Three-Dimensional Principal Strain Analysis for Characterizing Subclinical Changes in Left Ventricular Function

Gianni Pedrizzetti, PhD, Shantanu Sengupta, MD, Giuseppe Caracciolo, MD, Chan Seok Park, MD, PhD, Makoto Amaki, MD, PhD, Georg Goliasch, MD, PhD, Jagat Narula, MD, PhD, and Partho P. Sengupta, MD, *New York, New York; Trieste, Italy; Nagpur, India and Vienna, Austria*

Background: Subendocardial strain analysis is currently feasible in two-dimensional and three-dimensional (3D) echocardiography; however, there is a lack of clarity regarding the most useful strain component for subclinical disease detection. The aim of this study was to test the hypothesis that strain analysis along the direction of strongest and weakest systolic compression (referred to as principal and secondary strain, respectively) circumvents the need for multidirectional strains and provides a more simplified assessment of left ventricular subendocardial function.

Methods: Strain analyses were performed by using two-dimensional and 3D echocardiography in 41 consecutive subjects with normal results on electron-beam computed tomography, including 15 controls and 26 patients with systemic hypertension. The direction of principal strain referenced the myofiber geometry obtained from diffusion tensor magnetic resonance imaging of a normal autopsied human heart. The incremental value of principal strain over multidirectional two-dimensional and 3D strain was analyzed.

Results: In healthy subjects, 50 $\pm$ 3% of the subendocardial shortening occurred in the cross-fiber direction (left-handed helical); this balance was significantly altered in patients with hypertension (P = .01). The magnitude of longitudinal and circumferential strain was similar in patients with hypertension and controls. However, the alteration of the directional contraction pattern resulted in reduced secondary strain magnitude in patients with hypertension (P = .01), and the differences were further exaggerated when the secondary strain was normalized by the principal strain magnitude (P = .004).

Conclusions: Two-component principal and secondary strain analysis can be related to left ventricular myofiber geometry and may simplify the assessment of 3D left ventricular deformation by circumventing the need to assess multiple shortening and shear strain components. (J Am Soc Echocardiogr 2014;27:1041-50.)

Keywords: Strain, Left ventricle, Mechanics, Subclinical disease

Myocardial strain analysis can provide mechanistic insights into left ventricular (LV) systolic function to detect early cardiac dysfunction in a variety of disease states before abnormalities can be observed with traditional LV function measurements.[1] However, LV deformation is three-dimensional (3D); thus, three strain values (i.e., longitudinal strain [LS], circumferential strain [CS], and radial strain) must be defined. Although the amount of shortening or stretch in the tissue describes the strain, sliding of tissues parallel to a border is described as shear (i.e., circumferential-longitudinal, circumferential-radial, and longitudinal-radial shear, respectively). Circumferential-longitudinal shear is the largest and is also referred to as twist deformation. Strain and shear deformation together help define deformation in three dimensions, but there are several unresolved issues. First, it is relatively unclear how all of these components can be interlinked to simplify the clinical assessment of myocardial deformation. Second, the relations among the different strain or shear components and their anatomic correlation are still not completely understood.[2,3] Although the unique counterdirectional helical arrangement of cardiac fibers in the left ventricle is responsible for global LV deformation, LS, CS, and radial strain refer to geometric directions that do not correspond to any specific orientation of myocardial contractile elements and therefore could be inadequate for easily linking the structure and function of the left ventricle at the myocardial tissue level.

Principal strain analysis (PSA) is a method for describing multidimensional deformations that is widely applied in structural engineering.[4] It identifies the effective directions along which strain develops

From the Zena and Michael A. Wiener Cardiovascular Institute, Mount Sinai School of Medicine, New York, New York (G.P., S.S., G.C., C.S.P., M.A., J.N., P.P.S.); Department of Engineering and Architecture, University of Trieste, Trieste, Italy (G.P.); Sengupta Hospital and Research Center, Nagpur, India (S.S., P.P.S.); Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria (G.G.).

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Reprint requests: Partho P. Sengupta, MD, Mount Sinai School of Medicine, One Gustave L. Levy Place, PO Box 1030, New York, NY 10029 (E-mail: *sengupta.partho@mountsinai.org*).

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Abbreviations

CI = Confidence interval

CS = Circumferential strain

GPS = Global principal strain

GSS = Global secondary strain

LS = Longitudinal strain

LV = Left ventricular

PSA = Principal strain analysis

3D = Three-dimensional

3DFT = Three-dimensional speckle/feature-tracking

2D = Two-dimensional

and the entity of actual contraction therein. PSA is particularly well suited for biologic tissues with an underlying structure of muscular fibers along which the stress is generated. The direction along which strain develops, called the "principal direction," can be related to the actual fibers' direction. Therefore, application of PSA to myocardial deformation may be useful in characterizing effective LV contractile function corresponding to the underlying anatomic structure.[5,6] Application of PSA to the endocardium could permit referring to the volumetric change in terms of fiber shortening. The directional pattern of contraction, along with the values of principal and secondary strain, which develops along and orthogonal to the principal direction, respectively, help in providing an integrated perspective of myocardial shortening rather than using individual descriptions resolved along the longitudinal and circumferential directions, including circumferential-longitudinal shear or LV twist. Here, principal strain reflects the primary outcome of fiber shortening, while secondary strain better reflects the transversal connection between adjacent fibers. Given such a conceptual groundwork, PSA may simplify the assessment of tissue deformation, circumventing the need for multidirectional strain assessments.

