Tissue Doppler, strain, and strain rate echocardiography for the assessment of left and right systolic ventricular function

D Pellerin, R Sharma, P Elliott, C Veyrat

Heart 2003;**89**(Suppl III):iii9–iii17

Tissue Doppler (TDE), strain, and strain rate echocardiography are emerging real time ultrasound techniques that provide a measure of wall motion. They offer an objective means to quantify global and regional left and right ventricular function and to improve the accuracy and reproducibility of conventional echocardiography studies. Radial and longitudinal ventricular function can be assessed by the analysis of myocardial wall velocity and displacement indices, or by the analysis of wall deformation using the rate of deformation of a myocardial segment (strain rate) and its deformation over time (strain). A quick and easy assessment of left ventricular ejection fraction is obtained by mitral annular velocity measurement during a routine study, especially in patients with poor endocardial definition or abnormal septal motion. Strain rate and strain are less affected by passive myocardial motion and tend to be uniform throughout the left ventricle in normal subjects. This paper reviews the underlying principles of TDE, strain, and strain rate echocardiography and discusses currently available quantification tools and clinical applications.

For 30 years, the non-invasive ultrasonic assessment of myocardial function has relied on grey scale echocardiography and Doppler examination of intracardiac flow velocities. Technological advances in signal processing now make it possible to directly measure myocardial velocity and deformation in real time. Isaaz *et al*[1] were the first to introduce the concept of tissue Doppler echocardiography (TDE) to assess myocardial velocity using the pulsed Doppler technique. The use of colour TDE was subsequently reported by Sutherland *et al*[2] and Yamazaki *et al*.[3] Heimdal *et al* introduced real time strain rate calculation in the longitudinal axis in 1998.[4] TDE is now available on most modern cardiac ultrasound systems and can be used during a routine echo examination to assess global and regional left ventricular function. The origin of TDE myocardial velocities is related to myocardial architecture and fibre orientation. This paper reviews the underlying principles of TDE, strain, and strain rate echocardiography and discusses currently available quantification tools and clinical applications.

PRINCIPLES OF TISSUE DOPPLER ECHOCARDIOGRAPHY

Unlike conventional Doppler signals that are typified by high velocity and low amplitude, myocardial motion is characterised by relatively low velocity and high amplitude signals. Tissue motion creates Doppler shifts that are approximately 40 dB higher than Doppler signals from blood flow whereas velocities rarely exceed $\pm$ 20 cm/s.[1–3] To record low wall motion velocity, gain amplification is reduced and high pass filters are bypassed with the tissue signal directly entered into the autocorrelator.

During image acquisition, it is important to optimise the frame rate using an image sector as narrow as possible and to select the appropriate velocity scale. These parameters should be optimised at the time of imaging, as it is not possible to modify the frame rate and the velocity scale during post-processing image analysis.

MODALITIES OF TISSUE DOPPLER ECHOCARDIOGRAPHY

TDE has three modalities: spectral pulsed wave Doppler, two dimensional, and M mode colour Doppler.

Spectral Doppler

Spectral pulsed TDE has the advantage of online measurements of velocities and time intervals and an excellent temporal resolution (8 ms). Figure 1 illustrates a normal TDE waveform. According to the Doppler principle, tissue velocities moving toward the transducer are positive, whereas velocities moving away from the transducer are negative. Since the wall moves whereas the sample volume is fixed, the spatial resolution is poor and myocardial layers cannot be separately analysed. The ''onion bulb-like'' shape of the sample volume also decreases lateral resolution.

Colour Doppler

In colour TDE, red encodes wall motion towards the transducer (positive velocities), whereas blue encodes wall motion away from the transducer (negative velocities). On each side of the scale, the brightest shades correspond to the highest velocities. Colour images require digital acquisition and storage for off-line post-processing analysis. In contrast to spectral Doppler, endocardial and epicardial layers can be separately analysed. Peak and mean velocities, time velocity integral, and regional time intervals can be measured in each myocardial segment, in each myocardial layer, and in each phase of the cardiac cycle.

M mode colour encoded TDE has a high temporal resolution (5–10 ms). Colour two dimensional imaging has been limited by a slow frame rate, but parallel processing and advances in beam formation technology have increased the frame rate to a level adequate for analysis of most cardiac events (temporal resolution 10–100 ms).

QUANTIFICATION TOOLS FOR COLOUR TISSUE DOPPLER ECHOCARDIOGRAPHY RECORDINGS

There are three TDE quantification tools currently available: reconstructed spectral pulsed wave TDE, curved M mode colour display, and myocardial velocity gradient (MVG) analysis.

