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Mundigler G, Zehetgruber M

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G. Mundigler, M. Zehetgruber

Assessment of regional wall motion plays a major role in daily routine echocardiography. However, reliable visual analysis remains challenging in a significant number of patients. Tissue Doppler and strain rate imaging are new techniques which provide velocities of the myocardial wall during the cardiac cycle and therefore allow quantification of both regional and global systolic and diastolic function.

**Key words:** echocardiography, tissue Doppler imaging, strain rate imaging, myocardial velocity, systolic function, diastolic function

**Historical Review and Experimental Studies**

As early as 1973 Kostis et al. [1] first described pulsed wave Doppler technique for investigation of posterior wall velocities. Isaac et al. found that low peak systolic velocity was associated with abnormal wall motion [2]. 1992 McDicken and Sutherland introduced a new technique for producing images of the velocity of tissue motion within the myocardium [3]. Based on the autocorrelation signal processing [4] color Doppler flow images were used to obtain myocardial tissue velocities. 1994 Yamazaki et al. described this method for analysis of ventricular wall motion [5].

Several studies by Sutherland and Fleming et al. demonstrated the feasibility and reliability of color Doppler M-mode [6]. Measurements using a rotating phantom showed appropriate color coding allowing velocity assessment. By examining still images of agar and gel blocks, adequate axial and lateral resolution of 3 × 3 mm was documented, permitting accurate recognition of significant wall motion abnormalities.

In open chest pig animal models color coded tissue Doppler was able to identify wall motion abnormalities [7]. Miyatake et al. focused on measurement of the differences of velocity between the endocardial and epicardial sites of the ventricular wall, i.e. the myocardial velocity gradient (MVG) [8]. Recently, MVG was shown to differentiate transmural from nontransmural infarction in open chest dogs [9]. In a transgenic rabbit model of human hypertrophic cardiomyopathy TDI accurately identified the mutant rabbits even in the absence of left ventricular hypertrophy [10].

**Technical Principles of TDI**

Blood flow Doppler signals are characterized by high velocities and low amplitude. In contrast, Doppler signals from the myocardial wall exhibit low velocities (4–8 cm/s in healthy volunteers) with high amplitude. While in conventional Doppler techniques a high-pass filter prevents low-amplitude signal detection from the myocardium, in TDI this filter is bypassed and high frequency blood flow signals are eliminated by gain adjustment (Fig. 1).

**Color TDI**

In conventional echocardiography Doppler signals from red blood cells are detected at each sampling site along the ultrasound beam. The frequency shift is measured and converted into a digital format. By autocorrelation method different velocities are correlated with a preset color scheme and superimposed on the 2-dimensional image displayed as color flow on the monitor. Blood flow towards the transducer is color-coded in red shades while blood flow away from the transducer is color coded in shades of blue. Velocities exceeding the Nyquist limit lead to aliasing and to reversal of color and

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**Figure 1.** Left: Principle of conventional Doppler. High amplitude myocardial wall signals are eliminated by high pass filter. Right: Doppler signals from myocardial wall are extracted, blood flow Doppler signals are characterized by high velocities and low amplitude. In contrast, Doppler signals from the myocardial wall exhibit low velocities (4–8 cm/s in healthy volunteers) with high amplitude. While in conventional Doppler techniques a high-pass filter prevents low-amplitude signal detection from the myocardium, in TDI this filter is bypassed and high frequency blood flow signals are eliminated by gain adjustment.
In TDI, the same principles have been applied. The upper limit of measurable velocities is determined by the pulse repetition frequency, which is also the sampling frequency. With the latest techniques, frame rates of up to 240/s can be obtained. Because ventricular wall motion velocity at rest is about 10 cm/s or less and increases up to 15 cm/s during stress aliasing is unlikely under these conditions. As for pulsed wave and continuous Doppler, Doppler shift and hence temporal and spatial resolution are dependent on frame rate which itself is correlated to probe frequency, pulse repetition frequency and sector angle.

**Pulsed Wave Tissue Doppler Imaging**

In contrast to color-Doppler-TDI, pulsed-wave-TDI measures not mean but peak velocity instantaneously, hence obtained velocities are slightly higher than with color-TDI. Pulsed-wave-TDI provides real-time Doppler signals with high temporal resolution but allows only step by step evaluation of single sampling points of interest, reproducibility therefore may be lower than for color-Doppler-TDI.

