

## Review Article

## The Contribution of Doppler Echocardiography to the Assessment of Left Ventricular Long Axis Function

KONSTANTINOS A. TRIANTAFYLLOU, ATHANASIOS I. KRANIDIS, SPYRIDON G. KOULOURIS, STYLIANOS I. TZEIS, ANTONIS S. MANOLIS

*First Department of Cardiology, "Evangelismos" General Hospital, Athens, Greece*

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*Address:*  
Antonis S. Manolis

41 Kourempana St.,  
Agios Dimitrios,  
173 43 Athens, Greece  
*e-mail:*  
[asmanol@otenet.gr](mailto:asmanol@otenet.gr)

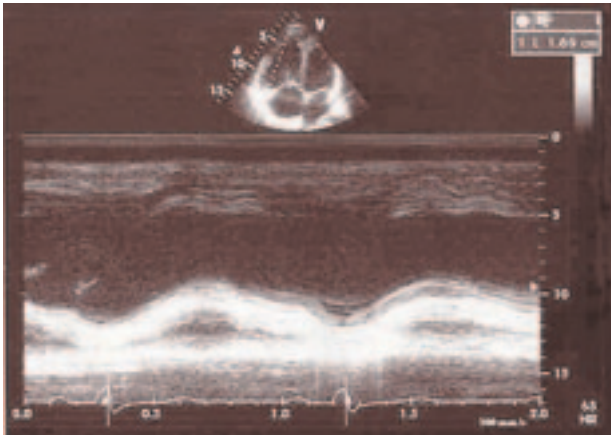
A plethora of data has hitherto accumulated concerning the study of left ventricular (LV) long axis function with different echocardiographic and Doppler techniques.<sup>1-4</sup> The data pertain to LV systolic and diastolic function, valvular heart disease, detection of ischemia or myocardial viability, and prognosis and outcome of cardiac diseases. More recently, the study of LV long axis function with new echocardiographic and Doppler techniques has made a major contribution to cardiac resynchronization therapy. In the present article a concise overview of these data is attempted.

### Left ventricular systolic function

The mean systolic excursion of the mitral annulus, measured by M-mode (Figure 1), has been shown to correlate closely with left ventricular ejection fraction (LVEF), mainly when there are no regional wall motion abnormalities ( $r=0.7$ ). Such a correlation exists because the mitral annulus systolic excursion expresses the contraction of the longitudinally arranged myocardial fibers, which are located in the endocardium and epicardium of the left ventricle.<sup>1</sup> In case of globally impaired LV systolic function, the weaker contraction of the longitudinal myocardial fibers will be expressed by

a decreased mean systolic mitral annulus excursion.<sup>5</sup> It has been shown that if the mean systolic excursion is  $>13$  mm, then the LVEF is  $>55\%$ , with a sensitivity of  $86\%$  and a specificity of  $93\%$ .<sup>6</sup>

However, in patients with ischemic heart disease and LV regional wall motion abnormalities, the assessment of the longitudinal systolic function by placing the sample volume in the mitral annulus and using tissue Doppler imaging (TDI) has shown a statistically stronger correlation between the mean velocity of the systolic wave and the LVEF, compared with the same correlation for the mean systolic excursion of the mitral annulus as assessed by M-mode (Figure 2). Moreover, it has been demonstrated that the systolic wave velocity that corresponds to asynergic left ventricular segments is significantly smaller than the velocity of non-asynergic segments.<sup>7,8</sup> These facts show that the study of long axis LV function provides information about the impairment of global as well as regional LV systolic function. The TDI technique also contributes to the assessment of regional systolic impairment. Importantly, the study of LV long axis function can reveal early signs of systolic impairment, whereas the most widely used index of systolic function, the LVEF, cannot. During examination of the long axis LV function a hypertensive

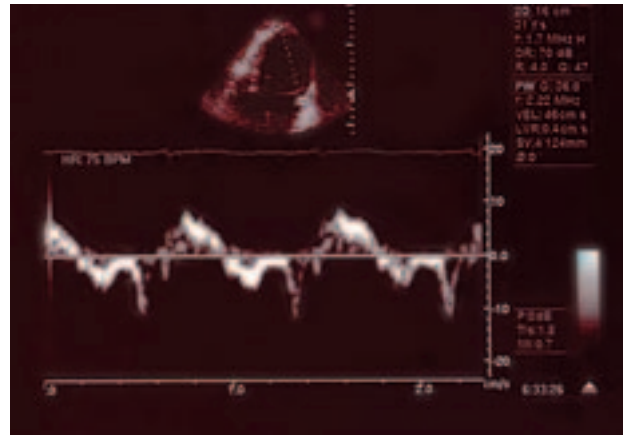


**Figure 1.** Apical four-chamber view. M-mode echocardiography shows the atrioventricular plane movement at the edge of the mitral annulus towards the lateral wall of the left ventricle.