Abbreviations: AV, atrioventricular; MVG, myocardial velocity gradient; TDE, tissue Doppler echocardiography

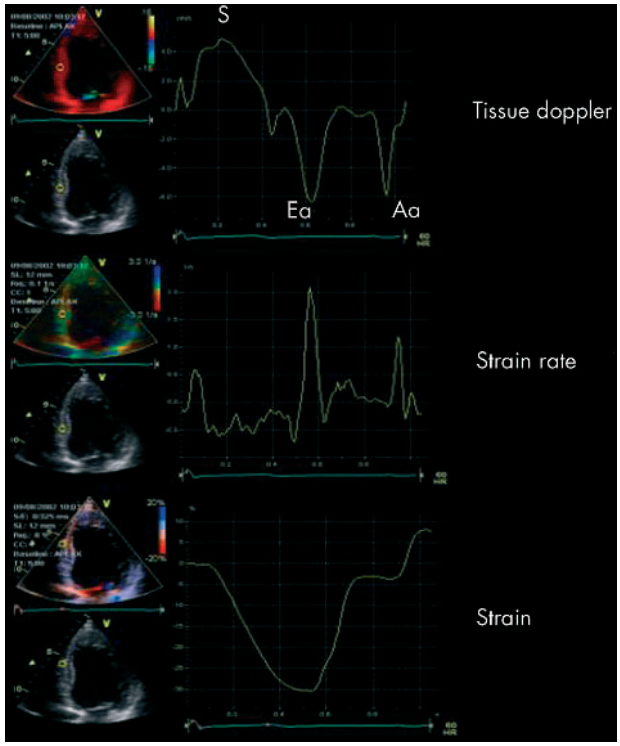

Figure 1 Tissue Doppler echocardiography (TDE), strain rate, and strain profiles of a normal subject obtained from an apical four chamber view. Time is on the horizontal axis. The region of interest is located in the mid inferoseptal segment. The TDE waveform consists of a first positive wave during the pre-ejection period, a systolic inward wall motion (S), followed by the isovolumic relaxation waves and by the outward wall motions Ea and Aa related to ventricular filling. Longitudinal strain rate profile is obtained from the same region of interest during the same cardiac cycle and shows corresponding waves. Negative systolic strain indicates longitudinal compression.

Reconstructed spectral pulsed wave Doppler

Simultaneous pulsed Doppler interrogation of multiple myocardial segments can be obtained off-line using high frame rate colour two dimensional TDE cine-loops in order to generate time−velocity plots. Velocities measured off line are lower than those obtained from online spectral pulsed TDE because they are derived from regional mean velocity rather than peak velocity. The major advantage of reconstructed spectral pulsed wave TDE is that information from several myocardial segments can be obtained within the same cardiac cycle.

Curved M mode colour display

The curved M mode colour velocity display is a reconstructed colour M mode recording along a manually traced line. Curved M mode reconstruction provides an instantly interpretable visual display of segmental asynchrony between myocardial segments. Regional delays can be calculated according to temporal resolution (currently 10−20 ms), which depends on the frame rate.

Myocardial velocity gradient

In the normally contracting heart, the endocardium moves faster than the epicardium. The consequent velocity gradient across the thickness of the wall from the endocardium to the epicardium reflects the rate of change in wall thickness and is equivalent to strain rate. Systolic MVG is an indicator of regional myocardial contraction that is independent of the translational motion of the heart. MVG is also little affected by the Doppler angle of incidence.[5 6] From the theoretical construct devised by Fleming in 1994,[7] a clinical method was proposed by several groups.[8–17] MVG was defined as the slope of the regression line between myocardial velocities and wall thickness. Units are s^{-1}. MVG can also be calculated as the difference between endocardial and epicardial velocities, divided by wall thickness.[10] Another MVG calculation algorithm has been proposed[17] using the time−velocity plot obtained by an automatic measurement of endocardial and epicardial velocities over time along a line parallel to endocardial or epicardial boundaries throughout the cardiac cycle. MVG calculations using this method correlate with that obtained by thickness−velocity plot and in addition provide automatic detection of peak velocity, timing, and duration of wall velocity changes over time.

TDE velocities have been validated using a rotating sponge model,[8] ventriculography and digitised M mode echocardiography,[1] myocardial length crystals, and high fidelity pressure and conductance catheters.[18] A correlation has been shown between time intervals assessed by TDE and time intervals assessed haemodynamically.[19] TDE velocities relate to the percentage of interstitial fibrosis and the myocardial β adrenergic receptor density.[20]

PRINCIPLES OF STRAIN AND STRAIN RATE ECHOCARDIOGRAPHY

Strain and strain rate are TDE derived modalities that are now available in real time. Strain rate measures the rate of deformation of a tissue segment and is measured in s^{-1}. Peak systolic strain rate represents the maximal rate of deformation in systole. An algorithm calculates spatial differences in tissue velocities between neighbouring samples within the myocardium aligned along the Doppler beam. A sample distance of 5−11 mm has been previously used. Strain is obtained by integrating strain rate over time and represents deformation of a tissue segment over time. Strain is expressed as the per cent change from the original dimension. Systolic strain represents the magnitude of deformation between end diastole used as a reference point and end systole (fig 1).