**Data Acquisition and Processing**

At the beginning of TDI color coded images were visually analyzed using color velocity scales. Now, TDI images can be obtained real-time and velocity curves may be analyzed later by postprocessing using integrated or external software. Echocardiographic images are obtained from the examined region using a standard phased array 3.5 MHz transducer and stored as digital cineloops. With recently available TDI software conventional 2-dimensional images now can be obtained without loss of grey scale image quality with simultaneous TDI acquisition. TDI provides a color-coded velocity map of cardiac structures. For velocity analysis one or more sample volumes simultaneously of predefined size, eg 3 × 3 pixels are positioned into the region of interest within the myocardium. Due to global cardiac motion an average of all mean velocities, which are moving within the sample region, are determined. As a special feature simultaneous movement of the sample volume during the cardiac cycle within the myocardial wall is possible by “fixing” it at the identical position. Doppler signals are converted into single or multiple velocity curves providing velocity profiles over the whole cardiac cycle. By Fourier analysis mean peak systolic and diastolic velocities are generated and displayed on a linear or logarithmic scale, velocities are measured as cm/s and time intervals in milliseconds (Fig. 2).

By using curved m-mode a myocardial region of various length can be analyzed. Wall movement is depicted color coded where spatial and temporal information is drawn on y-axis and x-axis respectively, which enables visual analysis of mechanical propagation during the cardiac cycle.

M-mode color Doppler techniques may provide improved spatial and temporal resolution, moreover, myocardial velocity gradients between epicardium and endocardium may be obtained. Due to angle dependency of Doppler signals this technique is limited to relatively small segments of parasternal views [11].

![Figure 2. Tissue Doppler velocity curve in a healthy volunteer. Apical 4-chamber view. The sample volume is positioned in the basal inferior septum. The initial positive excursion represents the isovolumic contraction phase (IVC), followed by the systole. The negative waves represent early (E') and late (A') diastole.](image-url)


TDI in Normal Subjects, Pathophysiologic and Technical Considerations

Previous studies using radio opaque markers implanted into the myocardial wall gave important information about regional heterogeneities of wall motion and distribution of velocities within the myocardium [12]. In the human heart muscular fibers are anatomically oriented in circumferential, radial and longitudinal manner, resulting contraction patterns are non-homogenous and complex. TDI can non-invasively visualize regional differences in mechanical activation and movement. Image acquisition from the parasternal short and long axis view allows assessment of myocardial velocity resulting from radial fiber contraction. Velocity of epicardial circumferential fibers can be evaluated only in small lateral and septal segments from the parasternal short axis. During systole basal and mid segments are moving not only inwards but also longitudinally towards a center of gravity, which is located between the second and third part of the long axis [13]. Contraction of subendocardial longitudinal fibers can be reliably assessed by TDI from the apical views. From base to apex a velocity gradient with highest velocities at basal segments can be observed, apical segments thicken during contraction but the epicardial apex remains relatively stationary. Accordingly, also in the normally contracting apex measured TDI velocities are very low. In addition to regional velocities, the total motion of the heart with translational and rotational motion during the heart cycle has to be taken into account for TDI analysis, measured velocities represent a sum of regional myocardial velocities and global intrathoracic cardiac motion. Therefore, for prevention of additional artifacts by total cardiac motion during breathing, it is recommended to perform image acquisition during apnea.

TDI Studies Evaluating Normal Subjects

Systolic and diastolic myocardial velocities and also distinct velocity patterns during specific cardiac phases in healthy individuals have been investigated for assessment of normal ranges [14], where aging was significantly correlated with changes in systolic and diastolic TDI-parameters [15–17]. Wilkenshoff found mean systolic peak velocities measured at rest between 2.46 ± 1.1 cm/s and 7.76 ± 1.85 cm/s in the apical septal region and the posterior wall respectively, similar ranges were found by Calcutto et al. [18, 19]. Garcia observed a similar range for each myocardial segment in 24 normal subjects for pulsed-wave-TDI assessed velocities and it was a similar range for each myocardial segment in 24 normal subjects [20–22]. In the short axis view, inferoposterior velocities are higher than in the anteroseptum, there is a gradient in peak systolic velocities within the myocardium with highest velocities at the endocardial site [23].

Coronary Artery Disease

Among cardiac imaging modalities 2-dimensional echocardiography plays an outstanding role in coronary artery disease. Abnormal myocardial wall motion at rest or during stress is a sensitive marker for myocardial damage or significant coronary stenosis, respectively. Akinia is defined by segmental wall thickening of less than 10 % and hypokinesia as wall thickening by less than 30 %. However, in routine echocardiography wall motion analysis is performed visually by “semi-quantitative” description. Unlike nuclear or magnetic resonance imaging techniques echocardiography still allows no reliable quantification of regional myocardial dysfunction, accurate wall motion analysis remains dependent on image quality and operator experience. In stress echocardiography observer experience is even more important and accurate assessment of regional function becomes more difficult at peak stress.

