Role of Tissue Doppler and Strain Echocardiography in Current Clinical Practice

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The motion of a muscle, is performed only by the Carnous fibers, and each Carnous fiber has a power of contracting itself. . . . The force of the whole Muscle is but an aggregate of the contractions of each particular fiber.

—William Croone in De ratione motus musculorum (On the Reason of the Movements), 1664

Visual or semiautomated tracking of the endocardial border provide estimates of cardiac volume, which are used to derive ejection fraction, a quantitative indicator of ventricular function. However, the heart is a complex mechanical organ that undergoes cyclic changes in multiple dimensions that ultimately affect a change in chamber volume that results in ejection of blood. Regardless of imaging technique, ejection fraction is unable to provide information on the underlying myocardial mechanical activity. Also, ejection fraction reflects the sum contribution of several regions and does not provide information on regional function. Regional function assessed visually is subjective and prone to error.1

Quantification of regional myocardial activity (deformation) was feasible only in experimental studies by use of markers attached directly to the myocardium, a technique not practicable in the clinical realm.2 Myocardial tagging with cardiac magnetic resonance (CMR) introduced the opportunity to noninvasively track regional myocardial mechanics.3,4 Modifications to the filter settings on pulsed Doppler to image low-velocity, high-intensity myocardial signal rather than the high-velocity, low-intensity signal from blood flow allows similar assessment by ultrasound. This technique is commonly referred to as tissue Doppler imaging (TDI) or Doppler myocardial imaging.5

Tissue Doppler Imaging

The TDI method depicts myocardial motion (measured as tissue velocity) at specific locations in the heart. Tissue velocity indicates the rate at which a particular point in the myocardium moves toward or away from the transducer. Integration of velocity over time yields displacement or the absolute distance moved by that point (Figure 1A and 1B).

Tissue Doppler–derived velocity can be obtained via pulsed Doppler (by placing a sample volume at a particular location), M-mode Doppler, or 2-dimensional color Doppler (Figure 1C and 1D).5 Color Doppler acquires tissue velocity information from the entire sector, and thus, multiple sites can be interrogated simultaneously. Individual segments are analyzed ex post facto. Although all of these methods yield the same mechanical information, differences in the peak values exist. Pulsed Doppler measures peak velocity, which is ≈20% to 30% higher than the mean velocity measured by color Doppler. This difference should be considered when one estimates left ventricular filling pressure using the E/e' ratio.6 Frame rates are highest with the M mode, lower with pulsed Doppler, and lowest with color Doppler TDI.

Tissue Doppler has been validated extensively and examined in a variety of cardiac pathologies.7,8 Although initial work reported tissue velocity from the septal or posterior wall in the parasternal projections, recent work almost exclusively interrogates tissue velocities in the longitudinal direction (apical projections). In the longitudinal direction, myocardial motion is such that the apex is generally immobile, whereas the base moves toward the apex in systole and away from the apex in diastole.9 This differential motion between base and apex results in a velocity gradient along the myocardial wall, with the highest velocities at the base and low or zero velocity at the apex (Figure 2). Because TDI interrogates motion at a single point in the myocardium with reference to a point outside the chest (the transducer), it is influenced by translational motion and tethering (normal apical segments pull an abnormal basal segment toward the apex). Moreover, single-point interrogation (depicting tissue displacement) does not fully capture true myocardial mechanics.

Strain Rate and Strain

Strain is a measure of tissue deformation and is defined as the change in length normalized to the original length (Figure 3). The rate at which this change occurs is called strain rate. Deformation in a 1-dimensional object, such as a thin bar, is limited to lengthening or shortening.10 Strain is how much the...
bar is shortened or lengthened relative to its original length (ie, reduction to half its original length is 50% strain, and an increase to one third longer is 33% strain). Strain rate is the speed at which this change occurs. Strain rate and strain are akin to shortening velocity and shortening fraction, respectively. Thus, to a certain extent, measurements otherwise restricted to experimental models can now be performed clinically. In general, peak systolic strain rate is the parameter that comes closest to measuring local contractile function in clinical cardiology. It is relatively volume independent and is less pressure independent than strain. In contrast, peak systolic strain is volume dependent and does not reflect contractile function as well.

