value of 16 segments.

2.3. Speckle-tracking analysis by 3D echocardiography

3D images were acquired from apical positions with the 3D transthoracic probe (PST-25SX 1–4 MHz phased array matrix transducer). Full-volume acquisition, in which four adjacent subvolumes were captured over four consecutive cardiac cycles, was performed during patient on breathhold to minimize the artifact between the subvolumes. Temporal resolution was between 15 and 23 frames per cardiac cycle, depending on the heart rate. Care was taken to include the entire LV cavity and myocardium, including the epicardium within the full-volume data set.

The resultant 3D-STE data sets were analyzed with 3D-wall motion tracking (3D-WMT) software (Toshiba Medical Systems) by an experienced investigator, under blinded conditions. After setting two reference points at the base of the LV at the mitral valve level and one at the apex on two orthogonal apical views at the end-diastolic frame, the 3D-WMT software automatically tracked the endocardial and epicardial contours on subsequent frames through the entire cardiac cycle in three different vectors simultaneously. The endocardial border and myocardial thickness could be manually adjusted to optimize boundary position and tracking. The global strain values (AS, CS, LS and RS) were automatically calculated by the software.

2.4. Reproducibility analysis

Intraobserver and interobserver variabilities of 3D data were evaluated in 20 randomly subjects by two sonographers blindly. Intraobserver and interobserver variabilities were evaluated by means of intraclass correlation coefficients (ICCs).

2.5. Statistical analysis

Statistical analysis was performed using SPSS software version 17.0. Continuous variables were expressed as mean ± SD and nominal variables as percentages. Continuous variables between groups were compared by analysis of covariance in general linear model with LSD posthoc analysis for subgroup comparisons, adjusted for age, gender and BSA. The p values after adjustment are presented. Categorical variables were compared between groups by the Chi-square test. Comparisons of 2D and 3D data were assessed using paired-samples t tests. Two-tailed values of $p < 0.05$ were considered statistically significant. The relationship between continuous variables was analyzed using linear regression analysis.

Table 1
Clinical characteristics.

	Control (n = 46)	HFPEF (n = 58)	HFREF (n = 45)	p-Value
Demographics				
Ages, years	48 ± 12	70 ± 10[a]	65 ± 9[a,b]	<0.001
Male, n (%)	18 (39)	35 (60)[a]	40 (89)[a,b]	<0.001
Body surface area, m^2	1.61 ± 0.17	1.66 ± 0.18	1.73 ± 0.18[a]	0.017
Body mass index, kg/m^2	22 ± 3	25 ± 4[a]	24 ± 4[a]	<0.001
Heart rate, bpm	67 ± 11	71 ± 15	66 ± 13	NS
Systolic blood pressure, mm Hg	123 ± 11	142 ± 18[a]	119 ± 15[b]	<0.001
Diastolic blood pressure, mm Hg	76 ± 8	75 ± 11	74 ± 10	NS
NYHA class I/II/III/IV (%)	/	(29/64/7/0)	(11/56/29/4)	0.006
Coronary artery disease (%)	/	53	62	NS
Hypertension, n (%)	/	46 (79)	25 (56)[b]	0.01
Diabetes mellitus, n (%)	/	12 (21)	17 (38)	0.056
Medications, n (%)				
β blockers	/	38 (66)	29 (64)	NS
ACEI/ARB	/	36 (62)	32 (71)	NS
Calcium channel blockers	/	31 (53)	1 (2)[b]	<0.001
Diuretics	/	24 (41)	29 (64)[b]	0.02
Spironolactone	/	2 (3)	2 (4)	NS
Digoxin	/	0 (0)	6 (13)[b]	0.004
Statins	/	36 (62)	25 (56)	NS

Data are presented as mean ± SD or percentages.
ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; HFPEF, heart failure with preserved ejection fraction; HFREF, heart failure with reduced ejection fraction; NYHA, New York Heart Association.
[a] $p < 0.05$ compared with the control group.
[b] $p < 0.05$ compared with HFPEF group.