Strain and Strain Rate Echocardiography and Coronary Artery Disease

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The echocardiographic assessment of regional myocardial function plays a critical role in the diagnosis and management of ischemic heart disease and in most laboratories relies on the visual detection of endocardial wall motion abnormalities and assessment of left ventricular (LV) ejection fraction. However, this approach is subjective and operator dependent, demands complete visualization of the endocardium, and is subject to the vicissitudes of cardiac loading and heart rate. Although estimation of myocardial shortening and thickening reflect the radial mechanics of the heart, the contribution of longitudinal (and to a lesser extent circumferential) myocardial deformation is largely neglected. Thus, there is a need for an objective, comprehensive, noninvasive measurement of myocardial performance and contractility with acceptable interpretative variability. Doppler tissue imaging, which measures the velocity of myocardium (in the longitudinal direction from apical windows and in the radial direction from short-axis scans) during systole and diastole is used to quantify ventricular function and is more sensitive to subtle changes in contractility than ejection fraction. However, tissue velocities are affected by translational movement and tethering, making it difficult to discriminate akinetic segments that are pulled (or tethered) from actively contracting segments. In addition, velocities are not uniformly distributed across the myocardium, decreasing from base to apex, making difficult the establishment of reference values.

Measurements of myocardial strain and strain rate (SR) are newer indices that have the potential to overcome these limitations. Strain and SRs represent the magnitude and rate, respectively, of myocardial deformation, which is an energy-requiring process that occurs in both systole and diastole. Abnormalities of myocardial deformation are seen early in the development of many pathophysiologic states, including ischemia, and thus provide a sensitive means for detecting regional myocardial dysfunction. The objective of this report is to review the use of strain and SR echocardiography in patients with coronary artery disease.

Principles of Myocardial Strain

Strain is the normalized, dimensionless measure of deformation of a solid object (such as a segment of myocardium) in response to an applied force or stress. Strain (ε) calculations may be either Lagrangian or natural. Lagrangian strain (ε_L) is defined as a deformation from its original length (L_0):

\[ \varepsilon_L = \frac{L(t) - L(t_0)}{L(t_0)}, \]

where L(t) is the length of the object at time instance t after deformation and L(t_0) is the length of the object when not subjected to external forces. Natural strain (ε_n) is defined as

\[ \varepsilon_n = \ln[1 + \varepsilon(t)], \]

where ln is the natural logarithm. Natural strain expresses the deformation relative to the length at a previous time instance (t, not t_0) and is more appropriate than Lagrangian strain when large deformations (as in the heart) are encountered; for small deformations (on the order of 5% to 10%), the latter approximates the former.

Because of 3D cardiac geometry and complex myofiber arrangements, there are multiple components or directions of strain (circumferential, longitudinal, and radial) that may be normal (ie, orthogonal or perpendicular) or shear. The direction of greatest deformation is called the principal strain. By convention strain can be either positive, which indicates lengthening, or negative, which indicates shortening. Values for normal circumferential and longitudinal strain are negative numbers, whereas those for radial strain are positive.

SR is simply the change in strain over time (ie, the rate of deformation, or mathematically, the temporal derivative of strain), and has the unit s^{-1}. Conversely, integrating SR values over time calculates strain.

Strain and SR can be assessed using either tissue Doppler velocities (Doppler stress imaging, or DSI) or by 2D echocardiographic (2D speckle-tracking or STE) techniques.

Doppler Strain (and SR) Imaging

Doppler strain (and SR) imaging are depicted in Figure 1. Using instantaneous tissue Doppler velocities, one can mathematically estimate SR by measuring the spatial velocity gradient as:

\[ SR \approx \frac{V_2 - V_1}{d}, \]

where \( V_2 \) and \( V_1 \) are instantaneous velocities measured at points 2 and 1, respectively, and d is the distance between the...
2 points. Finally, as alluded to above, myocardial strain can be derived by integrating all of the Doppler-derived SRs within a given time period, using the following equation4:

\[ \varepsilon_\text{strain} = \int_{t_0}^{t} \text{SR} \, dt, \]

where \( t_0 \) and \( t \) are the starting and ending time points, respectively. High frame rates and care to avoid aliasing are needed. This spatial description uses instantaneous lengths for reference length and therefore measures natural strain.