Systolic strain is positive and blue encoded when there is regional expansion. This is thickening in parasternal views and lengthening in apical views. Negative systolic strain is yellow−red encoded to denote regional compression, which is thinning in parasternal views and shortening in apical views. Infarcted myocardial tissue does not demonstrate shortening or lengthening activity and shows no or minimal systolic strain rate or strain, which is displayed as green. The technique of raw data storage and reconstruction permits the measurement of tissue velocity, peak systolic strain rate, peak early and late diastolic strain rate, and peak systolic strain from the same sample volume within the same cardiac cycle. Simultaneous interrogation of multiple myocardial segments and curved M mode colour display are also applicable to strain and strain rate.

Myocardial strain and strain rate have been validated in vitro using compressed gelatin phantoms[21 22] and in vivo using ultrasonic crystals,[23] pressure−volume loops,[24] or magnetic resonance imaging.[25] Peak posterior wall systolic strain rate accurately follows changes in myocardial contractility induced by adrenaline (epinephrine), β blockers, and pacing.[26]

The inter-observer and intra-observer variabilities of TDE, strain, and strain rate measurements were less than 15%.[27–30]

LIMITATIONS

As with flow Doppler, TDE velocity, strain rate, and strain measurements are angle dependent.[23 31] With the currently available technology, strain rate has a relatively poor signal-to-noise ratio and is load sensitive.[23] Strain measurements are

made along a single ultrasound scan line. Three dimensional TDE may overcome this limitation.[32] Limitations related to complex fibre architecture and to translation and rotation of the heart apply to all imaging modalities. Off-line analysis is required for colour images, which is time consuming.

ASSESSMENT OF GLOBAL SYSTOLIC LEFT AND RIGHT VENTRICULAR FUNCTION

TDE can be used to assess left ventricular ejection fraction using mitral annular velocity measurements during a routine study. This method is quicker and easier than the Simpson's rule with better reproducibility because tissue velocity assessment is not dependent on endocardial definition. Mitral annular velocity can be measured in more than 95% of patients.[33 34] Heart contraction is caused by complex myocardial fibre architecture and orientation and has three components: longitudinal, radial, and rotational between base and apex.

Long axis function

Long axis function is assessed from the apical window. Harvey Feigenbaum suggested the assessment of mitral annular motion by echocardiography as an index of left ventricular systolic function in 1967 using M mode recordings.[35] Velocities derived from the mitral annulus or the left ventricular base primarily reflect longitudinal motion. The longitudinally directed fibres are found in the subendocardium.[36 37] As the apex of the heart remains stationary, long axis changes are reflected in movements of the base.

Mitral annular systolic velocity can be used as an index of global ventricular function.[34 35 38 39] Several investigators have shown significant positive correlations between left ventricular ejection fraction and six-site average peak systolic mitral annular velocity.[33 34 40–42] When the patients were divided into two different groups with respect to an ejection fraction $\geqslant 0.50$ or < 0.50, a cut-off mean systolic mitral annular velocity of $\geqslant 7.5$ cm/s had a sensitivity of 79% and a specificity of 88% in predicting a preserved global left ventricular systolic function.[33] Peak mitral annular systolic velocity from the apical four chamber view (average from inferoseptal and lateral sites) correlated most closely with left ventricular ejection fraction as an individual view.[34]

Mitral annular peak systolic velocity is also a sensitive indicator of alterations in left ventricular contractility induced by low dose dobutamine infusion at 1, 2, 3, and 5 μg/kg/min.[43] Mitral annular systolic velocity significantly increased with only 1 μg/kg/min of dobutamine and further incremental increases occurred with each subsequent dose. A linear dose−response relation was demonstrated within this narrow dosage range. Routine measures of left ventricular ejection fraction by Simpson's rule did not detect increases until the 3 μg/kg/min dose. Another report showed that mitral annular systolic velocity can detect abnormal systolic function in patients with heart failure and a normal ejection fraction (diastolic heart failure).[44]

However, mitral annular velocity measurement cannot be used in patients with severe mitral annular calcification, prosthetic ring or prosthetic mitral valve.

Recently, mitral annular velocity has been shown to be a powerful predictor of cardiac death over the next two years and provides significant incremental prognostic value compared with clinical information and mitral deceleration time of the E wave < 160 ms.[45]

Tricuspid annular velocity can be used as an index of right ventricular function in patients with heart failure.[46] There was a good correlation between systolic annular velocity and right ventricular ejection fraction assessed by radionuclide ventriculography. A systolic annular velocity < 11.5 cm/s predicted right ventricular ejection fraction $< 45\%$ with a sensitivity of 90% and a specificity of 85%.[46] Tricuspid annular velocity may also be another prognostic index in patients with dilated cardiomyopathy.[47]

Myocardial acceleration during isovolumic contraction has recently been validated in experiments as a novel non-invasive index of right and left ventricular contractile function.[48 49]

Radial function

Radial function is assessed from the parasternal window. Systolic MVG can be used to assess ventricular function in patients with paradoxical septal motion. In patients with atrial septal defect and paradoxical septal motion seen on conventional echo recordings, septal MVG fitted within the range of control subjects.[50]

