Quantitative Evaluation of Global and Regional Left Ventricular Diastolic Function With Color Kinesis

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Background—Diastolic wall motion asynchrony is a major determinant of impaired left ventricular (LV) filling in patients with concentric hypertrophy and coronary artery disease. We evaluated the ability of Color Kinesis, a new echocardiographic technique that color-encodes endocardial motion, to quantitatively assess global and regional LV filling properties.

Methods and Results—Color Kinesis images and mitral and pulmonary vein flow Doppler data were acquired in 29 patients with LV hypertrophy and 29 age-matched control subjects. In addition, Color Kinesis data were correlated to coronary angiographic findings in 15 patients with suspected coronary artery disease. Segmental analysis of Color Kinesis images was used to obtain time histograms of regional diastolic fractional area change, wherein early and late peaks (peaks 1 and 2) reflected rapid LV filling and atrial contraction, respectively. Regional mean LV filling time and filling curves were used to objectively identify diastolic endocardial motion asynchrony in patients with LV hypertrophy and coronary artery disease. None of the mitral and pulmonary vein Doppler indices differentiated patients with normal mitral Doppler profile (n=13) from control subjects, whereas reduced peak1/peak2 ratio and prolonged mean filling time indicated augmented contribution of atrial contraction toward LV filling (P<.05). In 22 of 25 patients with LV hypertrophy and preserved systolic function and in all patients with coronary artery disease, delayed diastolic endocardial motion was observed in at least one segment.

Conclusions—Analysis of Color Kinesis images provides objective assessment of global and regional LV filling properties and allows identification of both diastolic dysfunction in patients with normalized Doppler indices and wall motion asynchrony. (Circulation. 1998;97:1053-1061.)

Key Words: echocardiography ■ diastole ■ hypertrophy ■ coronary disease

A bnormalities in left ventricular (LV) diastolic filling often precede systolic dysfunction in various disease states such as cardiac hypertrophy1 and coronary artery disease.2 LV diastolic properties are evaluated indirectly by measurement of transmural flow velocities with pulsed Doppler echocardiography. Distinct mitral inflow patterns have been used to differentiate abnormal relaxation from restricted filling.3 However, the diagnosis of diastolic dysfunction in patients with normalized mitral inflow patterns3 remains challenging.

Moreover, Doppler flow profiles provide information on global rather than regional LV diastolic properties. The ability to assess regional diastolic abnormalities, which may affect overall ventricular filling, depends on diagnostic techniques that require injection of contrast or radiopharmaceutical substances.4–6 Color Kinesis (Hewlett Packard) is an echocardiographic technique that allows objective evaluation of regional systolic wall motion.7 The aim of this study was to determine the feasibility of the use of Color Kinesis to assess global as well as regional LV diastolic properties. Accordingly, diastolic endocardial motion data obtained from Color Kinesis images acquired in patients with LV hypertrophy and age-matched control subjects were compared with traditional Doppler indices. In addition, the ability of Color Kinesis to objectively characterize regional LV diastolic asynchrony was evaluated in patients with LV hypertrophy and in patients undergoing coronary angiography for suspected coronary artery disease.

Methods

Color Kinesis: Principles of Operation

Color Kinesis analyzes regional backscatter in each acoustic frame in real time and classifies each pixel as either blood or myocardial tissue. Pixel transitions from tissue to blood during diastole are detected and color-encoded (Fig 1). Color overlays are updated on a frame-by-frame basis by adding one color at a time (30 frames/s). Thus a single end-diastolic frame provides an integrated display of the timing and magnitude of endocardial wall motion.

Study Population

Out of 100 screened subjects, 85 with good echocardiographic image quality and adequate tracking by Color Kinesis of ≥80% of LV endocardial boundary were selected for the study. From these, 12 patients were excluded because of (1) pericardial effusion and previous pericardotomy (n=3); (2) all types of arrhythmias and conduction abnormalities (n=2); (3) heart rates <55 or >100 bpm (n=2);
Assessment LV Diastolic Function With Color Kinesis

Figure 1. Principles of operation of Color Kinesis (A and B). Segmentation schemes used in the short-axis and apical four-chamber views (C). Ant indicates anterior; asp, anteroseptal; sp, septal; inf, inferior; pat, posterior; lat, lateral; b-lat, basal lateral; m-lat, mid-lateral; a-lat, apical lateral; a-sp, apical septal; m-sp, mid-septal; and b-sp, basal septal.