In addition to \( \varepsilon \) and SR, a few novel features of this technology may also have clinical utility for the diagnosis of ischemic heart disease. For example, postsystolic deformation (thickening or shortening) has been observed in ischemic areas of myocardium on color M-mode maps (Figure 2).5 Similarly, an increased time to onset of relaxation, also visible on color M-mode maps, of more than 20% has a sensitivity and specificity of 95% and 75%, respectively, for the detection of new wall motion defects.2

Several limitations to DSI should be noted. First, like all Doppler imaging techniques (and perhaps even more so), strain imaging is angle dependent. Given that strain is 3D with perpendicular vectors having opposite signs, angle deviation can have severe effects on SR calculations. Thus, the ability to align the ultrasonic beam parallel to the segment of interest is crucial to the accurate interpretation of SR data. Second, although myocardial deformation occurs in 3D space, Doppler-determined strain measurements are 1D; present imaging technology allows instantaneous strain assessment only along the axis of ultrasound propagation. Thus, only a limited number of strain components can be measured; apical views are used to record longitudinal strains and the parasternal short-axis view for recording radial strains. Finally, intraobserver and interobserver variability is substantial (10% to 15%),6 and image and signal quality influences and may limit measurement of SR; however, noise can be minimized by increasing the region of interest (at the expense of spatial resolution) and by integrating SRs (to obtain the less noisy strain measurement).

Validation of DSI
A number of animal and human studies have addressed the ability of DSI to quantify myocardial function in a variety of physiological and pathophysiologic states (Table 1). In a closed-chest pig model, radial strain and SR varied appropriately in response to atrial pacing, dobutamine infusion, and esmolol infusion, and SR correlated strongly with strain data obtained from sonomicrometry and appeared to be superior to myocardial velocities in distinguishing healthy and ischemic myocardium.

![Figure 1. Longitudinal DSI tracings. Longitudinal strain (A) and strain rate (SR) (B) in the mid lateral LV from a normal individual. C, Patient with cardiomyopathy; note the reduced peak SR.](image-url)
Similarly, Doppler-derived peak and mean myocardial strain correlated more strongly than systolic myocardial velocities with invasive hemodynamic measures of cardiac elastance in dogs treated with esmolol and dobutamine.

In human subjects, DSI has been compared with Doppler tissue velocities and tagged MRI. At present, tagged MRI is considered the gold standard for noninvasive myocardial strain imaging. Tagged MRI has the advantage of being able to evaluate strain in 3 dimensions. However, major disadvantages to MRI include its low sampling rate and limited temporal resolution, long acquisition and postprocessing times, expense, and availability—all factors that may limit the widespread use of MRI-derived strain in the clinical arena. In one study, dobutamine echocardiography was performed in 58 subjects that included patients with recent
myocardial infarctions, those with coronary risk factors, and healthy control subjects. Each subject was evaluated with Doppler tissue echocardiography, DSI, and tagged MRI. Longitudinal and radial strain derived from DSI correlated strongly with MRI-derived strains ($r = 0.89$ and $r = 0.96$, respectively). Longitudinal shortening detected by DSI increased appropriately with dobutamine infusion in healthy myocardial segments, whereas infarcted segments exhibited longitudinal lengthening and radial thinning with DSI. The results of these studies and others discussed below have demonstrated that DSI is feasible and can accurately and reproducibly assess myocardial function across a broad range of pathophysiologic states that occur in patients with ischemic heart disease.