Unlike conventional echo that does not show left ventricular wall motion during the pre-ejection period, TDE displays several colour strips within the walls representing wall motions with rapid changes in direction of motion. The velocity reversals had mirror signs in opposite walls, featuring successive inward and outward wall motions. In both walls, there was a simultaneous inward motion toward the left ventricular cavity centre.[16 51] Pre-ejection period inward motion velocity in the posterior wall correlated linearly with left ventricular systolic function.[16]

Aging

Transmitral inflow velocity, systolic and diastolic TDE velocity measurements vary with age. In contrast, there was no correlation between increasing age and systolic MVG.[10 52 53] An inverse relation has also been shown between age and systolic velocity at peak dose dobutamine, in both men and women.[54]

Relation between systole and diastole

A relation between systole and diastole has been described in patients with dilated cardiomyopathy evaluated by TDE.[55] TDE ejection and early diastole peak velocities have been measured in controls and patients with multi-vessel coronary artery disease and in patients with idiopathic dilated cardiomyopathy. TDE ejection velocities were strongly and positively correlated with early diastole velocities in the left ventricular posterior wall. Velocity increase from ejection to early diastole was $< 25\%$ in 78% of patients with ischaemic heart disease and might be useful in the non-invasive selection of patients with global severe left ventricular dysfunction and multi-vessel coronary artery disease.[56]

QUANTIFICATION OF REGIONAL WALL MOTION

TDE, strain, and strain rate have the potential to objectively quantify regional ventricular wall motion using high frame rate and high resolution acquisition systems, and off-line analysis of digital images.

Heterogeneity of ventricular wall motion in normal subjects

Normal values of TDE velocities have been reported[57 58] and regional differences in myocardial velocities have been described between individual wall segments using TDE.[5 52 58–60]

In the parasternal view, velocities are lower in the anteroseptal wall than in the posterior wall.[5 59 60] The translational motion of the heart in the chest during the cardiac cycle is anteriorly directed in systole and posteriorly directed in diastole. Velocities related to these components are superimposed on the intrinsic wall velocities, increasing velocity values at the posterior wall, and decreasing them in the septum. Systolic MVG was also lower in the anteroseptal

wall (1.69 (0.53) s^{-1}) than in the posterior wall (3.28 (0.67) s^{-1}).

In the apical view, the longitudinal velocity decreases from base to apex.[58 61] However, this may not represent intrinsic differences in tissue velocities, as this gradient was not seen when strain rate was measured by either echocardiography or magnetic resonance imaging.[25] Rather, the difference is a function of the greater motion of the whole heart at the base compared with the mid and apical regions. In addition, apical segments cannot be assessed using TDE because of the limited movement of the apex and unfavourable angle of incidence of apical myocardial motion with respect to the transducer position. Strain and strain rate are much less affected by passive myocardial motion and tend to be uniform throughout the left ventricle in normal subjects. The finding of MVG in a myocardial segment distinguishes active motion from passive translation.[62]

Longitudinal strain was lower than radial strain in controls. Longitudinal systolic strain and strain rate were –25 (7)% and –1.9 (0.7) s^{-1} respectively, whereas radial systolic strain was –57 (11)% and systolic strain rate was –3.7 (0.9) s^{-1}.[63]

Velocities at the lateral margin of the tricuspid annulus are higher than those of the lateral mitral annulus.[64] In the right ventricle, longitudinal strain and strain rate were higher than in the left ventricle and were heterogeneous with maximal strain and strain rate in the mid free wall segment.[63]

Ischaemic heart disease

Contraction of the ventricle in the longitudinal axis is mainly caused by subendocardial fibres[36] which are sensitive to ischaemia.[37 65] Experimental and clinical studies have shown that during acute ischaemia, myocardial peak systolic velocity and strain rate were notably reduced or reversed within 5 seconds after coronary occlusion and were delayed. In addition, there was positive velocity after the end of ejection.[6 29 66–68] Post-systolic shortening or thickening is a sensitive marker of ischaemia and can be easily recognised by high velocity, strain rate or strain occurring during the isovolumic relaxation period, often extending into the early filling period.[28 69 70] Accurate timing of the aortic valve closure is crucial for recognition of post-systolic shortening. However, post-systolic shortening is a normal finding in healthy subjects occurring in approximately a third of myocardial segments and, thus, is not always a marker of disease. Pathologic post-systolic shortening has high magnitude with coexisting reduction in systolic strain and strain rate, and its peak occurred later than in control subjects[71] (fig 2). Strain echocardiography has been shown to be a more sensitive technique than TDE for detecting regional ischaemic wall motion abnormalities during acute ischaemia.[29] Analysis of myocardial TDE velocities cannot distinguish between persistent ischaemia and stunning.[14] This can be achieved using MVG calculation across the thickness of the wall without dobutamine infusion.[72] However, ischaemia and stunning can be distinguished using a dobutamine infusion. In the case of ischaemia, strain and strain rate decreased with post-systolic shortening[28] in contrast with stunning.[69] Reduction in radial systolic strain occurred earlier that the reduction in tissue velocities or visually estimated wall motion score.[73]

