EDITORIAL COMMENT

Myocardial Strain: Can We Finally Measure Contractility?*

T. P. Abraham, MD  
R. A. Nishimura, MD, FACC  
Rochester, Minnesota

There existed a divine essence which was the life force of the heart, given the name “contractility,” the essence of the essence of life . . . In the discovery of “contractility” lay the key . . . but how to discover it?  
Adapted from “Contractility Revisited” in the Journal of Molecular and Cellular Biology, 1972.

The measurement of myocardial performance is of critical importance for the diagnosis and management of the patient with cardiac disease. Despite decades of investigation, the search for the optimal method to measure the contractile properties of the myocardium still continues. Extrapolations from experiments in isolated muscle preparations and the intact animal heart have resulted in invasive measurements of myocardial function such as peak positive dp/dt, cardiac output, and maximal elastance (1–3). The two former procedures can now also be measured noninvasively, but they are highly dependent upon the loading conditions of the heart and have not been routinely used in clinical practice. The latter is an accurate measurement of the intrinsic contractility of the left ventricle but is impractical for clinical assessment given the need for simultaneous measurement of pressure and volume under varying preload and afterload conditions (3).

WHAT IS MYOCARDIAL STRAIN?

Clinicians relied upon indirect parameters of ventricular function (such as systolic time intervals) until echocardiography was introduced, which provided a direct visualization of the myocardium. Two-dimensional echocardiography has become the procedure of choice for examining the status of the left ventricle, with direct real-time visualization of endocardial motion and wall thickening (4). The most commonly used parameter of systolic function from two-dimensional echocardiography is the ejection fraction (EF), which is now routinely requested from all echocardiographic studies and is used by the clinical cardiologist for diagnosis, prognosis, and to determine therapy. However, the EF itself has major limitations as a measurement of the status of the contractile properties of the left ventricle. The measurement itself is subject to error whether using a subjective visual estimate or quantitative analysis, the latter assuming that an accurate tracing of endocardial borders can be obtained. Also, EF is a global assessment of left ventricular performance and does not take into consideration regional contractile dysfunction, which is commonly seen in patients with coronary artery disease and primary myocardial disease.

Thus, there continues to be a clinical need for an objective measurement of the contractile state of the myocardium. Despite the initial enthusiasm, technological advances in noninvasive ultrasound imaging such as acoustic quantitation and color-kinetics have not been routinely incorporated into the daily clinical practice (5). In this issue of the Journal, Edvardsen et al. (6) and Gotte et al. (7) have reported on the utility of strain measurements for assessment of the regional contractile properties of the myocardium, the former by tissue Doppler echocardiography and the latter by magnetic resonance imaging (MRI). The question that arises is whether this new measurement of myocardial performance will be able to accomplish what is needed—namely, an objective reproducible assessment of regional myocardial contractile function.

Measurement of strain by MRI. The first noninvasive measurement of strain was introduced by Zerhouni et al. (15) in 1988 and a year later by Axel and Dougherty (16) using myocardial “tagging” during MRI. Local perturbation of magnetization of myocardial tissue persists for a large fraction of a second and can be exploited to study motion of the myocardium. Magnetization of tissue is used to produce an MRI signal, and local perturbation of the magnetization is seen as a line on the MRI image, occurring at the
interception of the tag plane and the image plane. While selective excitation creates a small number of tags, nonselective excitation with spatial modulation of magnetization can construct a series of parallel tags. A second series of tags located orthogonal to the initial series will produce a tag grid. The positions of the tags can be tracked to describe the motion of a fixed point within the heart wall. Strain can then be calculated as the differential motion between two points normalized for their initial separation. Strain calculations are axis dependent and thus may differ in different directions at the same position in the heart. Therefore, strain is usually expressed as principal strain, which is the direction and magnitude of greatest compression and expansion at a given location. The strain rate is the differential velocity between two adjoining points and corresponds to the time derivative of strain. The MRI myocardial strain can be measured in three directions: radial, circumferential and longitudinal.