By TDI, strain rate is the difference in velocity between 2 points along the myocardial wall (velocity gradient) normalized to the distance between the 2 points.12 A similar velocity gradient exists between the endocardium and the epicardium, because the endocardium moves faster. This concept is used to derive myocardial velocity gradient (radial strain rate).13 This velocity gradient depicts the rate of change of myocardial wall thickness during systole and diastole. Thus, strain rate measures the rate at which the 2 points of interest move toward or away from each other. Integration of strain rate yields strain, the normalized change in length between these 2 points.

Therefore, tissue velocity is obtained by interrogating a single point in the myocardium, with the reference point...
being the transducer on the chest wall. For strain rate, 2 points are interrogated in the myocardium. In the longitudinal direction, the points move closer to each other in systole and away from each other in diastole (online-only Data Supplement Movies Ia and Ib).

The use of strain (deformation) to examine the properties of the heart is not a new concept. Mirsky and Parmley used strain to study the elastic properties of the myocardium. Although myocardial strain is a 3-dimensional tensor, to simplify the discussion, the present review will focus on 3 primary directions of strain in the heart. The heart shortens and lengthens in the longitudinal direction, it thickens and thins in the radial direction, and it shortens and lengths in the circumferential direction (Figure 4A and 4B). A torsion or wringing motion also is present between the base and apex. When viewed from the apex, the apex rotates counterclockwise, and the base rotates clockwise in systole (twisting), with the opposite motion (untwisting) in diastole (Figure 4C). Strain rate and strain are theoretically less susceptible to translational motion and tethering artifacts and thus may be superior to tissue velocity in depicting regional or global myocardial function.

Tissue Doppler–derived strain variables have been validated with gel phantoms, isolated muscle preparations, sonomicrometric crystals in whole hearts, and tagged CMR imaging. Normal strain and strain-rate values have been published. Sample tracings are presented in Figure 5.

An extensive review of TDI/strain is beyond the scope of this article. The reader is referred to several excellent reviews that complement the present review and provide greater detail on specific issues. The present review will focus on the current clinical relevance of these novel techniques and examine the factors that influence their widespread and routine use.

Global Systolic Function

The current standard for global systolic function is the ejection fraction. Peak mitral annular velocity closely correlates with $\frac{dP}{dT_{\text{max}}}$ by high-fidelity, micromanometer-tipped catheters in the left ventricular cavity and with angiographic and radionuclide ejection fraction. Normal values for tissue Doppler velocities have been established. A peak mitral annular descent velocity >5.4 cm/s averaged from 6 annular sites predicts an ejection fraction >50%. Strain rate more closely correlates with invasively determined parameters of global function than systolic tissue velocity. Thus, either of these techniques could potentially be used in lieu of ejection fraction to quantify global function.

Regional Function

Detection of myocardial ischemia by visual assessment of wall motion is fraught with variability and low reproducibility. Wall motion can be quantified by TDI or strain echocardiography, respectively. Low systolic tissue velocities correlate with angiographic or echocardiographic wall-motion abnormality. Tissue velocities decrease with reduced regional perfusion, recover on reperfusion, and differentiate between transmural and nontransmural infarction. Regional strain rates and strain are reduced in ischemia and infarction. Strain and strain rate identify infarcted segments and correlate with extent of transmural infarction. Strain and strain rate are less susceptible to cardiac translational motion and tethering. The term “tethering” is used to describe the dragging of an akinetic basal segment toward the apex by normally functioning mid or apical segments (online-only Data Supplement Movie II). This theoretical advantage of strain/strain rate was confirmed in the clinical setting.