Myocardial strain rate and strain have the potential to discriminate acute from chronic ischaemia and myocardial infarction.[23] Infarcted myocardium is characterised by significantly reduced systolic and diastolic velocities, deformation rates, and MVG and by the loss of the homogeneous distribution of systolic strain rate from apical to basal segments.[9 27 33 74–77] In the border zone, systolic velocity and MVG were lower than in normal segments when there was a large myocardial infarction. Reduced systolic longitudinal velocities have been found in ischaemic segments even if there was normal wall motion on visual assessment.[76] Using MVG, it was possible to distinguish between transmural and non-transmural acute myocardial infarction after reperfusion therapy without inotropic stimulation.[72]

Quantification of stress echocardiography

Detection of ischaemia

Although clinically useful in its present form, the main limitations of stress echocardiography interpretation are the subjective visual analysis of endocardial motion and wall thickening and the necessity of adequate training. In addition, the low temporal resolution typically used in clinical stress echocardiography does not always allow accurate detection of small differences in asynchrony.[78] Myocardial velocity may provide a more objective correlate of ischaemia, reducing the expertise needed for interpreting stress echocardiography with improved reproducibility.

TDE criterion to detect stress induced ischaemia is a lack of increase in peak systolic velocity[79 80] (fig 2). Cut-off values for detection of ischaemia have been proposed.[81] These cut-off values were selected according to the lower 20th centiles of the velocity distribution in a normal population and gave diagnosis accuracy equivalent to expert interpretation in wall motion. In the MYDISE (myocardial Doppler in stress echo) study,[54] cut-off values were selected from receiver operator curves and were higher. A cut-off value of 10.3 cm/s for left anterior descending coronary artery disease, 10.8 cm/s for circumflex coronary artery disease, and 12.8 cm/s for right coronary artery disease were found in corresponding basal segments at peak stress.

Strain and strain rate may be superior to TDE velocity indices in the detection of induced ischaemia.[82] Measurements of endocardial velocity and conventional wall motion analysis did not reliably distinguish between ischaemic and non-ischaemic segments. In contrast an increase in MVG greater than 2.6 s^{-1} has been observed in non-ischaemic segments, whereas no ischaemic segment showed an increase in MVG greater than 1.5 s^{-1}.

The amplitude and timing of deformation were compared with conventional stress echocardiography, perfusion scintigraphy, and coronary angiography.[83] Post-systolic shortening was found in all ischaemic segments (fig 3). The ratio of post-systolic shortening to maximal segmental deformation was the best quantitative parameter to identify stress induced ischaemia and may be used as an objective marker of ischaemia during dobutamine stress echocardiography. Compared with conventional echocardiography, strain rate colour curved M mode analysis improved sensitivity and specificity from 81% and 82% to 86% and 90%, respectively.[83]

Time interval measurements are not influenced by the angle of incident ultrasound beam. Time to onset of myocardial relaxation in strain rate M mode display was delayed in ischaemic segments in patients with coronary artery disease.[30 84] During dobutamine stress echocardiography, time to onset of relaxation decreased in all non-ischaemic segments, whereas this decrease was blunted in ischaemic segments.[84] A change in time to onset of relaxation of 20% could identify new wall motion abnormalities with a sensitivity of 95% and a specificity of 75%.

Detection of viability

Quantification of regional left ventricular function may reduce the expertise needed for interpretation and improve the reproducibility for the identification of myocardial viability in patients with chronic coronary artery disease and severe left ventricular dysfunction.