(4) moderate to severe mitral or aortic regurgitation assessed with color-flow Doppler (n=2); (5) mitral or aortic valve stenosis (n=2); and (6) dynamic LV outflow tract obstruction (n=1). Finally, 29 patients (21 men, 8 women; age, 55±14 years; range, 30 to 81) with concentric LV hypertrophy secondary to long-standing systemic hypertension were recruited into the study as well as 29 age-matched normal subjects (13 men, 16 women; age, 54±14 years; range, 32 to 88) who were used as control subjects. LV hypertrophy was defined as LV mass index >2 SD above age- and sex-normalized values. Concentric LV hypertrophy was defined as septal thickness <1.3 times the thickness of the posterior wall when measured with M-mode in the parasternal short-axis view. Control subjects had (1) no history of cardiovascular disease, (2) normal two-dimensional echocardiographic study, and (3) LV mass index and mitral flow velocity pattern (E/A ratio and deceleration time) within the normal range.

In addition, 15 patients who underwent coronary angiography for suspected coronary artery disease (10 men, 5 women; age, 61±13 years; range, 45 to 84) were studied. Significant coronary artery stenosis defined as a reduction ≥50% of the arterial lumen was found in 7 patients (1 single-vessel, 3 double-vessel, and 3 triple-vessel disease). The remaining 8 patients had nonsignificant coronary artery atherosclerosis.

Data Acquisition
In all study subjects, a complete transthoracic echocardiographic study including M-mode, two-dimensional imaging, pulsed-wave Doppler, and color flow mapping of valvular orifices was performed with either a 2.5- or 3.5-MHz transducer (SONOS 2500, Hewlett-Packard).

Doppler Echocardiography
In all subjects, two-dimensional parasternal short-axis views were obtained at the mid papillary muscle level, followed by apical four-chamber views, and recorded on videotape for off-line measurements of LV mass index. Two-dimensional targeted M-mode imaging of the left ventricle was performed in the short-axis view to measure end-diastolic wall thickness. Mitral and pulmonary vein flow pulsed-wave Doppler velocity profiles were acquired during passive end-expiration, as previously described.

Color Kinesis Data Acquisition
Diasstolic Color Kinesis images were obtained from the LV mid papillary short-axis and apical four-chamber views as described previously. The timing of color encoding was set to begin at the first frame in which outward endocardial motion was noted, and its duration was set to its maximal value (19 frames). To minimize the effects of beat-to-beat variability, two nonconsecutive end-diastolic Color Kinesis images were acquired in each view and stored on an optical disk.

Data Analyses
Two-dimensional and M-Mode Measurements
LV mass index was measured with the two-dimensional area-length method.

Long-axis LV length was measured from the apical four-chamber view as the distance between the mid mitral annulus plane and the tip of the apical endocardial border. Both LV chamber dimensions and wall thickness were measured with the conventional leading edge technique.

Doppler Analysis
Measurements were performed off-line and values were obtained as the mean of three nonconsecutive beats. Isovolumic relaxation time was measured as the time interval between the aortic valve closure and the onset of the mitral valve inflow. Peak velocities during rapid filling (E) and atrial contraction (A) as well as the area under each peak (VTI and VTIA) were measured. Subsequently, the early to late diastolic mitral flow velocity E/A ratio and VTI/VTIa ratio were calculated, and the deceleration time was measured. Only cardiac cycles with linear deceleration and clearly defined peaks were used. In addition, we measured the time to half LV filling corresponding to 50% of the area under the mitral velocity profile. Pulmonary vein inflow velocities were measured at end-expiration. The ratio between peak forward flow velocity during ventricular systole and diastole (S/D ratio) as well as peak retrograde velocity at atrial contraction (A-pv) were measured.

Analysis of Color Kinesis Images
End-diastolic color-encoded images were divided into six segments (Fig 1C) with previously described custom software.