Coronary Artery Disease

Tissue velocities, strain rates, and strain are reduced in ischemia and infarction. Tissue velocities may not accurately reflect regional function due to tethering. Systolic tissue velocities, strain rates, and, to some extent, strain increase with dobutamine stimulation in the normal subject. This response is blunted in areas with induced
ischemia. Low systolic tissue velocity at maximal stress (<5.5 cm/s) predicts induced wall-motion abnormality. The MYocardial Doppler In Stress Echocardiography (MYDISE) study found that tissue velocities were predictive of angiographic disease. Isovolumic acceleration was more accurate than tissue velocity in predicting angiographic disease. Changes in systolic tissue velocity during dobutamine stress identify viable myocardium, predict outcomes in patients with an ischemic response or after a myocardial infarction, and may help identify false-positive wall-motion abnormalities. It is feasible to perform TDI during exercise.

Changes in strain precede those in wall motion or tissue velocity during dobutamine stress and can differentiate stunned from ischemic myocardium. Strain rate correlates with regional myocardial perfusion during dobutamine stress. Responses in strain and strain rate during dobutamine stress have been well summarized. Strain rate may be better than strain, and both are likely superior to tissue velocity in detecting CAD via stress echocardiography. Strain echocardiography is feasible during dobutamine and exercise stress echocardiography. Strain changes correlate closely with thallium perfusion abnormalities. Strain-rate response during low-dose dobutamine is superior to wall-motion analysis.

Figure 5. Representative strain rate and strain traces from a normal individual. Strain-rate tracings are a mirror image (across the “0” line) of the tissue velocity tracings in the longitudinal direction (see Figure 1). Therefore, systolic strain rate is negative (SRs), and early and late diastolic strain rates are positive (SRe and SRA). Strain rates depict the rates of deformation and strain depicts the extent of deformation of the region of interest. Dashed line indicates aortic valve opening and dotted line indicates aortic valve closure as measured by pulsed Doppler in the left ventricular outflow tract. Normal resting strain rate in the longitudinal direction is 1.0 to 1.5 s⁻¹, and normal strain is 10% to 15%.
and tissue velocity for identification of viable myocardium, \(^\text{49}\) and strain-rate data improve the sensitivity for prediction of functional recovery after revascularization. \(^\text{50}\)

Post-systolic strain may be seen in normal subjects and does not universally denote pathology. In abnormal myocardium, systolic strain is low, and post-systolic strain occurs later in diastole. \(^\text{51}\) Post-systolic strain identifies myocardial viability and inducible ischemia, \(^\text{52}\) and discussion is ongoing on whether it is an active or a passive phenomenon. \(^\text{53}\)

**Cardiomyopathy**

Tissue velocities, strain rates, and strain are reduced in cardiomyopathies and potentially could be used for preclinical detection of several inherited cardiomyopathies. Systolic and diastolic velocities were significantly reduced in transgenic rabbits with hypertrophic cardiomyopathy. \(^\text{54}\) Reduced systolic and diastolic velocities \(^\text{55}\) or reduced early diastolic velocities only \(^\text{56}\) have been demonstrated in patients with known mutations associated with hypertrophic cardiomyopathy without ventricular hypertrophy.

Early diastolic strain rates were significantly lower in asymptomatic, gene-positive patients with Friedrich’s ataxia. \(^\text{57}\) Similarly, early diastolic strain rates were lower in hypertrophic cardiomyopathy than in athletes or normal control subjects, \(^\text{58}\) and they are lower in restrictive than in normal or constrictive cardiomyopathy. \(^\text{59}\) Abnormal systolic and diastolic tissue velocities are reported in Fabry’s disease patients without ventricular hypertrophy. \(^\text{60}\) Systolic strain and strain rates improved after enzyme-replacement therapy in Fabry’s disease. \(^\text{61}\) Tissue velocities and strain rates are reduced in primary amyloidosis with and without evidence of cardiac involvement. \(^\text{62–64}\)

**Dyssynchrony Analysis**

Patients with low ejection fraction, conduction abnormality, and symptomatic heart failure despite optimal medical therapy experience significant benefits from cardiac resynchronization. \(^\text{65,66}\) Mechanical dyssynchrony as determined by TDI may be superior to electrocardiography in predicting response to this therapy. \(^\text{57,68}\)

Several reports suggest a low concordance between electrical and mechanical synchrony. \(^\text{69,70}\) Because TDI allows interrogation of the mechanical activity (Figure 6A), an operator is able to time the onset of systolic motion, peak motion, and end of systolic motion (Figure 6B) at various locations in the heart. In normal synchronous hearts, segmental systolic tissue velocities peak almost simultaneously (Figure 7A). In dysynchronous hearts, the lateral and/or posterior segments peak considerably later than the septum (Figure 7B), which results in inefficient ejection. Pacing of the delayed region allows synchronized mechanical activity and improves ejection. Severe mechanical dyssynchrony may be recognized visually; however, milder forms are not detectable and in either case cannot be quantified.