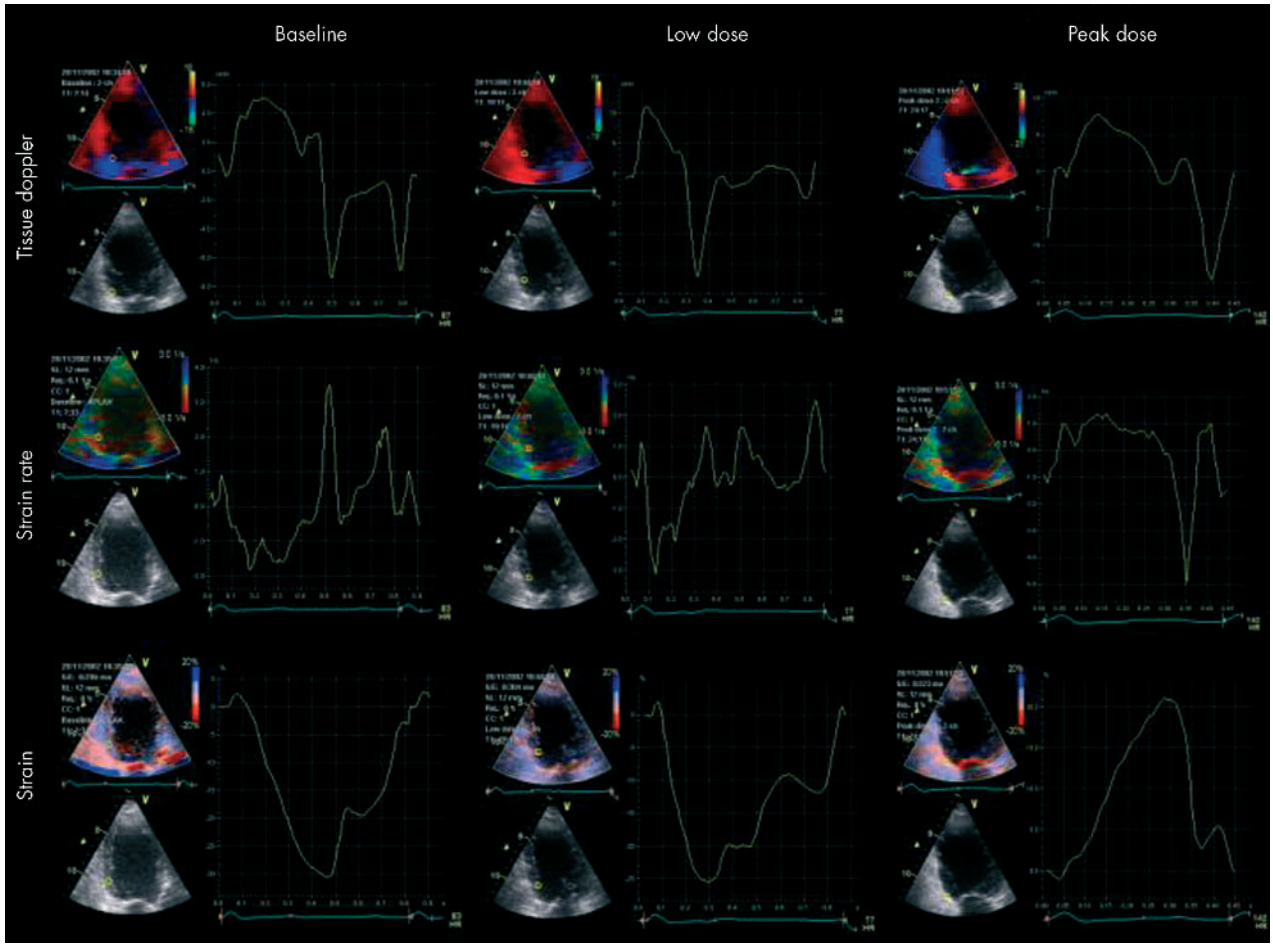

Figure 2 Quantitative analysis of a dobutamine stress echocardiographic study performed in a 53 year old patient who presented with atypical chest pain. Baseline, low dose, and peak dose dobutamine infusion have been recorded using colour high frame rate TDE. Strain rate and strain images were obtained and analysed off-line. The region of interest was located in the inferobasal segment where visual interpretation of changes in wall thickening and endocardial motion proved difficult. At baseline, longitudinal TDE, strain rate, and strain profiles showed a normal pattern with peak systolic velocity 5 cm/s, peak systolic strain rate −1.9 s^{-1}, and peak systolic strain −30%. During low dose dobutamine infusion, TDE velocity and deformation rate increased. Peak systolic TDE velocity was 11 cm/s and peak systolic strain rate was −3.1 s^{-1}. In contrast, peak systolic strain mildly decreased to −25%. During peak dose dobutamine infusion, peak systolic TDE velocity was reduced to 7.8 cm/s. The basal inferior region showed longitudinal expansion in systole with inverted and positive peak systolic strain rate +1.2 s^{-1} followed by pronounced negative strain rate during isovolumic relaxation (post-systolic shortening). Systolic strain was clearly positive as opposed to baseline and low dose dobutamine profiles. This segment, therefore, became ischaemic at peak stress and showed a biphasic response during incremental doses of dobutamine.