Two-Dimensional STE

Two-dimensional echocardiography STE analyzes myocardial motion by frame-by-frame tracking of natural acoustic markers (~20 to 40 pixels in size and variably referred to as “speckles,” “patterns,” or “fingerprints”) that are generated from interactions (ie, reflections, interference, scattering) between ultrasound and myocardium within a user-defined region of interest (Figure 3 and Figure 4). Unlike DSI, STE analyzes Lagrangian strain. Tracking algorithms may use either (1) a sum-of-absolute differences, which fits correlation-weighted data to a spatial polynomial curve to calculate regional strain at ~3-mm intervals of the LV circumference, or (2) Fourier analysis that assumes coherence of the geometry tracked using a sequence of intermediate passages from 2 cm down to 5-pixel bands; this method (vector-velocity imaging or VVI) also accounts for mitral annular motion, tissue-blood border detection, and the periodicity of the cardiac cycle. The different tracking algorithms may be clinically important, because the former was more accurate than the latter in a recent study that compared the 2 tracking techniques against tagged harmonic phase MRI Lagrangian strain. However, both methods are insonation angle-independent and allow measurement of longitudinal (from apical views), radial (from short-axis and apical views), and circumferential (from short-axis views) strains. More complex deformations, such as rotation, twist, and torsion (longitudinal circumferential shear) can be assessed, but a discussion of these deformations is beyond the scope of this article (reviewed in Reference 14). Intraobserver variability and interobserver variability are better with 2D than Doppler techniques and are less sensitive than Doppler to noise. Nevertheless, in patients with cardiomyopathy and myocardial infarctions, those with coronary risk factors, and healthy control subjects, each subject was evaluated with Doppler tissue echocardiography, DSI, and tagged MRI. Longitudinal and radial strain derived from DSI correlated strongly with MRI-derived strains ($r = 0.89$ and $r = 0.96$, respectively). Longitudinal shortening detected by DSI increased appropriately with dobutamine infusion in healthy myocardial segments, whereas infarcted segments exhibited longitudinal lengthening and radial thinning with DSI. The results of these studies and others discussed below have demonstrated that DSI is feasible and can accurately and reproducibly assess myocardial function across a broad range of pathophysiologic states that occur in patients with ischemic heart disease.

Table 1. Validation Studies of DSI and STE

<table>
<thead>
<tr>
<th>Species</th>
<th>DSI Standard (Reference)</th>
<th>STE Species</th>
<th>STE Standard (Reference)</th>
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<tbody>
<tr>
<td>Pig</td>
<td>dP/dt</td>
<td>Dog</td>
<td>Sono&lt;sup&gt;18,23&lt;/sup&gt;</td>
</tr>
<tr>
<td>Dog</td>
<td>Sono&lt;sup&gt;9&lt;/sup&gt;</td>
<td>Pig</td>
<td>Sono&lt;sup&gt;19,20&lt;/sup&gt;</td>
</tr>
<tr>
<td>Sheep</td>
<td>Elastance&lt;sup&gt;9&lt;/sup&gt;</td>
<td>Sheep</td>
<td>Sono&lt;sup&gt;17&lt;/sup&gt;</td>
</tr>
<tr>
<td>Human</td>
<td>MRI&lt;sup&gt;10,22&lt;/sup&gt;</td>
<td>Rats</td>
<td>Histology&lt;sup&gt;51&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Human</td>
<td>MRI&lt;sup&gt;10,13,18,21,22&lt;/sup&gt;</td>
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Sono indicates sonomicrometry.
dial infarction, strain and SR obtained using DSI and 2D STE were strongly correlated.\textsuperscript{16}

Frame rates of \(\sim 50\) to 70 are needed to avoid speckle decorrelation, and good image quality is needed for accurate tracking. Translation remains a problem using 2D acquisition methods as error is introduced to strain measurements when the heart swings out of the imaging plane. In addition, out-of-plane motion occurs as the result of rotation and motion of the heart;

\textbf{Figure 3}. Normal (A) and abnormal (B) circumferential strains from 2D STE. Six-segment model from the papillary muscle short-axis view. Curves denoted with a dashed line represent the LV volume-time curves. End-diastole and end-systole are denoted by dashed vertical lines. ESV indicates end-systolic volume; EDV, end-diastolic volume; and EF, ejection fraction.
as a result, only a portion of the real motion can be detected. The recent development of 3D wall motion tracking, which displays quantitative echo data from 3D ultrasound data sets and has been validated in sheep using sonomicrometry,\textsuperscript{17} has the potential to more accurately evaluate ventricular function in patients with ischemic heart disease.