The mechanical delay between the normal (early) and late segments predicts response to resynchronization. \(^\text{71}\) Among several proposed indices of mechanical dyssynchrony, the criteria commonly used in clinical practice are (1) septal to lateral wall delay \(>65\) ms \(^\text{68}\) and (2) the SD of time to peak

**Figure 6.** Two-dimensional TDI allows simultaneous interrogation of mechanical activity (myocardial motion) at several points in the image (A). Each TDI tracing (B) depicts when the area being interrogated started moving, which usually coincided with the onset of systole (white arrow), when peak motion occurred (hatched arrow), and when motion returned to its baseline state (black arrow). In general, these points coincide with beginning, peak, and end of systole, respectively. Each of these events is denoted, respectively, by when the tracing leaves the “0” line, the peak positive excursion, and when the tracing returns to the “0” line. S’ indicates systolic tissue velocity; e’, early diastolic tissue velocity; and a’, late diastolic tissue velocity. C, Measurement of mechanical synchrony: tracing from the basal septum. Time to peak tissue velocity (double-headed arrow) is measured as the delay between a reference point such as the onset of the QRS complex (white arrow, solid line) and the peak positive systolic wave (black arrow).
systolic velocity of 12 segments $>33$ ms. The relative value of TDI versus strain/strain rate in predicting response to resynchronization has not been resolved fully.\textsuperscript{73,74}

**Diastolic Function**

Early diastolic tissue velocity ($e'$) correlates with invasive measures of diastolic function.\textsuperscript{75–78} Despite early claims to the contrary, $e'$ is load dependent.\textsuperscript{77,79} Low $e'$ ($<3.5$ cm/s in the hypertensive population and $<3$ cm/s in patients with low left ventricular ejection fraction) predicts mortality in a manner incremental to clinical and echocardiography data.\textsuperscript{80,81} The ratio of mitral inflow E to $e'$ velocity ratio (E/$e'$) correlates closely with left ventricular filling pressure.\textsuperscript{75,82} The ratio predicts heart failure events in a manner incremental to clinical factors and ejection fraction.\textsuperscript{83}

The high temporal resolution of strain imaging allows interrogation of short-lived diastolic mechanical events. Patients with global diastolic dysfunction have higher numbers of segments with an altered early to late diastolic strain-rate ratio, and the number of altered segments increases with worsening global diastolic function.\textsuperscript{84} Evidence exists that changes in early diastolic strain rate can predict angiographic disease.\textsuperscript{85} Regional diastolic strain ratios are related to regional stiffness and can separate stunned from infarcted myocardium.\textsuperscript{86} Strain-rate–based time delays are related to regional perfusion and inducible wall-motion abnormality.\textsuperscript{45,87}

**Right Ventricular Function**

Evaluation of right ventricular function by echocardiography is challenging and often ignored in clinical practice. Tricuspid annular velocity correlates with right ventricular ejection fraction.\textsuperscript{88,89} Tricuspid annular excursion (tricuspid displacement) predicted 2-year survival in patients with pulmonary hypertension.\textsuperscript{90} Isovolumic acceleration, derived from tissue
velocity, is a load-independent measure of contractility and correlates with right ventricular end-systolic elastance. This correlation is less pronounced in clinical studies. More recent experimental data suggest a weak relationship between isovolumic acceleration and regional contractility. Systolic velocity and strain best correlated with invasively determined right ventricular stroke volume and dynamically tracked changes in right ventricular function during vasodilator infusion. Strain rates and strain quantitate regional right ventricular systolic function in various pathologies.