In this issue of the Journal, Gotte et al. (7) address the role of strain analysis of regional contractile function, using MRI in patients postmyocardial infarction. Thirteen patients following an anterior myocardial infarction were evaluated by MRI and were compared with findings from 13 age-matched healthy volunteers. Regional and global systolic function were obtained from cine short-axis images and expressed as percentage wall thickening, end-diastolic and end-systolic volume index, stroke volume index, and EF, respectively. Strain analysis was performed on tagged short-axis images. Principal lengthening strain, principal shortening strain and the angle between the maximum principal strain and the radial direction were calculated for the radial $(\varepsilon_r)$ and circumferential direction $(\varepsilon_\theta)$. Normal values for all parameters in each segment were established in the normal group. Values that exceeded 2 SDs from the normal mean were considered abnormal and labeled as dysfunctional myocardium. Although the percentage wall thickening was generally lower in all segments of the infarct group compared to the control group, no significant differences in percentage wall thickening were noted between the infarct and remote segments within the infarct group. This probably reflects the heterogeneity of regional contraction (17) and wide range of normal values (18), reducing the sensitivity of percentage wall thickening for distinguishing subtle differences in contractile function.

In contrast, strain analysis demonstrated significant differences in regional function among the infarct, infarct adjacent and remote areas. Both radial and circumferential strain values demonstrated a higher sensitivity for detection of dysfunctional myocardium when compared to percent wall thickening. Strain parameters showed better correlation with the global EF as compared to the percentage wall thickening. This study by Gotte et al. (7) confirms that strain parameters are more accurate in describing segmental function and correlate better with global measures of systolic function than percentage wall thickening.

There are some limitations to this study, however: 1) the study group was small; 2) the area of infarction was large enough to cause an overall drop in EF; 3) strain measurements were performed in radial and circumferential directions but not in the longitudinal direction; 4) only three short-axis slices were acquired for analysis; and 5) there was large variability of measurement of radial strain, especially in the lateral wall. Nonetheless, this study corroborates earlier animal data illustrating the usefulness of strain analysis in assessment of regional contractile function (19).

**Measurement of strain by tissue Doppler echocardiography.** Two-dimensional echocardiography has been described as the ideal imaging modality for assessment of global and regional ventricular function. By slicing the heart in multiple tomographic planes, real-time imaging of endocardial motion and wall thickening of the entire myocardium should be possible. Echocardiography is noninvasive, fast, portable and widely available at all cardiac centers. However, the actual application of echocardiography to regional myocardial function has been limited to a visual subjective assessment in most laboratories.

Tissue Doppler imaging (TDI) is an extension of conventional Doppler echocardiography that may provide additional information to two-dimensional echocardiography. Conventional Doppler echocardiography was originally developed to measure velocity and direction of blood flow (20). Modifications in the image acquisition process now enable direct measurement of tissue velocities (21,22). Ultrasound reflections from the fast-moving blood pool are high frequency and low amplitude, whereas those from slower-moving tissue are low frequency and high amplitude. By filtering out the high-frequency, low-amplitude echoes originating from the blood pool, the velocity of myocardial tissue can be measured. This is done using an autocorrelation technique, and the velocity profile is then shown either as a color or spectral display.

The initial application of TDI in quantifying myocardial mechanical activity was to measure the peak systolic and diastolic tissue velocities of a given segment (23). Investigators have shown that peak systolic velocity obtained by TDI can be a quantitative and objective measure of local systolic function both in rest and stress studies (24). However, this simplistic application of TDI does not efficiently discriminate between actively contracting and “tethered” myocardium, where a given akinetic segment will demonstrate motion in relationship to the fixed transducer if it is “pulled” by a more proximal contracting segment of myocardium (25).

The calculation of local velocity gradients (i.e., strain rates) can be made from TDI. Strain rate measures a vector component of regional myocardial contraction independent of the effect of tethering and translation. This technique directly compares the motion of two points along the ultrasound beam. These points move toward each other during contraction and away from each other during relaxation. Strain is the change in length corrected for the initial length, whereas strain rate is the rate of change. Strain rates
can be calculated from TDI data (strain rate imaging or myocardial velocity gradient) (25,26).

The potential advantage of strain rate imaging over conventional TDI in regional analysis of cardiac function is clearly demonstrated by Edvardsen et al. (6) in this issue of the *Journal*. In a setting of controlled ischemia during balloon inflation of a critically stenosed coronary artery, regional systolic function was quantified using TDI and strain rate imaging. Systolic dyskinesia was detected in the ischemic region in almost all patients by strain rate imaging but only in 65% of patients by TDI. In addition, reduced systolic velocities by TDI (suggesting abnormal systolic function) were found in the normally perfused basal septal segment in contrast to normal strain rate parameters in these segments. Again, limitations exist in this preliminary study: 1) small study group, 2) possible interplay of ischemic territories (only four patients in this group had isolated left anterior descending (LAD) artery stenosis, whereas 13 patients had additional circumflex or right coronary stenosis), and 3) no delineation of the exact territory supplied by the LAD artery. Overall, however, the study by Edvardsen et al. (6) demonstrates the clinical feasibility of strain rate imaging (technically acceptable images in 97% of the segments) in quantifying regional systolic function in a relatively objective manner and its superiority over TDI alone for analysis of regional myocardial function.