In the present investigation, we applied PSA in a cohort of healthy, young, normal controls. The principal directions of strain were compared with the myofiber geometry obtained using diffusion tensor magnetic resonance imaging (DT-MRI)[7,8] from an autopsied normal human heart. We also compared the control group with a cohort of asymptomatic middle-aged subjects with hypertension and normal LV ejection fractions as a model for the presence of subclinical LV dysfunction. Hypertension is the most prevalent risk factor for the development of diastolic dysfunction and heart failure in the community.[9] Recent investigations have suggested that patients with high normal blood pressure and systemic hypertension have subclinical myocardial dysfunction even before the development of LV hypertrophy.[10,11] The objectives of the study were (1) to measure principal and secondary strains from 3D echocardiography and verify their associations with the myofiber arrangement of the human left ventricle and (2) to evaluate the ability of this approach in revealing subclinical modification in LV contraction in patients with systemic hypertension with structurally normal hearts.

METHODS

We prospectively recruited 20 healthy volunteers from a tertiary care hospital in Nagpur, India. The control subjects were free from any type of cardiac disease and had normal results on echocardiography. The final analysis was restricted to 15 volunteers (mean age, 34 ± 8 years; eight women) because 3D imaging data were considered suboptimal in five subjects. For reference, high-quality DT-MRI data from an explanted normal human heart maintained in formaldehyde were obtained from publicly available data sets (http://gforge.icm.jhu.edu/gf/project/dtmri_data_sets/) provided by Drs Patrick A. Helm and Raimond L. Winslow at the Center for Cardiovascular Bioinformatics and Modeling at Johns Hopkins University (Baltimore, MD) and Dr Elliot McVeigh at the National Institutes of Health (Bethesda, MD). A total of 35 middle-aged Indian subjects with systemic hypertension were subsequently studied at the same center in Nagpur. The analysis was restricted to 26 cases (mean age, 47 ± 8 years; 13 women), because the data from the remaining nine patients were deemed suboptimal for 3D speckle-tracking. The diagnosis of hypertension was defined on the basis of the patients' clinical histories. All patients were taking antihypertensive medications at the time of study enrollment, and the medications were continued during the study period to more effectively reflect the clinically compensated situation. The enrollment criteria included normal LV function assessed by transthoracic echocardiography (ejection fraction > 55%), and sinus rhythm was required. The exclusion criteria included the presence of coronary artery disease, QRS duration ≥ 120 msec, arrhythmia, evidence of secondary hypertension, chronic renal failure, diabetes mellitus, valvular heart disease, liver disease, systemic inflammation, or other comorbidities that might affect cardiac function. The absence of subclinical coronary vascular disease was verified on the basis of screening electron-beam computed tomography. The ethics committee of the hospital in Nagpur, where all subjects were recruited, approved the study. Written informed consent was obtained from all patients and controls before their enrollment in the study. The final analysis of the echocardiographic images was performed in the Echocardiography Core Laboratory at Mount Sinai Hospital (New York, NY).

Standard B-Mode and Doppler Two-Dimensional (2D) Echocardiography

Standard 2D and Doppler transthoracic echocardiographic studies were performed using commercially available ultrasound systems (Vivid 7; GE Healthcare, Milwaukee, WI), and echocardiographic images were obtained according to the standard guidelines recommended by the American Society of Echocardiography.[12] The ultrasound settings were adjusted to optimize the endocardial definition. Routine standard echocardiographic examinations were performed, including measurements of LV systolic and diastolic dimensions, LV end-diastolic wall thicknesses, LV hypertrophy, LV end-systolic volume, LV end-diastolic volume, LV mass, and left atrial volume index. The LV ejection fraction was computed using the modified biplane Simpson's method from the apical four- and two-chamber views. The mitral early diastolic flow (E) and late diastolic flow (A) velocities were measured, and the E/A ratio was calculated. The deceleration time of the mitral E wave was also measured. Doppler tissue imaging was obtained from the apical four-chamber view. The septal and lateral wall tissues were measured using pulsed-wave Doppler tissue imaging at the septal and lateral mitral annulus and were averaged (over three-beat recording assessments) to obtain the mean early diastolic mitral annular velocity and the ratio of early diastolic transmitral flow velocity to early diastolic mitral annular velocity.

2D Strain Analysis

B-mode images were recorded at optimal frame rates for speckle-tracking echocardiography (≥30 frames/sec, also ensuring ≥30 frames/heartbeat) and optimal resolution for the myocardium by focusing the image on the entire left ventricle; images were stored