QRS Duration Alone Misses Cardiac Dyssynchrony in a Substantial Proportion of Patients with Chronic Heart Failure

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Background: **The primary determinate for the indication of cardiac resynchronization therapy in symptomatic chronic heart failure currently is a prolonged QRS duration. This is based on the premise that a prolonged QRS duration is a marker of left ventricular (LV) dyssynchrony. Tissue synchronization imaging (TSI) is an emerging technology that uses tissue Doppler velocities to determine the time to peak velocity of regions of the ventricular myocardium.**

Objectives: **Our objectives were to determine the prevalence of dyssynchrony in a cardiomyopathic population referred for echocardiography irrespective of QRS duration, to validate the novel technique of TSI in evaluation of mechanical LV dyssynchrony and to determine the accuracy of QRS duration in predicting significant LV dyssynchrony.**

Methods: **A total of 100 patients with significant LV dysfunction (Simpson's ejection fraction ≤ 35%) referred for echocardiography underwent TSI. Dyssynchrony was defined as a difference in time to peak contraction of greater than 105 milliseconds between opposing ventricular segments.**

Results: **Overall, 61 patients (61%) demonstrated significant dyssynchrony, whereas 52% had a QRS duration of greater than 120 milliseconds. Among those with a prolonged QRS duration, significant dyssynchrony was evident in 30 (58%). However, dyssynchrony was also common among those with a narrow QRS duration (<120 milliseconds) (31 patients [65%]). Of the 61 patients with dyssynchrony, 31 (51%) would have been missed if QRS criteria were used alone.**

Conclusions: **A substantial proportion of patients have dyssynchrony by TSI, but do not have a prolonged QRS duration. These patients may benefit from cardiac resynchronization therapy but on traditional criteria would be excluded from the therapy. Expanding the criteria for cardiac resynchronization therapy to include echocardiographic parameters may extend the benefit of this technology to a greater population in need.** (J Am Soc Echocardiogr 2006;19:1257-1263.)

Patients with chronic heart failure (CHF) have a poor prognosis and are highly symptomatic.[1] The added insult of left ventricular (LV) dyssynchrony increases morbidity and mortality.[2,3] Cardiac resynchronization therapy (CRT) involves the implantation of a biventricular pacemaker and has been shown to improve quality of life, symptoms,[4-6] and, more recently, mortality[7] in patients with drug-refractory CHF and prolonged electrocardiographic (ECG) QRS duration (≥120 milliseconds). CRT improves the ventricular activation sequence that coordinates the LV motion, giving improved ejection efficiency. However, CRT trials consistently show that 25% to 30% of patients with a prolonged QRS duration do not respond to CRT. This may reflect the absence of mechanical dyssynchrony in patients with a wide QRS indicating the need for additional or superior selection criteria to identify potential responders.[4-7] Moreover, it has recently been suggested that patients with CHF and a narrow QRS complex may also have mechanical LV dyssynchrony and, therefore, may benefit from CRT.[8,9]

The current criteria for CRT in patients with symptomatic CHF (New York Heart Association class III-IV) is an ejection fraction (EF) less than 35% and a QRS duration on ECG of longer than 120 to 150 milliseconds.[10] The premise being a prolonged QRS duration reflects cardiac dyssynchrony. Echocardiography and, in particular, Doppler tissue imaging (DTI) have been shown to demonstrate mechanical cardiac dyssynchrony noninvasively.[11-17] Tissue synchronization imaging (TSI) is a novel echocardiographic imaging modality that is able to rapidly assess LV mechanical dyssynchrony.[16,18,19]

Our aims were to: (1) determine the prevalence of significant dyssynchrony in a general cardio-

