Analysis of the Interaction Between Segmental Relaxation Patterns and Global Diastolic Function by Strain Echocardiography

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Background: **Strain echocardiography can depict segmental mechanical activity with high temporal and spatial accuracy, and may allow assessment of segmental relaxation not possible with conventional echocardiography.**
Methods: **Conventional and strain echocardiography were performed in healthy volunteers (young [group 1] and old [group 2]) and patients with normal 2-dimensional and stress echocardiography, with either normal global diastolic function (group 3a) or grade I or II global diastolic dysfunction (DD) (group 3b). Standard echocardiography criteria were used to define global DD. Early to late diastolic strain rate ratio less than 1.1 was defined as altered segmental relaxation.**
Results: **All participants had normal wall motion and ejection fraction. Participants of group 1 had normal segmental and global diastolic function. Participants of groups 2 and 3a demonstrated a wide range of altered segmental relaxation in the absence of global DD. All patients of group 3b had 12 or more segments with altered relaxation and global DD. Age and hypertension were associated with a larger number of altered segments, a lower mean early to late diastolic strain rate ratio, and global DD.**
Conclusions: **A wide range of altered segmental relaxation can exist in the absence of global DD. Age and hypertension are associated with altered segmental relaxation and global DD. Assessment of segmental relaxation may be beneficial in the elderly and patients with hypertension.** (J Am Soc Echocardiogr 2005;18:901-906.)

Heart failure caused by diastolic dysfunction (DD) is being increasingly recognized as the cause of significant morbidity, particularly in the elderly.[1] Global DD is most commonly identified by Doppler echocardiography.[2] Although it is assumed that there are interactions between regional and global diastolic function, the lack of appropriate techniques has prevented the characterization of this interaction. Strain echocardiography (SE) is a recently validated technique that can depict segmental mechanical activity with high temporal and spatial accuracy, and may allow assessment of segmental DD.[3,4] An understanding of the interaction between segmental relaxation mechanics and global flow/pressure-related phenomena (as depicted by transmitral Doppler and mitral annulus velocity) might yield important insights into the mechanisms of progression to global DD. We used SE in participants with preserved global and regional systolic function, with and without global DD, to better understand the interactions between changes in segmental relaxation and global DD.

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METHODS

Participants

This protocol was approved by the institutional review board. Three groups of participants were recruited: volunteers who were healthy and young (group 1); volunteers who were healthy and old (group 2); and patients (group 3). Those of groups 1 and 2 had no hypertension (blood pressure $< 130/85$ mm Hg), diabetes, or hyperlipidemia; were not taking any cardioactive medications; and had normal echocardiographic Doppler examination results including normal diastolic function. Members of group 3 were recruited from consecutive patients referred for clinical echocardiography with low to intermediate pretest probability for coronary artery disease (CAD) and a normal stress echocardiogram result. Of the 40 consecutive patients recruited, 20 had normal diastolic function

(group 3a) and 20 had grade I or II DD by echocardiographic Doppler criteria (group 3b). All participants had ejection fraction greater than 0.55 (by modified Simpson's method), no left ventricular hypertrophy (wall thickness $>$ 12 mm), and normal wall motion as assessed by an independent, experienced echocardiographer at rest and peak stress (group 3). All patients for group 3 had normal stress echocardiogram results.

Echocardiography

A system (Vivid 5, GE Medical Systems, Milwaukee, Wis) with a 3.5-MHz phased-array transducer was used for both conventional and SE imaging. Conventional echocardiography was performed using standard projections at rest and with stress,[5] whereas SE was restricted to apical projections only at rest. High frame rate SE (~200 frames/s) was performed with a narrow sector to yield the maximum temporal resolution (~5 milliseconds). Digital images were stored on magneto-optical disk and transferred to a workstation for offline analysis.

Global diastolic function. Standard echocardiographic Doppler criteria were used to grade the degree of global DD.[2] Transmitral Doppler flow was recorded at rest and during Valsalva's maneuver. A decrease in mitral early to late inflow velocity ratio of 0.5 during a Valsalva's maneuver was used to differentiate normal from pseudonormal (grade II) DD. Tissue velocities were measured at the lateral and septal mitral annulus and averaged to yield the final mitral annulus early (e') and late (a') velocity per subject.