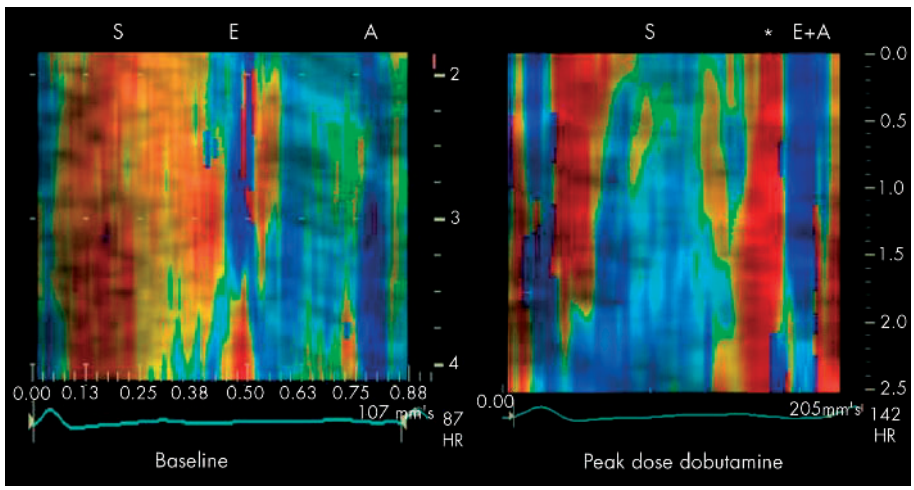

Figure 3 Colour curved M mode longitudinal strain rate images in the same patient as in fig 2 obtained in the inferobasal segment at baseline and peak dose dobutamine infusion. At baseline, there is negative systolic strain rate (red encoded) showing normal longitudinal shortening. During peak dose dobutamine infusion, there is positive systolic strain rate (blue encoded) showing longitudinal expansion or lengthening. The systolic strip is followed by a red encoded strip (*) occurring after aortic valve closure showing post-systolic shortening, another marker of ischaemia. Curved M mode reconstruction provides a visual analysis of segmental deformation rate of myocardial segments.

Sensitivity in the detection of viable myocardium was improved by using TDE velocity when compared with conventional echocardiographic parameters.[85 86] A combination of echo and TDE techniques was able to detect as many severely hypokinetic or akinetic but viable segments as rest−reinjection thallium tomography in patients with chronic coronary artery disease and low left ventricular ejection fraction.[87]

In patients after myocardial infarction MVG between endocardium and epicardium during dobutamine stimulation showed high sensitivity for the prediction of reversible dysfunction.[88] In patients with severe chronic three vessel disease and left ventricular dysfunction, transmural MVG could distinguish viable from non-viable segments when compared with rest−reinjection thallium tomography.[89] In viable segments, the highest velocities were found in the mid layer conferring a bell shaped pattern to the MVG. Contractile reserve was mainly caused by increased mid wall velocities (fig 4). These results suggest that the contractile properties of diseased but viable myocardium are mainly concentrated in the mid layer. The dramatic ultrastructural changes observed in hibernating myocardium may explain the heterogeneity of the MVG. In non-viable segments, the distribution of velocity was close to zero or anarchic with small variation and did not change significantly with dobutamine.[89]

Changes in regional function of stunned myocardium during inotropic stimulation were better characterised by strain rate than by strain values on experiments.[69]

Using ^{18}F-fluorodeoxyglucose positron emission tomography as reference, an increase in systolic strain rate of 0.23 s^{-1} during low dose dobutamine infusion has been shown to discriminate viable from non-viable myocardium with a sensitivity of 83% and specificity of 84%. In that study, strain echocardiography was superior to two dimensional or tissue Doppler imaging for the assessment of myocardial viability.[90]

Cardiomyopathy

Several studies have shown that TDE, strain, and strain rate echocardiography can detect subclinical dysfunction when conventional echocardiography is normal in patients with cardiomyopathy. One potential implication of this diagnostic sensitivity is the early detection of disease in asymptomatic gene carriers of familial cardiomyopathy.

Left ventricular hypertrophy is the clinical sign of familial hypertrophic cardiomyopathy and is absent in a significant number of subjects with causal mutations. In a transgenic rabbit model of human hypertrophic cardiomyopathy, TDE detected myocardial contraction and relaxation abnormalities, irrespective of cardiac hypertrophy.[91] Mitral annular systolic and early diastolic velocities also detected myocardial abnormalities in patients with hypertrophic cardiomyopathy and provided early diagnosis before and independently of hypertrophy.[92] Mitral annular systolic velocity < 12 cm/s and early diastolic velocity < 13 cm/s gave a sensitivity of 100% and a specificity of 90%. This pioneer work has to be confirmed by other reports.

In patients with secondary left ventricular hypertrophy, radial function may compensate for longitudinal dysfunction. Normal short axis systolic function may be associated with abnormalities in the timing and amplitude of apically directed myocardial velocities in these patients.[57]

Distinguishing physiological adaptive left ventricular hypertrophy caused by exercise, as in athletes, from a pathological process, as in hypertrophic cardiomyopathy, despite similar left ventricular hypertrophy has been achieved in patients[12] and in animal experiments[93] using MVG across the thickness of the left ventricular posterior wall. MVG values < 7 s^{-1} showed a positive predictive value of 96% and a negative predictive value of 94%.[12] This regional diastolic parameter was less sensitive in the older population. Long axis systolic and early diastolic velocities were decreased in patients with pathologic hypertrophy, but preserved in athletes. The best differentiation of pathologic from physiologic hypertrophy was provided by a mean systolic annular velocity < 9 cm/s (sensitivity 87%, specificity 97%).[94]

In restrictive cardiomyopathy, mitral annular velocity and posterior wall MVG were reduced whereas these parameters were within normal range in constrictive pericarditis.[95 96] MVG during isovolumic relaxation was positive in restrictive patients and negative in constrictive patients.