response during exercise testing has been found to co-exist with longitudinal left ventricular systolic dysfunction, while the LVEF remained within normal limits.<sup>9</sup> It is impressive that impaired long axis LV function, assessed by TDI, can contribute to the diagnosis of sub-clinical hypertrophic cardiomyopathy.<sup>10</sup> Impaired systolic function of LV longitudinal myocardial fibers has also been demonstrated in patients with myotonic dystrophy without heart failure symptoms.<sup>11</sup> Moreover, LV long axis systolic function impairment has been found in diabetics with normal LVEF by using TDI.<sup>12</sup> It is a fact that both mitral annulus systolic excursion (assessed by M-mode) and velocity (assessed by TDI) closely correlate with global and regional LV function. However, the latter seems to be better studied by the strain rate technique.<sup>13, 14</sup> The fact that LV longitudinal deformation is not load-dependent is very important.<sup>15</sup>

### Left ventricular diastolic function

The LV diastolic function has also been studied on its long axis and the findings are worth mentioning. Since the era of M-mode study of mitral annulus function, it has been found in healthy individuals that the ratio of the mitral annulus motion due to atrial systole to its total diastolic motion is a useful parameter for the assessment of diastolic LV filling. Moreover, the contribution of the mitral annulus motion M-mode study has been validated in the presence of coronary artery disease. Specifically, the aforementioned parameter has been shown to estimate diastolic LV filling and end-diastolic LV pressure quite accurately in patients with ischemic cardiomyopathy.<sup>3</sup> Such an assessment was most accu-



**Figure 2.** Velocities of mitral annulus movement during the cardiac cycle as recorded by the tissue Doppler imaging (TDI) technique.

rate in patients without regional LV wall motion abnormalities.<sup>16</sup> That is why this parameter has been found to assess LV diastolic function accurately in hypertensive patients without coronary artery disease, in particular defining the presence or absence of LV impaired relaxation.<sup>17</sup> In patients afflicted by ischemic cardiomyopathy, LV diastolic filling is also assessed by the early to late mitral annulus diastolic motion ratio, having as a drawback the dependence of this index on LVEF and heart rate.<sup>18</sup> The assessment of the early mitral annulus diastolic motion slope, acquired by M-mode, seems to reflect the systolic rather than the diastolic LV function. This constitutes evidence for LV systolic and diastolic function coupling.<sup>19</sup> It has also been found that during exercise the mitral annulus motion study can better demonstrate the LV diastolic function changes compared to the Doppler technique.<sup>20</sup> Concerning pseudo-normalization, a serious LV diastolic function abnormality, it can simply be detected by an early to late mitral annulus velocity ratio  $< 1$ , while the pulse wave Doppler trans-mitral flow study shows a normal early to late trans-mitral velocity ratio. Moreover, the waveforms of the mitral annulus diastolic velocities, as assessed by TDI, contribute significantly to the differential diagnosis of constrictive pericarditis from restrictive cardiomyopathy.<sup>21</sup>

### Valvular heart disease

In patients with mitral stenosis, both M-mode and TDI techniques have unraveled impaired LV longitudinal function despite normal systolic function as assessed by the LVEF index.<sup>22</sup> In patients with severe aortic steno-

sis, the mitral annulus motion study has been shown to be more sensitive than LVEF in demonstrating significant hemodynamic LV stress.<sup>23</sup> Furthermore, impaired LV long axis function has been discovered by TDI in patients with moderate-to-severe aortic stenosis and preserved LVEF.<sup>24</sup> In severe mitral regurgitation with LVEF >60%, LV long axis function study by TDI has shown that long axis systolic impairment may exist. This was found by systolic wave velocity measurement in the plane of the mitral annulus.<sup>25</sup> Subclinical LV dysfunction in patients with severe mitral regurgitation can also be detected with strain rate imaging. In such patients significantly lower end-systolic strain and peak systolic strain rate has been shown to predict reduced LV contractile reserve.<sup>26</sup> This is an important finding, having in mind that it can influence the decision for the timing of surgical intervention.