In each segment, colored pixel counts were used to calculate regional fractional area change, which was displayed as stacked time histograms. This display allowed clear identification of peak area change during rapid LV filling (peak 1) and during atrial contraction (peak 2). To facilitate intersubject comparisons, we used linear interpolation to obtain 20 values of segmental fractional area change in 5% increments of LV filling time. Thus irrespective of heart rate, LV filling time was 100% in each subject. The peak1/peak2 ratio was measured, and mean time of LV filling was computed for each segment and displayed as a bar diagram. Fractional area change was integrated with respect to

TABLE 1. Pulsed-Wave Doppler-Derived Indices and Parameters of Global Diastolic Function Obtained From Color Kinesis Data Obtained in Patients With Concentric Left Ventricular Hypertrophy and Age-Matched Control Subjects

<table>
<thead>
<tr>
<th></th>
<th>Isovolumic Relaxation Time, ms</th>
<th>E/A Ratio</th>
<th>VT1a/VT1b Ratio</th>
<th>Deceleration Time, ms</th>
<th>Time to Half LV Filling, ms</th>
<th>S/D Ratio</th>
<th>A-pv, cm/s</th>
<th>Peak1/Peak2 Ratio</th>
<th>Mean LV Filling Time, ms</th>
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<td></td>
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<tr>
<td>CTL</td>
<td>29</td>
<td>74±11</td>
<td>1.28±0.27</td>
<td>1.89±0.43</td>
<td>196±27</td>
<td>178±25</td>
<td>1.28±0.32</td>
<td>25±10</td>
<td>3.33±1.61</td>
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<tr>
<td>LVH</td>
<td>29</td>
<td>102±34*</td>
<td>1.28±0.97</td>
<td>2.13±1.36*</td>
<td>250±106*</td>
<td>186±60</td>
<td>1.30±0.53</td>
<td>28±12</td>
<td>2.94±3.32*</td>
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</table>

E/A indicates ratio between the peak velocities of early (E wave) and late (A wave) diastolic mitral inflow; VTI, velocity time integral; LV, left ventricular; S/D, ratio between the peak velocities of forward pulmonary vein flow during systole (S wave) and diastole (D wave); A-pv, peak retrograde velocity in the pulmonary vein at atrial contraction; SAX, short-axis view; A4C, apical four-chamber view; CTL, age-matched control subjects; and LVH, left ventricular hypertrophy.

Values are expressed as mean±SD. *P<.05 when compared with control subjects.
time and normalized to 100% in each segment. This normalization eliminated intersegmental differences in magnitude of regional endocardial motion, which was displayed as time curves reaching 100% of endocardial motion at 100% filling time. For each subject, data obtained from two Color Kinesis images in each view were averaged. Composite regional time curves obtained in all normal subjects were used as reference patterns of regional LV filling.

Study Design

Protocol 1
To determine the clinical value of Color Kinesis for the evaluation of global LV diastolic function, Doppler and Color Kinesis data were initially compared between patients with concentric LV hypertrophy and age-matched control subjects. Subsequently, patients were divided into three subgroups on the basis of their Doppler mitral inflow patterns1 by comparison of individual E/A ratios and deceleration times with the previously reported 95% confidence intervals, obtained in a normal population over a wide range of ages.2 Group 1 included 12 patients with an abnormal relaxation pattern (reduced E/A ratios and prolonged deceleration times). Group 2 included 13 patients with age- and sex-normalized E/A ratio. Group 3 included 4 patients with a restrictive filling pattern (increased E/A ratios with short deceleration times). In each group, Color Kinesis data were compared with conventional Doppler-derived indices. In addition, Color Kinesis and Doppler data were compared between groups and corresponding control subjects.

Protocol 2
To determine the ability of Color Kinesis to objectively assess regional diastolic function, the proportion of diastolic endocardial motion completed after the first half of LV filling time was determined for each regional time curve. These values were averaged and standard deviations used as an index of diastolic asynchrony. Data were compared between patients with LV hypertrophy and preserved systolic function (n=25) and control subjects. Regional curves obtained in normal subjects were averaged and a reference pattern of endocardial motion was defined in each segment as 1 SD around the mean. Delayed segmental endocardial motion was defined as decreased percentage of motion completed at 50% of filling time when compared with normal values.

