In Search of a Holy Grail
Predicting Cardiac Resynchronization Therapy Outcomes by Echocardiography

Zoran B. Popović, MD; James D. Thomas, MD

The contraction of ventricular segments can be quantified by myocardial velocities, strains, or strain rates. Whereas myocardial velocities simply represent a movement of a segment relative to some reference point, strains measure relative local deformation along 3 major cardiac axes. Plotting the changes of myocardial velocities, strains, or strain rates of individual segments through time can give us insight into ventricular function synchrony. Intraventricular dysynchrony can then be quantified by how much peak values of these segmental tracings vary in their timing or in their maximal values (amplitudes).

Early on, magnetic resonance imaging strain studies showed that left bundle-branch block leads to uncoordinated contraction of ventricular segments and results in intraventricular mechanical dyssynchrony.\(^6\) Magnetic resonance imaging studies have also shown that earliest contracting segments show mid-systolic blunting of contraction (because of late forceful contraction of lateral segments), often with late- (or even post-) systolic peak.\(^7\) In contrast, late contracting segments contract forcefully because of early stretch and activation of the Starling mechanism.\(^7\) Indeed, this interplay of early and late segments is the basis for using preexcitation of ischemic segments to prevent postinfarct remodeling.\(^8\) Magnetic resonance imaging studies also have shown that CRT decreases both time- and amplitude-based measures of intraventricular dyssynchrony.\(^6,9\) In addition to this intraventricular dyssynchrony, interventricular dyssynchrony also exists (as is well known to anybody who has auscultated a patient with bundle-branch block), although its importance is less well established.\(^10\)

Analysis of 3-dimensional segmental strains by magnetic resonance imaging is complex and not widely available. Therefore, the echocardiographic community has worked hard to develop predictive methods that are simple, robust, and efficient. Three major questions have emerged from nearly a decade of research: Should one measure dispersion in timings, or in the amplitude, of segmental signals? Should one use velocity- or strain-based measures? Should one measure timing of the onset of contraction or its peak?

The first methods to gain wide acceptance were velocity-based measures of dispersion in timing derived from tissue Doppler imaging. Several single-center studies have shown them to be accurate in predicting the outcome of CRT and to be superior to time-domain strain-based measures of dyssynchrony. Two recent studies that used time-based velocity dyssynchrony measures were not very encouraging, however. The multicenter Cardiac Resynchronization Therapy in Patients with Heart Failure and Narrow QRS (RethinQ) trial did not show that CRT was beneficial to patients with significant
dyssynchrony but narrow QRS complexes, whereas the large Predictors of Response to CRT (PROSPECT) trial showed that similar velocity-based temporal measures have little prognostic value, challenging their widely believed applicability.

Hence the study of Miyazaki et al and the search for something better. The investigators studied 45 patients before and after biventricular pacing, examining several proposed indices of dyssynchrony. They demonstrated that many of the most popular indices (using time to peak tissue velocity in a variety of segments) did not predict response to resynchronization, whereas time to peak strain showed much better correlation. This was somewhat surprising because several larger previous trials that compared strain and velocity dyssynchrony showed the opposite result. The reasons for this are unclear, though perhaps improvements in both instrumentation and technique (such as narrowing the acquisition sector width) may have allowed strain to overcome its prior problems of excessively noisy signals. On the other hand, failure of velocity data should not be entirely unexpected. Segmental velocities are affected by a number of factors, such as local tethering and apico-basal position. For example, it is fairly common that patients with nonischemic dilated cardiomyopathy and prominent left-to-right rocking during systole (ie, with “longitudinal rotation”) have depressed, double-peaked velocities of the basal lateral wall (Figure). This kind of velocity tracing is almost impossible to interpret by standard time-to-peak measures.

So, is this the end of a rainbow? We must recognize several problems with the study by Miyazaki et al. First, it represents a relatively small group of only 45 patients. Given the number of previous studies, some much larger than the present study, one has to be very cautious. Second, the strain measurements were derived from tissue velocity data, which are notoriously noisy and measure only the longitudinal strain component. Indeed, tissue velocity-derived strains may largely be a technique of the past, akin to videocassettes in the era of digital storage. It would have been more meaningful if the authors had used speckle tracking, which appears to present more robust strain data than does tissue velocity imaging. Speckle tracking also provides the potential to obtain not only longitudinal but also circumferential and radial strains that can provide information over and above the ones obtained from longitudinal strain. Also, one must wonder if strain rate, despite its noisy nature, would have provided a useful index, as it would seem to relate more specifically to delays in electrical activation, whereas strain itself has to integrate regional mechanical differences.

An even greater issue to consider is the persistent focus of the echocardiography community on time-based measures of dyssynchrony. Indeed, we have shown in a small study that an amplitude-based measure of dyssynchrony carries some prognostic weight. One could also speculate that methods that incorporate both time and amplitude information would be even more predictive. What is desperately needed, however, are ways to perform and interpret these studies more simply, allowing them to move out of the expert hands.
of just a few laboratories. One helpful tool would be a dynamic, bull’s-eye representation of the way strains change over time to provide an intuitive summary of the timing and magnitude of contraction. This type of display could help us define typical patterns of strain development during systole that underlie patient response to CRT. Ideally, in that situation, one could determine the necessity of CRT and the ideal location of the pacing electrode with the same certainty we have currently in determining the severity and pathoanatomic substrate of mitral regurgitation in patients with myxomatous mitral valve disease. Until that time, for clinical indications for CRT, we are left only with the crudest of tools: QRS complex duration and shape.

Sources of Funding
Dr Thomas is supported in part by the National Space Biomedical Research Institute through NASA Grant NCC9–58 (Houston, Tex) and the Department of Defense (Fort Dietrich, Md, USAMRMC Grant No. 02360007).

Disclosures
None.

References
3. Linde C, Gold M, Abraham WT, Daubert JC. Rationale and design of a randomized controlled trial to assess the safety and efficacy of cardiac resynchronization therapy in patients with asymptomatic left ventricular dysfunction with previous symptoms or mild heart failure—the RESynchronization reVerses Remodeling in Systolic left vEntricular dysfunction (REVERSE) study. Am Heart J. 2006;151:288–294.

Key Words: Editorials ■ echocardiography ■ cardiac resynchronization therapy ■ heart failure ■ pacing ■ pacemakers
In Search of a Holy Grail: Predicting Cardiac Resynchronization Therapy Outcomes by Echocardiography
Zoran B. Popovic and James D. Thomas

Circ Cardiovasc Imaging. 2008;1:3-5
doi: 10.1161/CIRCIMAGING.108.797175

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circimaging.ahajournals.org/content/1/1/3

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Cardiovascular Imaging can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Cardiovascular Imaging is online at:
http://circimaging.ahajournals.org//subscriptions/