Impact of Left Ventricular Size on Tissue Doppler and Longitudinal Strain by Speckle Tracking for Assessing Wall Motion and Mechanical Dyssynchrony in Candidates for Cardiac Resynchronization Therapy

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Background: Myocardial dysfunction and left ventricular (LV) geometry deformation may reduce the accuracy of tissue Doppler imaging (TDI) in assessing myocardial contractility.

Methods: In 92 patients with heart failure who underwent cardiac resynchronization therapy (CRT), we assessed the impact of LV end-diastolic volume on the accuracy of peak longitudinal velocity (TDI) and strain (ϵ_L by speckle tracking) to assess regional wall motion and LV dyssynchrony.

Results: Peak-ϵ correlated to normal ($-13\% \pm 6\%$, n = 259), hypokinetic ($-10\% \pm 5\%$, n = 347), and akinetic ($-7\% \pm 5\%$, n = 498, $P < .0001$) wall motion independent of LV size. In contrast, velocity failed to distinguish normal from dysfunctional segments in patients with severe LV dilatation (end-diastolic volume > 250 mL). The 12 standard deviation of time to peak systolic velocity and the opposing septal-lateral wall delay by strain and TDI failed to predict response to CRT, whereas the 12 segment standard deviation of time to peak ϵ correlated to end-systolic volume reduction ($r = -0.39$, $P < .001$).

Conclusion: Accuracy of TDI in assessing LV wall regional motion is limited in severely dilated ventricles and probably affects LV dyssynchrony measurement. (J Am Soc Echocardiogr 2009;22:695-701.)

Keywords: Cardiac resynchronization therapy, Tissue Doppler, Speckle tracking

Several large clinical trials have confirmed the sustained benefit of cardiac resynchronization therapy (CRT) in patients with symptomatic severe left ventricular (LV) dysfunction and wide QRS duration.[1-8] The beneficial effects of CRT include improvement of symptoms,[1-8] ejection fraction,[2,4,8] mitral regurgitation,[1,4] LV remodeling,[1,2,4] and survival.[8] Despite these encouraging results, approximately 30% of patients selected according to QRS duration criteria do not respond to CRT.[8] Observational studies have consistently demonstrated that the main predictor of responsiveness to CRT is mechanical rather than electrical dyssynchrony.[9-14] Measurement of regional longitudinal myocardial electrical-mechanical events at the base of the heart using velocity data acquired with tissue Doppler imaging (TDI)[12,15] has been proposed to enhance the identification of mechanical dyssynchrony and thus patient selection for those likely to respond to CRT. In patients with heart failure (HF), TDI has had an ever increasing clinical utility because peak systolic longitudinal velocity is used for assessing ventricular function.[16] However, in patients with HF, spherical LV deformation affects the base of the heart predominantly and increases the misalignment of Doppler incidence angle along with myocardial motion. Together with reduction of tissue velocity caused by myocardial dysfunction, the reduction in signal/noise ratio could explain the lesser accuracy of TDI to reliably represent myocardial motion in patients with HF. In the present study, we evaluated the impact of LV size on the accuracy of peak velocity and time to systolic velocity by TDI to quantify LV regional wall motion and dyssynchrony in patients with HF before CRT compared with peak and time to peak strain (ϵ) by two-dimensional (2D) speckle tracking.

MATERIALS AND METHODS

Study Population

The study included 92 patients with symptomatic HF and QRS duration > 120 ms who had conventional TDI and longitudinal ϵ analysis by 2D speckle tracking before implantation of a biventricular device. The study was conducted in a retrospective and prospective consecutive group of patients.

The retrospective group was selected from 589 consecutive patients with HF who underwent implantation of a biventricular device

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at the Cleveland Clinic between January 2005 and December 2006. Patients were selected if they had a complete baseline echocardiographic study performed 3 months before device implantation on a Vivid 7 system (GE, Vingmed System 7, Horten, Norway) and an echocardiographic follow-up (>3 months) was available (120/589). Complete baseline echocardiography included standard grey scale and color TDI in the apical views (2, 3, and 4 chamber) with high frame rates (>35 frame/sec). Of these 120 selected patients, 50 were excluded (5 had implants < 3 months after an acute coronary syndrome or cardiac surgery, 41 had > 2 nonanalyzable segments by 2D speckle tracking [n = 30] or TDI [n = 17], and 4 had permanent atrial fibrillation). After device implantation, 5 additional patients were excluded (inadequate CRT delivery, ie, LV pacing rate was < 50%, 3 with paroxysmal atrial fibrillation, and 2 with an increased LV lead threshold). Ultimately, 65 patients were included in the retrospective group.