Protocol 3
To evaluate the ability of Color Kinesis to detect delayed diastolic endocardial motion in LV regions supplied by coronary arteries with various degrees of stenosis, regional motion was correlated with perfusion territories on a segmental basis. As in protocol 2, the index of diastolic wall motion asynchrony was calculated from Color Kinesis images. Regional delayed endocardial motion was defined as a downward shift of individual segmental Color Kinesis time curves relative to the corresponding reference profile at 50% of the total filling time. The presence or absence of delayed endocardial motion was correlated with coronary angiographic findings on a segmental basis.11

Statistical Analysis
Intergroup comparisons were performed with either the Student’s t test or the Mann-Whitney rank-sum test whenever data failed the normality test. Nonparametric Spearman correlation coefficients were computed and tested for differences between the Doppler VTIE/VTIA ratios and Color Kinesis peak1/peak2 ratios (P≤.05 considered significant).

Results

Protocol 1
Assessment of Global LV Diastolic Function
LV mass index was greater in patients with hypertrophy when compared with normal subjects (178±52 versus 67±14 g/m², P<.0001). No intergroup differences were noted in heart rate (71±12 versus 65±9 bpm), mitral inflow E/A ratio, time to half LV filling, pulmonary venous flow S/D ratio, and A-pv (Table 1). In contrast, isovolumic relaxation and deceleration times were prolonged, and VTIE/VTIA ratio significantly decreased in patients with LV hypertrophy (Table 1).

Figure 2. End-diastolic Color Kinesis images obtained in a patient with concentric left ventricular hypertrophy (LVH) and an age-matched normal subject (CTL), in the short-axis (top) and apical four-chamber (bottom) views. Note the presence of thick yellow and orange bands in the patient with LVH in late diastole (see color scale in Fig 1), which reflects the greater dependence of left ventricular filling on atrial contraction. In contrast, in the normal subject, blue and green colors corresponding to early diastolic filling are predominant.

Fig 2 shows an example of end-diastolic Color Kinesis images obtained in a patient with concentric LV hypertrophy and an age-matched control subject. The magnitude of diastolic endocardial motion was similar between both subjects. However, despite similar heart rates, the patient exhibited more late colors (yellow and orange), reflecting augmented contribution of atrial contraction toward LV filling. Even though mean regional diastolic fractional area change was not significantly different between patients with LV hypertrophy and control subjects (74±9% versus 68±19% and 46±10% versus 47±15% in the short-axis and apical four-chamber views, respectively), the proportion of late diastolic filling was greater in patients with LV hypertrophy.

Fig 3 shows time histograms of regional diastolic fractional area change averaged for patients with LV hypertrophy and for age-matched control subjects. The ratio of the early to late peaks (peak1/peak2) was lower in patients (Table 1), while the timing of both peaks was similar between groups. The mean LV filling time was prolonged in patients with LV hypertrophy.

Characterization of LV Filling Profiles
With the exception of patients with a restrictive pattern (group 3), all patients and control subjects had normal LV systolic function. Mitral and pulmonary venous flow Doppler indices obtained in the three subgroups of patients and corresponding control subjects are shown in Table 2. The isovolumic relaxation time was prolonged in patients with abnormal
relaxation (group 1) and normalized mitral flow Doppler (group 2) and decreased in patients with a restrictive pattern (group 3). The time to half LV filling was increased in group 1 and decreased in group 3, whereas it was similar to control subjects in group 2. The pulmonary vein S/D ratio was increased in group 1 and decreased in group 3, relative to control subjects. The A-pv was only nonsignificantly augmented in group 3. In contrast, in patients with normalized mitral inflow profiles, none of these Doppler parameters were statistically different from control subjects (Table 2).

When compared with control subjects, patients in groups 1 and 3 exhibited distinct diastolic endocardial motion patterns (Fig 4). Patients with abnormal relaxation exhibited augmented atrial contribution toward LV filling. In contrast, insignificant atrial contribution was noted in patients with restrictive mitral inflow profiles. The time histograms were similar to mitral inflow profiles in normal subjects and in patients with LV hypertrophy and preserved systolic function (group 2). The pulmonary vein Doppler parameters (Table 2). The atrial contribution in this group was similar to group 1 (Fig 5, middle). Accordingly, peak1/peak2 ratio was diminished in patients with abnormal relaxation (Fig 5, left) and markedly increased in patients with restrictive patterns (Fig 5, right). This ratio correlated with VTIE/VTIA ratio in both views (r=.81 and .73, respectively; P<.001). Mean LV filling time was prolonged in group 1 and shortened in group 3 (Table 3).