Cardiac AL (primary) amyloidosis is characterised by an early impairment in systolic function at a time when fractional shortening remains normal. This abnormality precedes the onset of congestive heart failure and can be detected by systolic strain and strain rate but is not apparent by TDE systolic velocity.[97]

Fabry cardiomyopathy is diagnosed by detection of left ventricular hypertrophy in patients with α-galactosidase A deficiency. Conventional non-invasive tools are unable to provide a pre-clinical diagnosis allowing prompt institution of enzymatic therapy. Early detection of Fabry cardiomyopathy has been obtained by TDE before development of left ventricular hypertrophy.[98]

In patients with Friedrich's ataxia who were homozygous for the GAA expansion in the smaller allele of the Friedrich's ataxia gene,[99] systolic and early diastolic radial MVG was lower than in age matched control subjects. A uniform reduction of strain and strain rate indices has also been

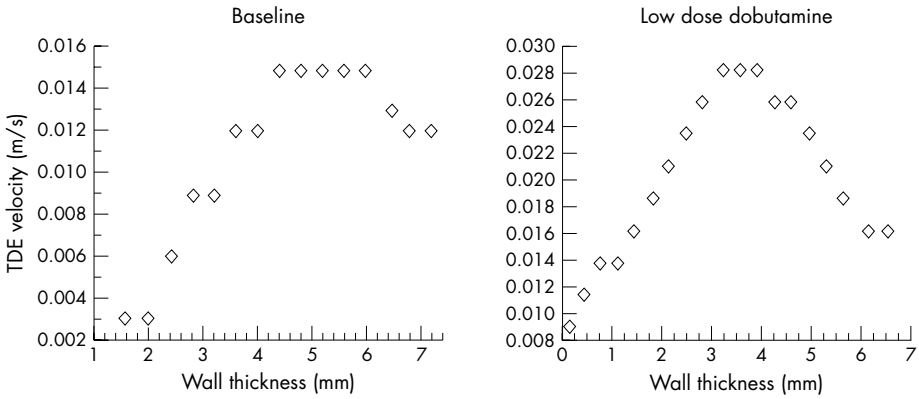

Figure 4 Quantitative analysis of stress echocardiography for the detection of viable myocardium in a 63 year old man with severe three vessel coronary artery disease and a left ventricular ejection fraction of 32%. Transmural myocardial velocities across the thickness of the wall were measured in a severely hypokinetic but viable segment assessed by echocardiography and rest−reinjection thallium tomography. The highest velocities were located in the mid layer conferring a bell shaped pattern to the myocardial velocity gradient in contrast with the usual pattern of linearly decreasing velocity from endocardium to epicardium. During low dose dobutamine infusion contractile reserve was mainly caused by increased mid wall velocity.

shown in hypertrophic and non-hypertrophic left ventricular myocardium in patients with Friedrich's ataxia whereas no changes occurred in the right ventricle.[100]

In patients with dilated cardiomyopathy, intraventricular mechanical asynchrony can be assessed by analysing the temporal relation of myocardial velocities between various segments of ventricular walls. The prevalence of left ventricular systolic and diastolic asynchrony was 51% and 46%, respectively, in patients with narrow QRS complexes, and 73% and 69%, respectively, in patients with wide QRS complexes.[101] As QRS complex duration is not a determinant of systolic asynchrony, intraventricular synchronicity has to be assessed by TDE when considering cardiac resynchronisation therapy. Detection of the most delayed left ventricular wall may guide left ventricular lead implantation and could be detected by the assessment of time to peak systolic velocity[102] and interval between the end of the A wave and beginning of the next E wave using DTE[103] in basal segments.

Multisite pacing

After device implantation, several atrioventricular (AV) intervals are tested to optimally programme the device. The optimal AV delay is chosen as the shortest AV interval to obtain the longest left ventricular filling time without interruption of the A wave.[104] Improvement of asynchrony, duration of left ventricular filling, duration of ejection as well as mitral regurgitation, and left ventricular remodelling are assessed.[105]

CONCLUSION

Tissue Doppler, strain, and strain rate echocardiography provides additional information to conventional echocardiography. A quick and easy assessment of left ventricular ejection fraction is obtained by mitral annular velocity measurement during a routine study, especially in patients with poor endocardial definition or abnormal septal motion. Tissue Doppler, strain, and strain rate echocardiography provides quantification of regional wall motion at rest and during stress. However, time consuming off-line analysis of colour images is required in the present state of technology.

Strain rate and strain are less affected by passive myocardial motion and tend to be uniform throughout the left ventricle in normal subjects.

These non-invasive techniques are rapidly evolving and expanding. Further refinements in signal processing and quantitative analysis are likely in the near future.

ACKNOWLEDGEMENTS

The authors would like to thank Mrs Harriet St Pierre for her technical assistance.

Authors' affiliations

D Pellerin, R Sharma, P Elliott, The Heart Hospital, London, UK
C Veyrat, Institut Mutualiste Monsouris, Paris, France

Correspondence to: Dr Denis Pellerin, The Heart Hospital, 16–18 Westmoreland Street, London W1G 8PH, UK; denis.pellerin@uclh.nhs.uk

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