\textbf{Validation of STE}

Two-dimensional strain has been validated against DSI\textsuperscript{15} and strain measured using sonomicrometry\textsuperscript{18,19,20} and tagged MRI (Table 1).\textsuperscript{10,18,21,22} Sonomicrometer-determined strains were highly correlated with 2D strain ($r=0.90, P<0.001$), with excellent agreement in anesthetized dogs subjected to intra-

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure4.png}
\caption{Normal (A) and abnormal (B) radial strains from 2D STE. Six-segment model from the papillary muscle short-axis view. Curves denoted with a dashed line represent the LV volume-time curves. End-diastole and end-systole are denoted by dashed vertical lines. ESV indicates end-systolic volume; EDV, end-diastolic volume; and EF, ejection fraction.}
\end{figure}
venous saline loading and brief coronary artery occlusion.\textsuperscript{18}\nIn an open-chest porcine model of ischemia, 2D strain at rest and during dobutamine infusion correlated significantly with sonomicrometer-determined strain (\(r=0.77\) and 0.80, \(P<0.001\) for longitudinal strain; \(r=0.57\) and 0.63, \(P<0.05\) for radial strain; and \(r=0.74\) and 0.58, \(P<0.001\) for circumferential strain).\textsuperscript{20} In another study, longitudinal, radial, and circumferential strains determined with speckle tracing and tagged harmonic phase MRI were similar in patients with known or suspected coronary artery disease.\textsuperscript{21}

VVI, which incorporates speckle-tracking and endocardial contour tracking, was validated in canines using sonomicrometry during 5-minute coronary occlusion/reperfusion cycles followed by dobutamine and esmolol infusions. Good correlations were reported between circumferential and longitudinal systolic strain by VVI and sonomicrometry in the ischemic zone (\(r=0.88\) and 0.83, respectively, both \(P<0.001\)) and in nonischemic basal segments (\(r=0.94\) and 0.90, both \(P<0.001\), respectively), with excellent interobserver and intraobserver variability.\textsuperscript{23} In view of the known transmural gradient of strain (ie, greatest in the endocardium), differences in the absolute value of strain in that study were explained by implantation of sonomicrometers in the midmyocardium, whereas VVI more closely tracked the endocardium. DSI and STE are compared in Table 2 and are compared with tagged MRI in Table 3.

### Table 2. Comparison of DSI and STE

<table>
<thead>
<tr>
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<th>DSI</th>
<th>STE</th>
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<tbody>
<tr>
<td>Doppler technique</td>
<td>Two-dimensional echo technique</td>
<td>Good temporal and spatial resolution</td>
</tr>
<tr>
<td>High temporal and spatial resolution</td>
<td>Well validated</td>
<td>Well validated</td>
</tr>
<tr>
<td>Measures natural strain</td>
<td>Measures Lagrangian strain</td>
<td>Measures Lagrangian strain</td>
</tr>
<tr>
<td>Unaffected by translational motion</td>
<td>Affected by translational motion</td>
<td>Independent of insonation angle</td>
</tr>
<tr>
<td>Highly insonation angle dependent</td>
<td>Independent of insonation angle</td>
<td>Measures multiple deformations</td>
</tr>
<tr>
<td>Longitudinal and radial strain</td>
<td>Requires high frame rates (&gt;100 to 130)</td>
<td>Requires high quality image, more modest frame rates</td>
</tr>
<tr>
<td>Substantial interpretative variability</td>
<td>Less sensitive to noise; better interpretative variability</td>
<td>Less sensitive to noise; better interpretative variability</td>
</tr>
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</table>