### Detection of ischemia

Echocardiographic study of post-exercise mitral annulus motion has been found to contribute significantly to the demonstration of ischemia. Specifically, Alam et al discovered that a reversible reduction of the mitral annulus motion  $\geq 3$  mm at its junction with one or more LV walls is linked to the presence of ischemia with a sensitivity of 80% and a specificity of 100% in patients with possible coronary artery disease.<sup>27</sup> Others, though, have found that by dobutamine-atropine administration in healthy subjects there is an initial increase and a subsequent decrease of the mitral annulus systolic excursion, which means that the method is not so accurate for ischemia demonstration.<sup>28</sup> Moreover, it has been found that after dobutamine administration, a mean mitral annulus systolic excursion increase of <0.25 correlates with great sensitivity and specificity with coronary artery disease in patients without regional LV wall motion abnormalities.<sup>29</sup>

The mitral annulus excursion of each LV side is reduced in the case of asynergy of the examined side or significant coronary artery stenosis.<sup>30</sup> The LV long axis function study during dobutamine infusion discerns coronary artery disease among heart failure patients with greater sensitivity than wall motion index measurement.<sup>31</sup> New techniques such as TDI and strain rate (Figure 3) can assess the segmental LV long axis function. Regional ischemia is more accurately demonstrated by the strain rate technique than by the classic TDI method during dobutamine stress echocardiography.<sup>32</sup> If the LV is longitudinally divided into 3 segments, the reversal of exercise-induced ischemia is not

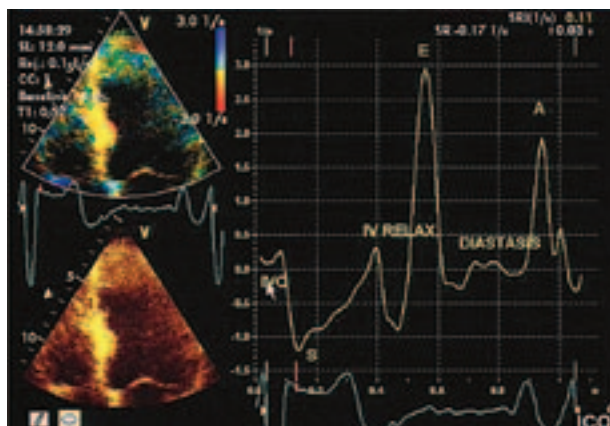


Figure 3. Mitral annulus strain rate curves.

ed earlier in the apical segment.<sup>33</sup> Moreover, it has been found that in patients with chest pain without segmental LV wall motion abnormalities, an increase of the interval from the R peak of the QRS complex to the S wave peak of the TDI signal is related to ischemia.<sup>34</sup>

Successful differential diagnosis between ischemic or dilated cardiomyopathy is of paramount importance, more so when left bundle branch block exists. The LV long axis function assessment has recently been found to contribute in such cases. Specifically, Duncan et al found that during dobutamine infusion, failure of the early diastolic velocity, as measured by TDI at the mitral annulus plane, to increase to 1.1 cm/s is suggestive of ischemic cardiomyopathy.<sup>31</sup> Finally, the post-systolic thickening measured by the strain rate technique at the LV long axis can show regional ischemia and segmental scarring in patients with ischemic heart disease.<sup>35</sup>

### Detection of myocardial viability

The LV long axis function has been used to demonstrate myocardial viability. Specifically, a >2 mm increase of the mitral annulus systolic excursion, measured by M-mode from the apical views at the interventricular septum, the lateral, the anterior and the inferior walls, is related to viable myocardium in the respective wall. Moreover, it has been found that such an increase accurately predicts the asynergic segments that will improve after revascularization.<sup>36-38</sup> Recently, the correlation between systolic mitral annulus velocity and myocardial viability has been explored by TDI. It has been demonstrated that a systolic velocity increase  $\geq 2.0$  cm/s is suggestive of the presence of viable myocardial tissue.<sup>39</sup>

### Prognosis and outcome of cardiac diseases

The mitral annulus longitudinal displacement, an index reflecting the LV long axis function, has been shown to correlate with prognosis in patients with coronary artery disease.<sup>40</sup> Willenheimer found that the measurement of the total mitral annulus displacement, which expresses both systolic and diastolic function, contributes to the detection of patients who will develop heart failure.<sup>41</sup> In patients with dilated cardiomyopathy, however, the prospective follow up of LV long axis function has a role in prognosis as well. Specifically, Faris et al found that the prospective improvement of LV long axis function is linked to a better prognosis.<sup>42</sup> It has also been demonstrated that in patients with chronic atrial fibrillation an impaired mitral annulus motion, which represents LV long axis function, affects prognosis unfavorably.<sup>43</sup>