Regional diastolic function. An 18-segment modification of the American Society of Echocardiography model was used for segmental analysis (6 apical segments vs 4). Peak systolic and diastolic Doppler tissue velocities and strain rate (SR) were determined for each echocardiographic segment. Analogous to transmitral Doppler, SE diastolic tracings record an early and late diastolic peak (Figure 1). SR signal can be contaminated by background artifact and peak amplitudes may vary depending on the angle of the incident ultrasound beam and image quality. We used the early to late diastolic SR (SR_{EA}) ratio to define normality. We used data from group 1 to define the normal values for the SR_{EA} ratio. Segments with SR_{EA} ratios below 2SD of the mean value were labeled as having an altered relaxation pattern as compared with young participants (altered segments). The number of altered segments was determined for each participant. The SR_{EA} ratio was generated for each segment and averaged to yield a participant SR_{EA} ratio (participant SR_{EA} ratio = sum of SR_{EA} ratio for 18 segments/18). A mean peak systolic SR was similarly calculated per participant.

Statistics

Using existing preliminary data, the minimum detectable difference in participant SR_{EA} ratio was calculated as 0.25 (assuming n = 10/group, respectively) for 80% power and $\alpha = 0.05$. Differences among groups were tested using the χ^2 statistic for discrete variables and the rank sum test for continuous variables. Pearson correlation coefficient was used to assess the association between continuous variables. Univariate and multivariate logistic regression models were used to test the relation of age and hypertension to SR ratios. A P value less than .05 was considered significant.

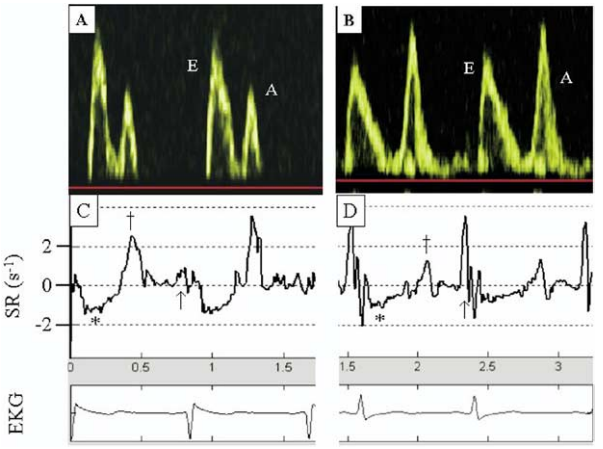

Figure 1 Transmitral Doppler flow velocity tracing illustrates normal (E/A ratio $>$ 1.0) (**A**) and abnormal (E/A ratio $<$ 0.75) (**B**) global diastolic function. Strain rate (*SR*) imaging illustrates normal (early-late diastolic SR ratio $>$ 1.1) (**C**) and abnormal (early-late diastolic SR ratio $<$ 1.1) (**D**) segmental relaxation. Peak (*), early (†), and late (*arrow*) diastolic waves. *Lower panels* in **C** and **D** show electrocardiographic (*EKG*) trace for time reference.

RESULTS

Participants

In all, 20 volunteers and 52 patients were enrolled. Twelve patients were excluded because two or more echocardiographic segments were suboptimal for SE analysis. Group 3 was significantly different from the control groups with regard to prevalence of chest pain, dyspnea, medications, hypercholesterolemia, diabetes, and hypertension (Table 1) (Table 2). In group 3, there was normal diastolic function in 20 patients; global DD was classified as grade I in 14 patients and grade II in 6 patients. The ratio of early mitral inflow to mitral annular velocity (E/e') was higher in group 3 compared with groups 1 and 2 (17 $\pm$ 5 vs $P < .001$). All patients had normal ejection fraction and normal segmental wall motion by visual interpretation. Peak systolic SRs were statistically similar among all groups (1.38 $\pm$ 0.29, 1.25 $\pm$ 0.22, and 1.39 $\pm$ 0.25 s^{-1}, respectively; $P = .3$).

Diastolic Function

All volunteers for groups 1 and 2 had normal global diastolic function as judged by standard