specific uses of strain and sr echocardiography in coronary artery disease

### Specific Uses of Strain and SR Echocardiography in Coronary Artery Disease

**Detection of Coronary Artery Disease**

Because strains and SRs are homogenously distributed across the myocardium, the detection of even subtle changes in either measure suggests myocardial dysfunction (Table 4). Although strain imaging has a potential role in the diagnosis and management of virtually any disease that affects the myocardium, arguably its greatest potential is in the detection of ischemic heart disease. Because longitudinal mechanics predominate in the ischemia-vulnerable subendocardium, either Doppler- or 2D-derived strain can be used because both analyze the longitudinal component of deformation. In the appropriate patient at rest, subclinical LV systolic dysfunction has been shown to correlate with the presence of obstructive coronary disease. Thus, Doppler longitudinal systolic strain and SRs were significantly abnormal in visually normokinetic segments supplied by stenotic (>70%) arteries.\textsuperscript{24} In a prospective, observational study, tissue Doppler systolic and early diastolic strains in the basal anterior segment of patients with left anterior descending (LAD) coronary artery disease remained depressed for 1 hour after exercise (whereas velocity and SR quickly normalized), suggesting that strain-identified regional postischemic dysfunction (ie, myocardial stunning) may be diagnostic in patients with chest pain in whom the ECG has normalized.\textsuperscript{25} In a study of 2D strain imaging, a peak systolic longitudinal SR of \(-0.83\) s\(^{-1}\) and an early diastolic SR of 0.96 s\(^{-1}\) predicted significant (>70%) stenosis with a sensitivity and specificity of 85% and 64% and 77% and 93%, respectively, suggesting the potential for early diastolic deformation to improve diagnostic accuracy. In another study of 108 patients undergoing coronary angiography, a 2D longitudinal strain of \(-17.9\%\) discriminated severe 3-vessel or left main disease from lesser coronary artery disease with a sensitivity and specificity of 79% and 79%, respectively.\textsuperscript{26} Finally, in a cohort of patients with normal ejection fraction at increased atherosclerotic risk and/or with stable chest pain, a progressive impairment of 2D global strain and SR (the former with lower variability and higher reproducibility than the latter) was directly related to increasing severity of coronary disease.
as determined from multislice computed tomography. A global longitudinal strain (the average of segmental longitudinal strains) ≥17.4% provided high sensitivity and specificity (83% and 77%, respectively) in identifying patients with obstructive coronary disease.28 Taken together, these studies support the use of DSI or STE longitudinal strain to identify and risk-stratify atherosclerotic coronary disease with good accuracy and reproducibility.

Dobutamine Stress for Detection of Coronary Artery Disease

Despite the accuracy and clinical utility of dobutamine stress echocardiography (DSE) for the diagnosis of coronary artery disease, the need for good image quality, the subjective nature and expertise required for proper interpretation, difficulties with moderate coronary stenosis, and (laboratory) site variability of interpretable thresholds are important limitations. The incremental value of quantitative strain imaging to DSE and its ability to overcome these limitations have been tested in several investigations. In a closed-chest porcine model of noocclusive coronary stenosis (LAD angioplasty balloon inflation), peak Doppler radial systolic SR and time to regional lengthening predicted a dobutamine-induced reduction in regional myocardial blood flow (measured with colored microspheres) with a sensitivity and specificity of 81% and 91% and 65% and 91%, respectively, in the absence of any change in global hemodynamics.29 A study in patients undergoing both DSE and coronary angiography compared DSI with conventional visual assessment for the detection of regional ischemia using perfusion scintigraphy as the gold standard.30 DSI improved the sensitivity and specificity of dobutamine echocardiography from 81% and 82% to 86% and 90%, respectively. This study also suggested that the ratio of postsystolic deformation (shortening) to maximal motion analysis scoring32 and therefore has the potential to increase the clinical utility of strain analysis during DSE.

STE has also been studied as an adjunct to DSE. In response to a flow-limiting stenosis at rest and a non–flow-limiting stenosis during dobutamine infusion in open-chest pigs, longitudinal and circumferential (but not radial) strain was reduced. Radial strain decreased only in the presence of a flow-limiting stenosis during dobutamine, suggesting that longitudinal and circumferential mechanics are altered earlier than radial mechanics in the ischemic cascade.20 The incremental value of postprocessed 2D and tissue Doppler longitudinal strain to the stress-echocardiographic diagnosis of coronary artery disease was compared in 150 consecutive patients undergoing dobutamine infusion.33 Diagnostic accuracy of strain (and wall motion analysis) was similar for ischemia in the left anterior descending territory and similar (but not as good as wall motion analysis) for the left circumflex territory; however, tissue Doppler strain was more sensitive than either 2D strain or wall motion analysis in the right coronary territory. In another study, the optimal cutoff values for longitudinal, circumferential, and radial strains at peak dobutamine stress derived from 62 patients with a coronary angiographic reference to detect significant coronary stenoses were −20%, −26%, and 50%, respectively; the diagnostic accuracy derived from an additional 40 patient validation group was 85%, 76%, 70%, and 82% for longitudinal, circumferential, radial strains, and wall motion score index, respectively, and the combination of longitudinal strain and wall motion scoring yielded diagnostic accuracy that was incremental to either alone.34 In addition, 2D strain measured in early diastole may increase the accuracy of detecting coronary disease during stress. Delayed LV relaxation detected by radial strain from apical views (transverse strain) during the first third of diastole 5 and 10 minutes after exercise (“diastolic stunning”) identified significant coronary stenosis with a sensitivity of 97% and specificity of 93%.35 These encouraging data suggest that quantitative strain data are sensitive and provide incremental diagnostic information in DSE.