**Differences between MRI and TDI in assessment of strain.** Although both MRI and TDI are noninvasive, significant differences exist between the two in their assessment of myocardial function. The major difference is that these two techniques measure different parameters. Tissue Doppler imaging by echocardiography measures the velocity at two locations along the Doppler sample beam, whereas MRI measures the motion of two distinct points in the myocardium. Also, MRI measures Langrangian strain, while TDI measures natural strain. Whether these differences will translate into a clinical difference is unclear.

The advantage of measurement of strain and strain rate by echocardiography is that these values can be obtained in real time with high temporal and spatial accuracy. Both acquisition and storage of image clips are relatively easy and quick, and off-line strain analysis usually takes approximately 5 min per projection and about 15 min per patient. A major limitation of the echocardiographic technique is that measurements of strain are usually performed using apical projections alone and thus only the longitudinal strain is assessed. Although estimation of longitudinal strain may suffice, the incremental value of strain measurements in other dimensions has not been systematically assessed in disease states. As with all echocardiographic measurements, the measurement of strain and strain rate is limited by image and signal quality. The velocity profile signal tends to be noisy with current technology, and determination of peak velocities can be difficult. The tissue Doppler signal is angle dependent, and strain values are significantly different if the angle of the incident beam is over 20° (27). Strain analysis is affected by the quality of the gray scale image. Artifacts such as reverberation could lead to erroneous strain rates.

Magnetic resonance imaging can obtain data in three dimensions and thus is able to determine strain in all three directions. However, this estimation utilizes certain assumptions that may introduce an error (19). As spatial resolution increases, it may be theoretically possible to differentiate intramyocardial strains and therefore calculate subendocardial and subepicardial strains. The major disadvantage of MRI is that it is expensive, with limited availability. Acquisition times are long, requiring gating of multiple beats. The temporal resolution is currently suboptimal, and analyzing individual phases of the cardiac cycle (early diastole, for example) may be difficult. If combined with contrast imaging, a tagging study would have to be performed first as contrast agents shorten relaxation times and thus the tag would fade more rapidly. Postprocessing of tagged MRI images is time-consuming.

The clinical application of strain analysis by either technique will depend on the parallel development of faster acquisition and analysis programs. In echocardiography, “cleaning up” the signal will enable reliable and reproducible strain value measurements during routine clinical imaging. The use of real-time strain rate imaging, clutter filters and imaging with second-harmonic Doppler should help resolve some of these issues. Also, incorporation of techniques such as speckle tracking may allow measurement of motion of a certain point within the myocardium rather than a point in space. Simple measures such as narrow sector angle and “clean” gray scale images may improve the velocity and color Doppler data quality. Also, on-line user-friendly analysis packages and real-time strain rate display may hasten routine clinical use. Faster acquisition programs will significantly shorten MR scan times, and on-line, rapid analysis packages will allow wider applicability of this technique. New analysis techniques such as harmonic phase MRI (28) may facilitate routine application of tagged MR strain analysis.

**FUTURE DIRECTIONS**

To standardize the interpretation of echocardiographic strain analysis and given the heterogeneity of strain in the myocardium, normal reference values and variability of strain parameters will need to be established (29). It would be logical to extend the work presented by Edvardsen and Gotte by investigating the utility of strain analysis in evaluation of acute MI and stunned and hibernating myocardium. Although initial reports of the use of strain parameters in stress interpretation are encouraging (30,31), these results will have to be replicated in larger and more diverse patient groups. In addition to regional systolic function analysis, strain imaging may allow interrogation of regional myocardial diastolic function (32). Furthermore, echocardiographic strain imaging at high frame rates can significantly enhance temporal resolution and allow metic-
ulous timing of regional cardiac mechanical activity, introducing new paradigms in the assessment of coronary artery disease (33).

Finally, noninvasive implementation of strain analysis resurrects an old muscle physiology concept to help resolve current shortfalls in regional myocardial assessment. Initial studies indicate that this technique is feasible, correlates closely with invasive parameters of ventricular function and may be superior to conventional visual regional wall-motion analysis. However, key advances in acquisition and analysis technology as well as parallel clinical investigation are needed for this new technology to mature into a new standard for regional myocardial assessment.

Reprint requests and correspondence: Dr. R.A. Nishimura, Section of Publications, Mayo Clinic, 200 First Street, SW, Rochester, Minnesota 55905.

REFERENCES