### Cardiac resynchronization

Doppler echocardiography, mainly by LV long axis function studies, makes a major contribution to cardiac resynchronization therapy, a therapeutic approach for the treatment of symptomatic patients with severely impaired LV function. The assessment of *interventricular delay* is accomplished by measuring the maximum systolic velocities of the right ventricular wall and the LV lateral wall from the apical long axis view, and the time interval [ $T_{S(\text{systolic})}$ ] from the beginning of the QRS complex to their appearance. Yu et al demonstrated that the difference between  $T_s$  of the LV lateral wall and  $T_s$  of the right ventricle constitutes an index of interventricular mechanical delay, which is reduced with biventricular pacing.<sup>44</sup>

The LV long axis function study is of special value when one intends to assess the electromechanical activation delay of different LV segments. The most widely used parameter is the *intraventricular delay*, defined as the time difference between the appearance of the maximum systolic velocity of the basal lateral wall and the basal interventricular septum. Intraventricular delay measurements  $>60$  ms characterize significant intraventricular dyssynchrony.<sup>45,46</sup> Furthermore, LV intraventricular delay can also be assessed after measuring the timing of maximum systolic velocity ( $T_s$ ) at basal and mid segments of septal, lateral, anteroseptal, posterior, anterior and inferior walls and subsequent estimation of the maximum  $T_s$  difference between two of the above segments and additional calculation of the standard deviation ( $T_s$ -SD) of  $T_s$  among them. The higher the  $T_s$ -SD value, the greater the LV intraventricular dyssynchrony.<sup>44</sup> Using a  $T_s$ -SD value  $>32.6$  ms ( $+2$  standard

deviations of the distribution in normal subjects) as the criterion for significant dyssynchrony, Yu et al<sup>44</sup> have shown that intraventricular dyssynchrony exists in 43% of heart failure patients with a narrow QRS and in 64% of cases with a wide QRS.

Strain rate and tissue tracking are two new echocardiographic techniques, which are based on LV long axis function assessment and have also been used to estimate intraventricular dyssynchrony. These methods are based on the direct measurement of myocardial wall shortening or stretching, during systole and diastole respectively. The myocardial deformation rate is assessed by measuring the segmental velocity gradient between two adjacent myocardial wall segments (the velocity difference between two points with distance  $l_0$  between them, divided by this distance [ $V_2 - V_1/l_0$ ,  $s^{-1}$ ]).<sup>45-49</sup> The main advantage of this method is the ability to differentiate active systolic myocardial wall motion from the passive motion found in patients with ischemic cardiomyopathy and scar tissue.

Three-dimensional echocardiography is an emerging modality, promising to improve the reproducibility of ultrasound studies made to assess LV mechanical dyssynchrony. Examination of LV function at its long axis with real-time three-dimensional echocardiography combined with TDI has been used to devise a systolic dyssynchrony index (SDI) derived from time-volume analysis of all 16 LV segments. This index is a numeric expression of the dispersion of time to minimum regional volume in each of the 16 LV segments. It has been shown to be able to quantify global LV function and increases with worsening LV systolic function. The systolic dyssynchrony index could also estimate mechanical dyssynchrony in patients with and without QRS prolongation.<sup>50</sup>

The findings of many studies support the value of intraventricular dyssynchrony as a predictive index of a favorable response to cardiac resynchronization therapy. Bax et al have demonstrated that the only predictive parameter for LVEF improvement after cardiac resynchronization was the presence of significant LV dyssynchrony.<sup>46</sup> In fact, patients with intraventricular delay  $>60$  ms had a high probability of LVEF improvement after biventricular pacemaker implantation. In one of their recent studies, Penicka et al<sup>47</sup> reconfirmed the value of intraventricular delay as a predictor of a favorable response to cardiac resynchronization therapy, but have also demonstrated that the index with the highest predictive accuracy (high sensitivity and specificity) is the sum of interventricular and intraventricular delay, with the limit set at 102 ms.