Myocardial Infarction

Longitudinal strains are reduced in patients with myocardial infarctions36 and correlate with infarct size and ejection fraction37,38 and predict LV remodeling and clinical events39 and response to reperfusion strategies.40–42 In a study of patients with recent first myocardial infarctions and matched control subjects, e and SR but not tissue Doppler velocities could differentiate normal from abnormally contracting segments.43 In a subpopulation of the same study who also underwent both DSI and coronary angiography, longitudinal Doppler strain data displayed 85% sensitivity and specificity for the detection of infarct-involved segments using strain and SR cutoffs of −13% and −0.8 s⁻¹, respectively. DSI and regional myocardial blood flow (contrast echo) predicted LV remodeling (≥20% increase in end-diastolic diameter) in 10 patients 4 to 6 months after reperfused ST-elevation myocardial infarction (area under the curve [AUC] for strain, 0.95; SR, 0.85; and regional myocardial blood flow, 0.90) and correlated with an LV functional improvement (ejection fraction increase ≥10%) in an additional 19 patients.40 In 27 patients, percutaneous coronary intervention increased the early diastolic SR in ischemic (but not nonischemic) segments and was associated with an increase in the early diastolic transmittal filling velocity; systolic SRs in ischemic and nonischemic segments were unchanged.41 In 20 patients with severe angina ineligible for revascularization, an improvement in New York Heart Association angina class was associated with improvement in DSI (peak systolic strain), and systolic and diastolic myocardial and diastolic transmittal velocities with enhanced external counterpulsation.42
Viability
The assessment of myocardial viability based on wall motion scoring during low-dose dobutamine infusion is subjective and often difficult. DSI measures may be useful to identify viable myocardium. Stunned myocardium displays reduced systolic SRs that improve with dobutamine infusion or recovery. Additionally, an increase in systolic SR of ≥0.23 s⁻¹ during low-dose dobutamine infusion had a sensitivity and specificity of 83% and 84%, respectively, for the detection of viable myocardium when using ¹⁸F-fluorodeoxyglucose cardiac PET as the gold standard. The incremental value of segments with or without contractile reserve.

50% and occurred equally in nontransmurally infarcted segments with or without contractile reserve. Abnormal segments that recovered function (146 of 369 segments) had lower wall motion score and strain and SRs (and SRI increments), with similar sensitivity and specificity for predicting functional recovery; however, the combination of wall motion score and SRI parameters increased the sensitivity for prediction of functional recovery over wall motion scoring alone without a change in specificity. In contrast, postsystolic shortening may better represent scarring than viability. The prevalence of color Doppler SRI postsystolic shortening was increased in transmural versus nontransmural infarcted segments as determined from late-enhancement gadolinium MRI (96% versus 50%) and occurred equally in nontransmurally infarcted segments with or without contractile reserve.

STE parameters also identify viable myocardium. The viability of myocardial segments (96 segments, 12 rats) after coronary occlusion-reperfusion was assessed with histology (TTC staining) and 2D strain imaging. Segments with greater than 50% area of infarct had lower end-systolic radial and circumferential strains and longer time to peak strains than those with lesser degrees or no infarct, and an end-systolic radial strain less than 2% had a sensitivity and specificity of 88% and 95% for detecting infarcted areas greater than 50%. A study in patients compared the ability of STE radial strain and contrast-enhanced MRI (ceMRI) to predict recovery of 463 segments in 53 patients 9 months after revascularization. Segments that failed to recover had lower peak radial strain (15.2% versus 22.6%) and greater hyperenhancement, and, using a cutoff of 17.2% for peak radial strain, functional recovery was predicted with high accuracy (AUC, 0.859) similar to MRI (AUC, 0.874). The same group later reported similar findings in 512 dysfunctional segments at baseline; the accuracy to predict functional recovery 9 months after revascularization was similar for peak systolic radial strain (AUC, 0.846) and ceMRI (AUC, 0.834). The combination of strain and hyperenhancement improved diagnostic accuracy (AUC, 0.861) and their predictive power.