Time histograms obtained in group 2 exhibited a disproportionate contribution of atrial contraction toward LV filling despite normalized mitral Doppler profiles (normal E/A ratios with prolonged deceleration time, n=7; normal E/A ratios with normal deceleration time, n=6) (Fig 4) and normal pulmonary vein Doppler parameters (Table 2). The atrial contribution in this group was similar to group 1 (Fig 5, middle). Accordingly, peak1/peak2 ratio were decreased and mean LV filling time prolonged (Table 3). As a result, in these patients, VTIE/VTIA ratio correlated poorly with the Color Kinesis peak1/peak2 ratio (r=.43; P=0.02).

### Protocol 2

In patients with LV hypertrophy and preserved systolic function (n=25), the proportion of diastolic fractional area change

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**TABLE 2. Pulsed-Wave Doppler-Derived Indices Obtained in Three Subsets of Patients With Concentric Left Ventricular Filling Hypertrophy and in Corresponding Age-Matched Control Subjects**

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Isovolumic Relaxation Time, ms</th>
<th>E/A Ratio</th>
<th>VTIE/VTIA Ratio</th>
<th>Deceleration Time, ms</th>
<th>Time to Half LV Filling, ms</th>
<th>S/D Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal relaxation</td>
<td>12</td>
<td>122±34*</td>
<td>0.73±0.18*</td>
<td>1.46±0.39*</td>
<td>316±108*</td>
<td>227±38*</td>
<td>1.67±0.42*</td>
</tr>
<tr>
<td>Control subjects</td>
<td>12</td>
<td>75±11</td>
<td>1.26±0.32</td>
<td>2.01±0.42</td>
<td>199±34</td>
<td>181±21</td>
<td>1.32±0.35</td>
</tr>
<tr>
<td>Normalized mitral inflow profile</td>
<td>13</td>
<td>100±24*</td>
<td>1.21±0.46</td>
<td>2.00±0.88</td>
<td>235±58</td>
<td>179±40</td>
<td>1.19±0.40</td>
</tr>
<tr>
<td>Control subjects</td>
<td>13</td>
<td>74±12</td>
<td>1.20±0.27</td>
<td>1.81±0.44</td>
<td>192±21</td>
<td>180±31</td>
<td>1.26±0.31</td>
</tr>
<tr>
<td>Restrictive mitral inflow profile</td>
<td>4</td>
<td>57±8*</td>
<td>3.15±1.36*</td>
<td>4.56±2.01*</td>
<td>102±19*</td>
<td>81±23*</td>
<td>0.57±0.16*</td>
</tr>
<tr>
<td>Control subjects</td>
<td>4</td>
<td>73±7</td>
<td>1.29±0.12</td>
<td>1.79±0.43</td>
<td>198±27</td>
<td>162±16</td>
<td>1.09±0.13</td>
</tr>
</tbody>
</table>

*Same abbreviations as in Table 1.
*Values are expressed as mean±SD. *P<.05 when compared with control subjects.
completed during the first half of the LV filling in both the short-axis and apical four-chamber views was reduced when compared with control subjects (62 ± 6% versus 74 ± 7% and 66 ± 9% versus 76 ± 5%, respectively, \( P < 0.01 \)). Regional diastolic endocardial motion was more heterogeneous in patients with LV hypertrophy, as reflected by increased index of asynchrony (10.4% versus 6.9%, \( P < 0.01 \), short-axis; 11.2% versus 8.9%, \( P = 0.05 \), apical four-chamber views).

The patterns of regional LV endocardial motion were consistent and relatively uniform in normal subjects, as demonstrated by the homogeneous profiles of regional time curves (Fig 6, top). In contrast, patients with LV hypertrophy frequently exhibited diastolic endocardial motion asynchrony (Fig 6, middle), corroborated by the wide intersegmental variability in the regional LV filling times (Fig 6, bottom). Although groups 1 and 2 had normal LV systolic performance, 22 of 25 (88%) patients exhibited delayed endocardial motion during early diastole (Fig 7) in at least one segment (97 of 300 total segments). Late diastolic endocardial motion occurred most frequently in the septal, anteroseptal, and anterior segments in the short-axis view (13, 14, and 11 segments, respectively) and in the basal septal, mid septal, and lateral segments in the apical four-chamber view (7, 8, and 19 segments, respectively).