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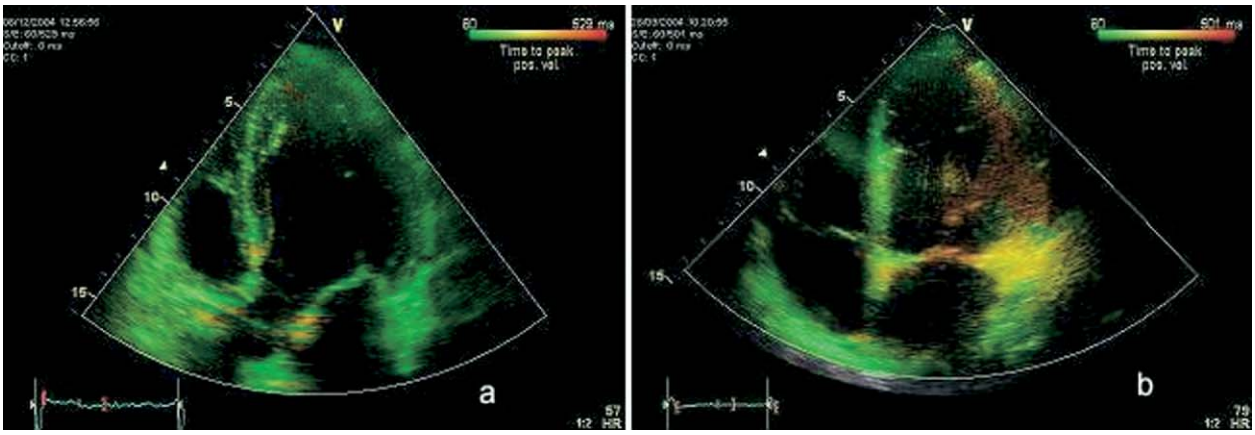

Figure 1 Tissue synchronization imaging. Apical 4-chamber views demonstrating normal time to peak velocity data (*green*) (**A**) and significant lateral wall delay (*red*) with no significant delay seen in septal region (**B**).

myopathic population; (2) validate TSI as a marker of mechanical LV dyssynchrony; and (3) determine the accuracy of QRS duration in predicting significant LV dyssynchrony.

METHODS

This study was approved by our research ethics committee.

Patients

The population consisted of 100 consecutive patients with CHF referred for an echocardiogram with a Simpson's EF of 35% or less and having had an ECG within 1 month of the echocardiogram being performed. All studies were performed on commercially available equipment (Vivid 7; GE Healthcare, Sydney, Australia). Patients with CRT, with a pacemaker in situ, or in atrial fibrillation were excluded from this study.

Echocardiography

Biplane Simpson's EF was calculated from the apical 2- and 4-chamber views. Diastolic function was assessed according to standard criteria.[20] Significant diastolic dysfunction was deemed as being present if there was a pseudonormalized or restrictive filling pattern evident from the mitral inflow pulsed wave Doppler profile.

During the echocardiographic study, each apical view (2, 4, and long axis) was overlayed by the DTI color map, optimized to give the highest frame rate by reducing depth and sector size and then 3 or more cardiac cycles for each view were digitally stored. All images were analyzed offline (EchoPac, GE Healthcare). Only DTI with a frame rate of greater than 100 cycles/s were considered for analysis.

TSI Assessment

The timing of mitral and aortic valve opening and closure were determined using the pulsed wave Doppler spectral tracings from each of these valves. Using these timings the TSI interval start time was manually set to begin analysis at aortic valve opening and cease analysis at aortic valve closure to reduce interference from postsystolic contraction.

TSI analyzes tissue Doppler velocity signals within the ventricular myocardium, to determine the timing from the QRS to the peak systolic velocity. This time to peak velocity information is assessed for every pixel in the region of interest, and is color coded over the 2-dimensional image according to the timing. The time to peak velocities are color coded green for normal timing, yellow for moderate delay, and red for a severe delay. Therefore, a ventricle with normal time to peak velocities is color coded green over the myocardium (Figure 1, *A*) and a ventricle with a significant delay in one of the walls is color coded yellow or red over the delayed wall (Figure 1 *B*).

For quantitative assessment the TSI picture was frozen, scrolled to end systole, and regions of interest (each 6 × 12 mm) placed manually on opposing walls within the LV myocardium at a basal and midlevel on the following walls: septal, lateral, inferior, anterior, posterior, and anteroseptal. The time to peak numbers were recorded for each apical view giving 12 measures of time to peak velocity (Figure 2). This 12-segment model of dyssynchrony is the same as the model used by Yu et al[11,19] and has been found to be a reliable assessment of mechanical dyssynchrony. The time to peak velocities of opposing walls at the same level (ie, basal to basal and midwall to midwall) were subtracted from one another to determine the delay between the opposing walls giving 6 measurements of delay.