Global LV strain (averaged peak systolic strain using semiautomated software) in 147 patients with an acute myocardial infarction was correlated with a viability index derived from single-photon emission-computed tomography (r=0.79) and predicted an improvement in ejection fraction 1 year after the index infarction (sensitivity and specificity for improved ejection fraction ≥5% of 86% and 74%, respectively) using a global LV strain cutoff of −13.7%.

Extent of Myocardial Infarction
A related issue—differentiating nontransmural from transmural infarction—has important implications for management, insofar as transmural segments worsen prognosis are unlikely to improve after revascularization. Radial SR and ε responses to dobutamine infusion were compared in a study of closed-chest pigs with chronic nontransmural and transmural infarctions. Before infarction, dobutamine produced a linear increase in SR and a biphasic (increase with low dose, decrease with high dose) ε response. In nontransmural infarcts, baseline SR and ε were reduced compared with control; during dobutamine infusion, ε did not change and the SR response became biphasic. In transmural infarctions, both SR and ε were considerably reduced and failed to respond to dobutamine. Postsystolic deformation occurred in both nontransmural and transmural infarctions (although markedly so in the latter). DSI and ceMRI were compared in 47 patients with a first myocardial infarction (21 transmural, 15 nontransmural ≥50%, and 11 subendocardial <50%) and 60 volunteers. An SR >−0.59/s detected transmural infarction with high sensitivity and specificity (90.9% and 96.4%, respectively) and a −0.98/s>SRI>−1.26/s discriminated subendocardial infarction from normal myocardium with very good sensitivity and specificity (81.3% and 83.3%, respectively).

The ability of STE to assess infarct scar size (histology) and infarct-induced LV remodeling (end-systolic diameter) was examined in rats 4 to 10 weeks after LAD ligation. Circumferential and radial strains were both significantly decreased after infarction and were lowest in the infarcted segments, but segmental circumferential strain was dependent to a similar extent on segmental fibrosis and end-systolic diameter, whereas segmental radial strain was more dependent on end-systolic diameter. The ability of STE to differentiate the transmural extent of infarction measured with ceMRI and dobutamine stress echo was tested in 80 patients with chronic LV ischemic dysfunction. Segments with transmural scar had lower circumferential strain and SRs than subendocardial (1% to 50% wall thickness) infarcts and normal myocardium. However, neither radial nor longitudinal deformation indices discriminated transmural from subendocardial scar, although longitudinal strain and SR (unlike dobutamine stress wall motion analysis) distinguished subendocardial infarct from normal segments. In contrast, a regional longitudinal strain cutoff value of −4.5% distinguished nontransmural from transmural infarction with high sensitivity and specificity (81.2% and 81.6%, respectively), and a segmental radial strain cutoff value of 16.5% distinguished nontransmural from transmural infarctions with reasonable sensitivity and specificity (70.0% and 71.2%, respectively), as did a circumferential strain cutoff value of −11.1%.

Global strains derived from DSI and STE were assessed acutely and at 10 days in 36 patients after ST-elevation myocardial infarction treated with thrombolysis and were compared with infarct size and transmurality using ceMRI. LV global circumferential strain (from 6 segments) and particularly LV global peak systolic longitudinal strain (from 16 segments) correlated with infarct size; segmentally, circumferential strain better distinguished transmural from sub-
endocardial necrosis than longitudinal strain (sensitivity and specificity of circumferential strain to predict transmural necrosis of 80% and 74%, using a cutoff of −13.3%). Reproducibility was better with STE than DSI. In a study of 61 patients with non–ST-elevation myocardial infarction, LV global longitudinal strain before revascularization (28% surgical, 69% percutaneous coronary intervention) predicted infarct size (as did wall motion score index) 9 months after infarction. A global longitudinal strain $>−13.8\%$ (and a wall motion score index $>1.3$) identified patients with infarcts involving $>12\%$ of myocardium. Global circumferential and global radial strains were not as predictive. Thus, measurement of regional deformation and global strains with either DSI or STE, ideally in multiple directions, has the potential to identify infarct size and the transmural extension of a myocardial scar and therefore the extent of nonviable myocardium. Variable cutoffs between laboratories that may be explained in part by methodologic, analytic, and experimental design differences remain problematic.