**Table 1.** Applications of studies of left ventricular long axis function.

Left ventricular systolic function	<ul style="list-style-type: none"> <li>– Mitral annulus mean systolic excursion (M-mode)</li> <li>– Mitral annulus mean systolic wave velocity (TDI)</li> </ul>
Left ventricular diastolic function	<ul style="list-style-type: none"> <li>– Ratio of mitral annulus motion due to atrial systole to its total diastolic motion (M-mode)</li> <li>– Ratio of early to late mitral annulus diastolic motion (M-mode)</li> <li>– Mitral annulus diastolic velocities (TDI)</li> </ul>
Valvular heart disease	Detection of early systolic dysfunction at long axis: <ul style="list-style-type: none"> <li>– Mitral stenosis (M-mode, TDI)</li> <li>– Aortic stenosis (M-mode, TDI)</li> <li>– Mitral regurgitation (TDI, strain/strain rate)</li> </ul>
Detection of ischemia	Stress echo assessment of : <ul style="list-style-type: none"> <li>– Mitral annulus systolic excursion (M-mode, TDI)</li> <li>– Mitral annulus early diastolic velocity (TDI)</li> <li>– Post-systolic thickening</li> </ul>
Myocardial viability	<ul style="list-style-type: none"> <li>– Increase of mitral annulus systolic excursion (M-mode) and systolic velocity (TDI), assessed at interventricular septum, anterior, lateral and inferior walls</li> </ul>
Prognosis	<ul style="list-style-type: none"> <li>– Coronary artery disease: total mitral annulus displacement</li> <li>– Dilated cardiomyopathy: follow up of long axis function</li> <li>– Atrial fibrillation: mitral annulus motion assessment</li> </ul>
Cardiac resynchronization	<ul style="list-style-type: none"> <li>– <i>Interventricular delay</i>: Time difference between maximum systolic velocity of right ventricular free wall and left ventricular lateral wall, measured from QRS (TDI)</li> <li>– <i>Intraventricular delay</i>:               <ol style="list-style-type: none"> <li>1. Time difference between maximum systolic velocity of basal interventricular septum and basal lateral wall, measured from QRS (TDI).</li> <li>2. Measurement of the maximum difference of timing of maximum systolic velocities between basal and mid septal, anteroseptal, anterior, lateral, posterior and inferior walls (TDI). Additional assessment of the standard deviation of the above values.</li> </ol> </li> </ul>

TDI – tissue Doppler imaging.

LV long axis function study can be used to assess a successful response to cardiac resynchronization therapy and the actual accomplishment of cardiac resynchronization. Yu et al<sup>44</sup> have shown that biventricular pacing resulted in LV reverse remodeling and improved function, attributed mainly to the reduction of inter- and intraventricular LV dyssynchrony. Penicka et al<sup>47</sup> have found improved LV function six months following biventricular pacing in patients with inter- and intraventricular delay documented by TDI. Kawaguchi et al<sup>51</sup> have demonstrated, with the aid of contrast echocardiography, that LV only pacing in patients with dilated cardiomyopathy improves dyssynchrony in 50% of them and abolishes the interventricular septum's paradoxical motion.

#### Limitations of echocardiographic techniques for the assessment of LV long axis function

It is undeniable that echocardiographic assessment of LV long axis function has had a major impact and pro-

vides important information for clinical decision making. However, each of the above mentioned techniques used for such an assessment carries certain limitations. For example, in the assessment of myocardial viability mitral annular motion assessment by M-mode may be influenced by left atrial hemodynamics and left ventricular end-diastolic pressure. Furthermore, since M-mode is performed at the mitral annulus level, measured values might be influenced by the infarct zone or the wall motion of non-infarcted regions.<sup>36</sup> When regional systolic mitral annular motion velocity is assessed with TDI, it must be kept in mind that the point velocity of a specific LV region does not differentiate between active contraction and passive drawing motion related to translation and rotation of the whole heart or contraction of adjacent segments.<sup>39</sup> Strain rate imaging is considered independent of passive tethering effects from other regions. However, the current technology used for this technique is characterized by signal noise, which increases with higher heart rates and sub-optimal

image quality. In addition, the analysis of strain by Doppler echocardiography is very angle-dependent.<sup>45</sup> Since the echocardiographic assessment of myocardial viability carries the important duty of correctly detecting ischemic patients with reversible left ventricular dysfunction, such limitations must always be taken into account.

## Conclusion

Left ventricular long axis function study via echocardiography is quite useful in a variety of clinical settings (Table 1) and should be performed on a routine basis. These echo-Doppler techniques can reliably assess LV systolic and diastolic function in a variety of underlying cardiac diseases, including ischemic and non-ischemic cardiomyopathy and valvular heart disease. They can also contribute to the detection of myocardial ischemia or viability and assess the prognosis in coronary artery disease, dilated cardiomyopathy and atrial fibrillation. Finally, echocardiographic assessment of the LV long axis function has had a major impact in cardiac resynchronization therapy, whereby measurement of the inter- and intraventricular delay appears to be of paramount importance in detecting responders to cardiac resynchronization therapy, but also in the optimal programming of cardiac resynchronization devices, thus contributing to a better outcome of heart failure patients fitted with such devices.<sup>52,53</sup>

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