Atrial Function

Assessment of atrial function by conventional echocardiography is challenging. Modesto et al demonstrated that strain parameters may provide a simple, quantitative assessment of atrial function in amyloidosis. Atrial function has since been examined with strain echocardiography in other conditions and has been shown to predict successful maintenance of sinus rhythm after cardioversion for atrial fibrillation.
Cautions

Conceptually, it is worthwhile to bear in mind that the complex mechanics of the heart are likely best represented by a 3-dimensional strain tensor, whereas most current methods measure strain in a single or 2 dimensions. The primary practical limitation of tissue velocity or strain analysis is reproducibility. Tissue velocity signals are generally more robust than strain. However, in either parameter, it is not unusual to move the sample region minimally to find wide variations in signal quality with significant differences in amplitude and phase (timings), with obvious implications for its clinical implementation. For instance, with multiple lines of evidence to demonstrate its superiority in analysis of dyssynchrony, tissue velocity analysis is being increasingly used to select patients for cardiac resynchronization therapy. However, unless operators are cautious, cursor positions can be manipulated to “dial in” the desired dyssynchrony timing. Pulsed TDI traces may be challenging for timing measurements because they often do not yield distinct peaks. Similarly, multiple systolic peaks in the TDI signal are often difficult to adjudicate (Figure 8). Although recommendations have been made that the earlier and larger of the peaks is the “true” peak, this approach is not totally immune to error, because moving the sample often changes the amplitude and character of the peaks. Although not intuitive, the angle of insonation does influence timing of TDI events when angles exceed 20°. A significant yet steep learning curve exists in acquisition, analysis, and interpretation of TDI/strain data. We clinically report TDI or strain only when the signal is consistent. We do not report or insert a disclaimer when working with images that yield highly variable TDI/strain values. We believe, as most publications suggest, that indices of mechanical dyssynchrony will be essential in selecting patients for cardiac resynchronization therapy; however, it is our opinion that at the present time and with available technology, the use of TDI and/or strain analysis for dyssynchrony analysis requires substantial training and technology improvements before it can be applied in the wider clinical arena. Despite several years of experience in TDI/strain, we find analysis challenging in a reasonable number of cases. The judicious and cautious application of TDI/strain data in clinical decision making is suggested given that most, if not all, dyssynchrony studies using TDI/strain are not randomized or blinded.

The angle dependence of tissue Doppler–based velocities and strain should be kept in mind when one is working with full-sector images. Non-Doppler–based techniques overcome this limitation. Strain/TDI technologies cannot be retrofitted, and most vendors require the purchase of new platforms/programs to enable tissue velocity and strain analysis. Strain has been validated clinically with tagged CMR used as the standard. Some issues related to validation are worth noting. Most validation is performed with both a normal and a significantly abnormal population (eg, myocardial infarction), which results in 2 large, significantly separated clusters of data and consequentially high correlation between techniques. How this correlation translates into a clinically useful tool can only be addressed in large clinical trials with blinded analysis. Clinical studies yield lower correlations between ultrasound strain and CMR than those reported in experimental studies (r values of 0.40 to 0.50). Our (unpublished) experience in unselected patient populations has been similar.

The spatial resolution for strain analysis by tagging is not usually similar to that in cine CMR. Magnetic resonance tags are usually 7 to 10 mm apart, and thus, the in-plane (radial and circumferential) resolution for strain is 7 to 10 mm. The
slice thickness is usually 8 to 10 mm; thus, the longitudinal spatial resolution is 8 to 10 mm. In patients, strain imaging by tagged CMR can also be noisy at times. Nonetheless, CMR remains the best validated, most robust, and most reproducible technique for noninvasive strain measurements and is the ideal method for validation of strain in a clinical study. Lack of correlation alone does not suggest that either technique is inaccurate, because the mathematical derivation of strain is different between CMR and ultrasound. Reference values for strain for each technique will most likely be different. Newer semiautomated CMR programs such as harmonic phase (HARP), strain-encoded MRI (SENC), and displacement encoding with stimulated echoes (DENSE) may have better resolution and are likely more robust.104–106

Strain by TDI is obtained through integration of the strain rate signal. Because integration reduces noise, strain signal will always be “cleaner” than strain rate. It is not uncommon to find a significantly noisy (and meaningless) strain rate signal that yields a deceptively clear strain signal. Data based on such a strain signal are of questionable value.