**Prognosis**

Although many studies have reported on the diagnostic accuracy of strain and SR for detecting coronary disease, only a few studies have examined its prognostic value. Peak wall motion score index, mean and segmental SRs, and segmental strain independently predicted mortality over a 7-year follow-up in a study of 646 patients undergoing dobutamine stress echocardiography using automated segmental strain analysis; moreover, prediction from models based on clinical data were improved by wall motion score index and further increased by adding either segmental or mean SRs to the model. In a study of 358 patients, anatomic M-mode SR stress echocardiography (dobutamine, bicycle, and treadmill) was used to risk-stratify 358 patients followed nearly a year for death and myocardial infarction. Abnormal SR at rest was defined as being $>−1/s$ (or green-yellow hue by subjective visual assessment), whereas an ischemic SR was defined by the development of postsystolic shortening or a SR $>−2/s$ (or brown hue) during stress. Event rates were greater in those with an abnormal (7.2%) than those with a normal SR stress response (0.5%), and independently predicted events (relative risk, 1.75). Surprisingly, although wall motion score index was concordant with SR imaging, the index itself was not predictive. In another study, the ability of dobutamine–VVI strain and SR to predict events (mortality, myocardial infarction, revascularization) over an 18-month follow-up was tested in 84 patients with left bundle-branch block (which may be problematic during stress testing). The average SR at peak stress was the only independent predictor of outcome when echocardiographic variables were added to a clinical model (hazard ratio, 2.38/0.2/s; $P<0.001$); event-free survival in patients with an average SR at peak stress lower (more negative) and higher than $−0.5/s$ were 89.9% and 45.9%, respectively. Finally, 659 patients were followed for 21±13 months after myocardial infarction (48% with multivessel disease, LAD culprit vessel in 48%; ejection fraction, 46±8%); after adjustment for clinical and traditional echocardiographic predictors, the global LV longitudinal strain and SR were independently related to the primary (all-cause mortality) and secondary end point (a composite of revascularization, reinfarction, and hospitalization for heart failure). Thus, patients with a global strain and SR $≥15.1\%$ and $−1.06/s$ had 5 and 4 times the risk of all-cause mortality and 2 and 5 times the risk of a secondary event, respectively. Owing to the small number of events and the relatively short follow-up, these intriguing and promising studies should be regarded as preliminary.

**Perspective**

Despite considerable data suggesting that deformational analysis has clinical utility in patients with known or suspected coronary artery disease, DSI has not become standard, daily practice because it requires expertise and highly trained operators and time-consuming data acquisition and processing with high interobserver variability. In addition, its 1D and highly angle-dependent nature and its limited spatial resolution and reduced signal-to-noise ratio are important limitations. In contrast, STE is more likely to become standard practice because it may be semiautomated and therefore less time consuming, and, compared with DSI, has increased reproducibility, greater signal to noise, no angle dependency, and is multidirectional. Nonetheless, variable cutoffs and algorithms, rapidly changing software, and a paucity of normative values remain impediments to the use of strain imaging. For example, although normal mean peak systolic longitudinal, circumferential, and radial strains are $≈17\%$ to 25%, 21% to 26%, and 37% to 39%, respectively, these values are based on small numbers of subjects and are highly variable and dependent on age, sex, ventricular region, and algorithm. Finally, although temporal and magnitude markers of regional strain and changes in the strain curve (eg, postsystolic shortening) will find importance in specific situations, global longitudinal strain, which correlates with LV ejection fraction and predicts functional recovery and cardiovascular morbidity and mortality, has the potential to become a routine clinical measurement in the evaluation of CAD.

**Conclusions**

Doppler-derived and 2D echocardiographic–derived myocardial strain imaging represent exciting advances in the field of noninvasive cardiac imaging. Strain and SR are sensitive (detect early disease), correlate well with other measures of cardiac function, and detect changes in myocardial contractility, both normal and abnormal, across a wide range of ischemic syndromes. They provide novel insights into the complex deformations of the left ventricle and appear likely to enhance detection of coronary artery disease and viable myocardium and predict the sequelae of myocardial infarction, the response to reperfusion, and prognosis. With further study, technological refinements, automation, and establishment of normative values, echocardiographic strain imaging will add greatly needed objectivity to the evaluation of cardiovascular disease, especially in the patients with coronary artery disease.

**Disclosures**

Dr Hoit is a speaker for Philips Medical.
References

Assessment of segmental myocardial viability using regional myocardial perfusion and deformation imaging in patients with left bundle branch block.

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