Previously described quantitative echocardiographic methods such as acoustic quantification or color – kinesis have many disadvantages and as yet have not found their way into daily clinical practice. TDI is a new technology, which has been proposed for quantification of regional systolic and also diastolic regional function. MVG between endo-, and epicardium was suggested as a valid quantitative parameter for regional wall motion [11] however, due to angle dependency its use is restricted to a few segments only. During ischaemia longitudinal endocardial fibers are primarily affected, hence velocity changes can be detected by apical approach. During acute coronary occlusion peak systolic velocities decrease, a reversal of isovolemic relaxation velocity and reduction of early and late diastolic velocities can frequently be observed. These changes are reversible during reperfusion [24, 25]. Compared to healthy subjects, in patients after myocardial infarction reduced peak systolic velocities were measured at 4 different sites of the mitral annulus, velocities significantly correlated with ejection fraction. A cut-off point of ≥ 7.5 cm/s had a sensitivity of 79 % and a specificity of 88 % in predicting preserved systolic function or ejection fraction of ≥ 0.50 or < 0.50, respectively [26]. In addition to systolic velocities, diastolic E' (mitral annulus)-deceleration time and E'/A' ratio have also been shown to correlate with wall motion abnormalities. However, in apical segments overlap reduces accuracy for discrimination between normal- hypo- or akinetic segments in this region [27]. Goresan et al. found a significant correlation of several TDI indices, such as time to peak systolic velocity, systolic duration or systolic time velocity integrals with the degree of regional dysfunction [21].

Stress echocardiography

Stress echocardiography gains increasing importance as a valuable, non-invasive diagnostic tool in coronary artery disease or in determination of myocardial viability. However, dependency on image quality and subjectivity of the visual analysis remain major limitations. TDI should provide quantification of wall motion abnormalities, therefore enhancing objectivity and accuracy. Katz et al. found significantly lower systolic velocities at peak stress in abnormal than in normal segments (3.1 ± 1.2 cm/s vs. 7.2 ± 1.9 cm/s). However, in apical abnormal segments the velocity response could not be distinguished from normal controls. A peak stress velocity response of ≤ 5.5 cm/s was useful in identifying abnormal segments in all but apical segments [28]. Wilkenshoff et al. examined healthy volunteers during exercise with TDI and observed significant increases in systolic velocities for most myocardial segments during each workload step [19]. As an indicator independent from translational motion MVG was found to increase during dobutamin stress in nonischaemic segments and remained unchanged in ischaemic segments [29, 30]. Pasquet found lower peak velocities in both ischaemic and scar segments than in normal segments at rest and during exercise treadmill test [31]. In an ongoing multicenter study increased accuracy for diagnosis of myocardial ischaemia could be obtained with TDI by using an adjusted model rather than cut-off-values [32] (Fig. 3a, b).

Viability assessment of DSE in combination with TDI improved accuracy and showed comparable results to thallium-201 tomography [33]. In PET non-viable segment systolic peak velocities were significantly lower and demon-
strated a reduced response during dobutamine stress compared to PET-viable segments [34, 35].

**Global Systolic Function**

Echocardiographic evaluation of global left ventricular function is most commonly obtained by visual semiquantitative analysis. Measurements of fractional shortening (FS), stroke volume or left ventricular ejection fraction (LVEF) are frequently assessed parameters. However, in many patients accurate estimation is limited by poor image quality. Less dependent on endocardial definition, TDI has been evaluated in different patient groups for assessment of LVEF. Measurement of longitudinal shortening of the left ventricle to assess LV-function has gained growing importance during the last years [36]. Left ventricular long axis contraction is reflected in mitral annular descent, which can be evaluated by TDI at different sites. In comparison with radionuclide ventriculography the septal and lateral average velocities were well correlated with LVEF under identical conditions, this relationship was not significantly affected by wall motion abnormalities. A six-site peak mitral annular descent velocity of >5.4 cm/s identified LVEF within normal range with reasonable sensitivity and specificity [37]. However, as for LVEF it has to be taken into account that mitral annulus-TDI velocities are dependent on loading conditions, atrial haemodynamics and heart rate as well. Yamada et al. found significant positive correlations of endocardial peak systolic velocity for the LV posterior wall with FS and LVEF in different patient groups but no correlation between FS or LVEF and peak velocity of the ventricular septum [38]. Oki et al. described separation of the PW-TDI obtained systolic velocity curve into 2 peaks (SW1 and SW2) and suggested SW1 along the long axis to be a useful parameter for evaluation of isovolumic myocardial LV contractility. However, difficulty of clear separation of SW1 and SW2, regional asynergies and abnormal septal movement are frequent limitations [39].