Prospective

The study was prospectively conducted in a cohort of patients with HF who were recruited consecutively before biventricular device implantation at the Cleveland Clinic from January 2007 to May 2007. Patients were included if they met all the following criteria: symptomatic HF, age between 18 and 75 years, left ventricular ejection fraction (LVEF) < 35%, and sinus rhythm with QRS duration > 120 ms. Exclusion criteria were recent cardiac event (<3 months after an acute coronary syndrome or cardiac surgery), inadequate CRT delivery after 3-month follow-up (LV pacing rate was < 50%), and > 2 nonanalyzable segments by speckle tracking or TDI. Patients in the study (n = 27) underwent 2D echocardiography before implantation on a Vivid 7 system with high frame rate and color TDI in the apical views. At 3 months, 2D echocardiography was repeated to quantify reverse remodeling after CRT. All patients had given informed consent, and the study protocol was approved by the Cleveland Clinic Review Board.

Biventricular Pacemaker Implantation

CRT was provided in the standard fashion with 3 transvenous leads. The right atrial and ventricular (apical site) leads were positioned conventionally. The LV lead was inserted through the coronary sinus and positioned into the lateral (n = 33), posterolateral (n = 41), anterolateral (n = 8), or middle cardiac vein (n = 4). Lead position was defined by coronary sinus angiogram data. Epicardial implantation was required in 6 patients. Biventricular pacing devices used included Medtronic (Minneapolis, MN, n = 54), Saint Jude Medical (Sylmar, CA, n = 25), and Guidant-Johnson and Johnson (Boston, MA; n = 13). After implantation, the atrioventricular interval was adjusted for optimal diastolic filling using Doppler echocardiographic assessment of mitral inflow, and V-V timing was programmed to be simultaneous in all cases. All devices were systematically interrogated within 3 months after the CRT procedure to ascertain their proper functioning.

Follow-up

Baseline and 3-month clinical characteristics were extracted from medical reports. Responders were defined by the presence of significant reverse remodeling (LV end-systolic [LVES] volume reduction > 15% by Simpson biplane method) at 3 months after CRT.

Quantification of Myocardial Function

Regional wall motion was graded semiquantitatively as normal, hypokinetic, and akinetic in the 12 apical segments (mid and base) of the ventricle by 2 independent experienced physicians blinded to strain values. A consensus grading was used for segments with discordant scoring. The apical segments were not analyzed because of the unfavorable angle of apical myocardial motion and geometry with respect to the transducer orientation. End-diastolic volume (EDV) and end-systolic volume were determined using biplane Simpson method to compute LVEF by an experimented physician blinded to strain and TDI data.

Peak Velocity (by Tissue Doppler Imaging) Analysis

Basal and midventricular velocity curves (n = 12) derived from color TDI sequences (EchoPac, GE Vingmed, Horten, Norway) were exported for off-line analysis. Peak and time to peak velocity were automatically computed on Excel (Microsoft Corp, Redmond, WA). The reference timing point was defined at the end diastole (at the peak of the R wave on the electrocardiogram tracing) with the timing of systole defined as aortic valve opening and closure determined by sampling LV outflow tract pulsed Doppler flow. When the velocity curve was exclusively negative during the systolic ejection period, time to peak velocity was defined at end systole and peak velocity was considered to be zero. Significant LV dyssynchrony was considered when the 12-segment standard deviation of time to peak systolic velocity (12SD-TDI) and the septal-lateral opposing wall delay were > 33 ms[15] and > 65 ms,[12] respectively.

Peak Longitudinal Strain by Speckle Tracking Analysis

To compute longitudinal ϵ curves by 2D speckle tracking (EchoPac), end diastole was chosen as the reference time point. Mid and basal ventricular segment strain curves were exported for an automatic analysis in Excel. Peak ϵ and time to peak ϵ in the 12 segments was defined as the minimum value of the ϵ curve within the cardiac cycle and the time to this minimum value, respectively. The 12 segment standard deviation of time to peak ϵ (12SD-ϵ)[17] and the opposing septal-lateral strain delay were used to define LV dyssynchrony.

Statistical Analysis

Normally distributed continuous variables were expressed as mean ± SD. Dichotomous data were expressed as percentages. We assessed the impact of segment location and LV size on the accuracy of peak systolic velocity and strain to evaluate wall motion by using 2-way analysis of variance. To compare numeric data between 2 groups, paired and unpaired Student *t* tests were used as appropriate. Dichotomized comparisons were assessed by the chi-square test or Fisher's exact test. Linear correlation was used to compare continuous variables. SD-TDI and SD-ϵ were adjusted to RR interval according to Bazett's formula[18] for comparison. Interobserver and intraobserver variability were assessed in 10 random patients and expressed as the SD of the difference between 2 paired measurements and as a percentage of variability (SD was divided by the average value of the variable). Two-tailed probability values less than .05 were considered statistically significant.

RESULTS

The study population had an average age of 63 ± 13 years, 66 were male, and 93% (n = 86/92) were severely symptomatic (New York Heart Association class III) with a mean LVEF of 25% ± 9%, a QRS duration of 154 ± 29 ms, and a mean EDV of 235 ± 90 mL (Table 1).