Because lateral resolution of Doppler-based strain is influenced by beam width, it is unclear whether reliable resolution exists to separate endocardial from epicardial strain in long-axis imaging; however, such analysis may be feasible in the axial direction. In addition, tissue velocity and strain parameters are sensitive to load,46,77 and load should be considered when tissue velocity or strain is compared at 2 time points.

Despite the burgeoning evidence of incremental value over conventional echocardiography in myriad clinical conditions, tissue velocities have found limited clinical use, and strain has found virtually no routine clinical use, except in a few centers. Unfortunately, several impediments exist to the routine clinical application of these technologies. Although the concept is not new and is well-founded in myocardial physiology, it is unfamiliar territory to the cardiologist and the sonographer. This results in significant inertia in learning and implementing the technology. The concept is nonintuitive. Unlike the visualization of an obvious morphological abnormality (eg, flail mitral leaflet), tissue velocity and strain data offer no real-time feedback. Data are collected and spirited away for off-line analysis, with considerable delay between acquisition and data availability. Sonographers are not yet comfortable with data acquisition and less so with data analysis. This translates to significant physician time commitment. The manual analysis and signal noise/variabil-
may exacerbate this commitment and reduce enthusiasm for clinical use.

Potential solutions include advancements that result in a robust and reproducible signal that lends itself to semiautomated programs that may reduce analysis time. Availability of real-time feedback during image acquisition that informs the operator of image acceptability would reduce the number of unanalyzable images. Analysis of tissue velocity and strain from conventional images would reduce the time and effort spent in collecting separate TDI images. Lastly, parametric imaging in which a parameter of interest is displayed in a color-coded image, such as a bull’s eye plot, may help with physician interpretation.

The interaction of ultrasound with the myocardium produces unique acoustic patterns, or “speckles.” These speckles can be tracked over time and speckle displacement used to calculate tissue velocity and strain.\(^\text{107}\) This method is relatively angle independent, because it is not based on the Doppler principle.\(^\text{108}\) Published data suggest that radial strain by this method is not as reproducible as longitudinal strain.\(^\text{109,110}\)

Because speckle tracking is automated, this technique lends itself to semiautomated measurements of strain. One such method allows the generation of bull’s eye plots of longitudinal segmental strain (Figure 9). Another similar technique uses arrows to display the direction and amplitude of motion at various points in the heart (Figure 10). Speckle tracking imaging can use preexisting B-mode images; however, it is performed at much lower frame rates (40 to 90 frames per second) and may not be as accurate in timing mechanical events as Doppler-based imaging (100 to 250 frames per second).

Tissue velocity and strain have facilitated the interrogation of torsional movements in the heart.\(^\text{111}\) The Table summarizes the potential clinical value of tissue velocity and strain parameters. The parameters are considered useful if substantial clinical evidence is available in relatively large sample sizes and from multiple sources. Parameters are considered probably useful if the evidence is from smaller studies but has been reproduced in multiple centers.

At the present time, tissue velocity and strain data appear to be of optimal value if the images are acquired carefully, analysis is meticulous, and the interpretation is judicious and balanced. To conclude, tissue velocity and strain echocardiography allow detailed interrogation of regional and global mechanics and offer substantial incremental information on myocardial function compared with conventional echocardiography. Both techniques characterize fundamental concepts in cardiac physiology and represent a paradigm shift in the application of echocardiography in clinical practice. Evidence is increasing that the information from these novel techniques will help with clinical decision making and the prediction of outcomes. Education in these new concepts, ample hands-on training, and improvements in imaging technology will help cardiologists gain familiarity with these techniques and better implement them in practice. Randomized and blinded studies in larger populations will help define their eventual role in clinical practice. Ongoing advances that reduce operator interaction may improve reproducibility and facilitate wider clinical use.

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