In failing human hearts betareceptor density decreases and myocardial cells will be replaced by interstitial fibrous tissue with subsequent impairment of left ventricular function [40]. Shan et al. examined myocardial velocities by TDI at rest and during low dose dobutamine stress. Systolic and diastolic velocities were strongly related to both the number of myocytes and myocardial beta receptor density [41].

**Diastolic Function**

Left ventricular filling is a complex sequence of multiple systolic and diastolic properties of the left ventricle combined with the transmural pressure gradient and the atrial systole. Analysis of both the mitral inflow pattern and pulmonary venous flow allows the differentiation of various diastolic filling patterns, correlating with the severity of diastolic dysfunction. However, in clinical routine, the echocardiographer is faced with several drawbacks in mitral and pulmonary inflow interpretation when several haemodynamic alterations (changes in preload, heart rate, relaxation) occur simultaneously or when pulmonary ve-
Hypertrophic Cardiomyopathy

Yamada et al. measured significantly reduced peak velocities in the hypertrophied septum and the posterior wall, however, velocity gradients were only slightly reduced compared to normals. In the septum, transmural velocity profiles were also less uniform than in the posterior wall, possibly reflecting the degree of myocardial disarray [47]. Impairment of systolic velocities was found not only in the hypertrophied interventricular septum but also in nonhypertrophied regions suggesting these segments also being affected by the pathologic process [48].

Arrhythmias

Today with both, pulsed-wave-TDI and color-Doppler-TDI frame rates of > 200 and temporal resolution of 5 ms can be achieved by reducing the sector angle. Velocity profiles assessed at different sampling sites show regional variations also in healthy individuals [49]. In previous studies, in patients with Wolff-Parkinson-White syndrome TDI even with frame rates of 38/5 was able to detect early contraction sites. TDI diagnosis for the left-sided pathways correlated also well with the ablation site, where feasibility was remarked lower in right sided pathways. For TDI acceleration mode, a special feature of TDI, an agreement of 90 % between TDI and accessory pathway localized by invasive electrophysiological testing was found, and TDI was effective for localizing left sided accessory pathway in particular in the anterior, anterolateral and inferior walls. Reim et al. reported a case where complete atrioventricular dissociation inherent to ventricular tachycardia was detected by fetal echocardiography with M-mode-TDI. Moreover, the onset and pattern of propagation of the tachycardia could be identified by 2-dimensional TDI [50]. However, accuracy is dependent on adequate image quality with clear delineation of endocardial and epicardial borders, visual analysis underlies subjective interpretation and may be time consuming. Whether this method will be helpful in patients with preexcitation, eg as non-invasive screening technique requires further investigations [51–54].

As a promising tool in treatment of patients with heart failure and inter/intraventricular desynchronisation biventricular pacing has been suggested. TDI could evaluate asynchrony between different wall segments by simultaneous measurement of time intervals helping to discriminate patients who will benefit from this new therapy [55].

Limitations

Unsatisfactory reproducibility is still a main limitation of TDI. For pulsed wave TDI interobserver reproducibilities for peak systolic velocity have been reported from 4 % for the lateral annulus to 24 % for the short axis, reproducibility was better in the long axis than in the short axis view and in general was dependent of observer experience [57, 58]. Katz et al. reported a relatively good interobserver variability of 3.8 ± 16.5 % for color coded TDI [28]. For myocardial velocity gradients the mean difference between two observers was 0.9 ± 0.5 cm/s [29]. Reproducibility in general is better in basal than in apical segments and can be invariably high in segments obtained from the parasternal long axis. In a multicenter trial, coefficients of variation for basal, mid-ventricular, and apical segments were 8–13 %, 11–21 %, and 13–47 %, respectively. For anteroseptal segments reproducibility in the parasternal long axis was 104 % [59]. Several reasons contribute to this problem. As for conventional echo image minor changes in transducer position during image acquisition can lead to significant changes, which gain increased importance when serial examinations as for stress echo are necessary. As described above, artifacts and regional heterogeneities within the myocardial wall may result in large velocity differences, hence sample volume position has to be “standardized” when comparison of images is required. Unlike PW-TDI color Doppler-TDI has the advantage of offline postprocessing and analysis however, identical positioning of the sample volume may be challenging as well.
although Doppler signals are less influenced by poor image quality TDI analysis may be impossible when there is no delineation between myocardium and surrounding structures or when signal to noise ratio is low, subsequently black zones may occur.

For both, evaluation of global or regional systolic and diastolic function whole cardiac motion and tethering effects in scar regions may limit accuracy by substantial “false” velocity increase of dysfunctional segments, since it cannot differentiate whether velocities are caused by active or passive movement. Translational motion to a varying degree occurs, eg, after orthotopic heart transplantation, from right ventricular overload, or during catecholamine stress. While longitudinal shortening is less affected, whole cardiac motion may significantly lead to overestimation of assessed velocities of the posterior wall in the parasternal long axis.

As in conventional Doppler, error occurs with increasing angle between ultrasound beam and investigated segments. Velocities may therefore vary according to the incidence angle of Doppler signal and investigated region, eg in parasternal short axis view lateral wall velocities cannot be measured reliably. For comparative examinations as for stress echo angle dependency plays a minor role since velocities within the same region are compared side by side at different steps.

Time is still another crucial limitation of this method. Although lateral resolution is less in apical views, due to the heterogeneity of longitudinal velocities also within small segments and artifacts it takes time to find the best position for the sample volume. Screening the whole myocardium therefore is time consuming with commercially available software.

Strain Rate Imaging (SRI)

As a technical consequence of the limitations of TDI mentioned above and based on the myocardial velocity gradient SRI was introduced in 1997. Strain means tissue deformation due to applied stress. Elongation of the myocardium is positive strain whereas shortening is negative strain, according to the equation \( S = \Delta l/l_0 \), where \( S \) = strain, \( \Delta l \) = change in length and \( l_0 \) = basal length. Additionally, as a temporal derivative of strain, strain rate (SR) measures the rate of deformation, which is equivalent to the MVG. In contrast to TDI, the velocity gradient between two points within the myocardium, with a predefined offset can be assessed also in the longitudinal view and regional strain can be calculated. The resulting information gained from the region of interest is depicted color coded, eg as curved M-mode or as a velocity curve, where strain rate is measured as \( s^{-1} \) (Fig. 4).

In a pilot study of Heimdahl et al. real time SRI was able to differentiate clearly normal from reduced left ventricular function [60]. In akinetic segments strain rate was zero compared to hypokinetic areas with SR of 0–0.8 \( s^{-1} \). Similar results were found by Voigt et al. who found values of 19% for systolic longitudinal strain (=shortening) in normokinetik segments, which corresponded well to strain obtained by MRI. Measurement differences between 2 observers were 15%, 13% for systolic strain rate and strain respectively [61]. In experimental models systolic strain increased during dobutamine infusion while SR reduction occurred with coronary occlusion, this well correlated with strain by sonomicrometry [62, 63].

Although SRI has the potential for playing a notable role in diagnosis of coronary artery disease several limitations still remain to solve. SRI is based on calculation of Doppler signals and measures distances along the ultrasound beam and not in tissue. Consecutively, angle dependent errors can occur, leading to reduced or even inverted strain rates [60, 62, 64]. In contrast to TDI, SRI should be less affected by translational cardiac motion and segmental tethering effects, however, local interactions between segments with different elastic properties, and also different loading conditions can influence SR values [61, 63]. Normal SR values in larger cohorts of healthy subjects, influence of different pathologies such as hypertension, but also changes due to aging processes with respect to systole and diastole have to be defined. At present also spatial and temporal resolution is limiting the diagnostic accuracy. Below 10 mm samples signal to noise ratio becomes too low. Moreover, random noise frequently occurs, rendering interpretation of strain rate tracings difficult.

Future Aspects

Accurate quantification of the normal and impaired myocardial motion with respect to timing and amplitude remains a key target. In future, automated 3-dimensional data acquisition including TDI and SRI will be commercially available, instantaneously providing tissue Doppler Bull’s eyes and myocardial time-velocity maps of the whole heart in real time as already described.
 previously [65–67]. Higher frame rates, improved signal processing, and time saving by automation will facilitate quantification of wall motion abnormalities hence increasing the value of this method in terms of sensitivity and specificity.

Conclusion

As a matter of fact, pathologic processes due to numerous different reasons are reflected by changes and impairment of the normal systolic and diastolic velocity patterns. These patterns of velocity curves and numerical values are already well described for healthy individuals and in a broad spectrum of cardiac diseases. Due to wide overlaps particularly in the apical regions, age dependency, and a lack of specificity of velocity patterns, differentiation between normal and pathologic may still be challenging in the individual patient. However, for the first time, TDI and SRI provide “numbers” hence enabling quantification of wall motion. Nevertheless, TDI and SRI are still experimental methods and so far the only recommended and reliable clinical application for TDI is assessment of diastolic function.

The new acquisition and analyzing techniques may overcome present limitations and offer TDI and SRI as useful complementary tools in clinical echocardiography.

References

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