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>SAX</th>
<th>A4C</th>
<th>SAX</th>
<th>A4C</th>
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</thead>
<tbody>
<tr>
<td>Abnormal relaxation</td>
<td>12</td>
<td>1.67 ± 0.74*</td>
<td>1.57 ± 0.53</td>
<td>255 ± 33*</td>
<td>255 ± 21*</td>
</tr>
<tr>
<td>Control subjects</td>
<td>12</td>
<td>3.48 ± 1.74</td>
<td>2.31 ± 1.86</td>
<td>198 ± 22</td>
<td>193 ± 19</td>
</tr>
<tr>
<td>Normalized mitral inflow</td>
<td>13</td>
<td>1.86 ± 1.03*</td>
<td>1.71 ± 1.05*</td>
<td>236 ± 34</td>
<td>226 ± 35*</td>
</tr>
<tr>
<td>profile</td>
<td>13</td>
<td>3.20 ± 1.70</td>
<td>2.49 ± 0.71</td>
<td>227 ± 31</td>
<td>201 ± 24</td>
</tr>
<tr>
<td>Control subjects</td>
<td>13</td>
<td>10.27 ± 3.62*</td>
<td>5.52 ± 3.17</td>
<td>120 ± 12*</td>
<td>135 ± 24*</td>
</tr>
<tr>
<td>Restrictive mitral inflow</td>
<td>4</td>
<td>3.00 ± 1.31</td>
<td>2.56 ± 0.91</td>
<td>205 ± 24</td>
<td>192 ± 15</td>
</tr>
<tr>
<td>Control subjects</td>
<td>4</td>
<td>1.63 ± 1.54</td>
<td>1.59 ± 0.53</td>
<td>255 ± 33*</td>
<td>255 ± 21*</td>
</tr>
</tbody>
</table>

Same abbreviations as in Table 1. Values are expressed as mean ± SD. * \( P < 0.05 \) when compared with control subjects.
Protocol 3
The index of asynchrony obtained in patients with nonsignificant coronary artery lesions was not significantly different from that of the control group (9.4% versus 6.9%, short-axis; and 8.5% versus 8.9%, apical four-chamber views; NS). In contrast, in patients with coronary artery disease this index was significantly increased (17.1% versus 6.9%, short-axis; and 12.9% versus 8.9%, apical four-chamber views; $P<.05$) when compared with the control group because of delayed regional endocardial motion. Similarly, patients with coronary artery disease had larger index of asynchrony compared with patients with nonsignificant coronary artery lesions (17.1% versus 9.4%, short-axis; and 12.9% versus 8.5%, apical four-chamber views; $P<.05$). In patients with coronary artery disease, diastolic endocardial motion was delayed in 28 of 84 segments studied (33%) (Fig 8), whereas in patients with nonsignificant coronary lesions, regional diastolic abnormalities were only observed in 8 of 96 segments analyzed (8%). Coronary angiograms revealed that 70 LV segments were supplied by narrowed coronary epicardial arteries ($\geq 50\%$ of arterial lumen). Delayed regional diastolic endocardial motion was observed in 27 of these segments and remained within the normal profile in 43 LV segments. A total of 110 LV segments were perfused by coronary arteries with nonsignificant lesions. In 9 of these segments, Color Kinesis analysis detected delayed endocardial motion, whereas in 101 LV segments, normal regional diastolic displacement was noted.

Discussion
Considerable efforts have been recently directed toward the development of noninvasive techniques capable of accurate and serial assessment of LV diastolic properties. However, currently available methods such as Doppler and acoustic quantification$^{12,13}$ only provide information on global rather than regional LV filling. Moreover, diastolic dysfunction may be difficult to identify in patients with normalized Doppler indices.$^{14}$ Global LV diastolic function is adversely affected by heterogeneities in regional contraction and relaxation.$^{15,16}$ Consequently, regional diastolic properties need to be fully elucidated to better understand this relationship.

Figure 7. Example of regional filling curves obtained in a patient with concentric left ventricular hypertrophy (LVH) and normal systolic function. For each segment, a reference profile of diastolic endocardial motion was generated by averaging curves obtained in normal subjects ($n=29$); dashed lines represent 1 SD around the mean. In this case, the curves in the anterior, anteroseptal, and septal segments reflect delayed endocardial motion during early diastole. For each segment, mean time of filling (in milliseconds) is displayed (open bars) together with the normal values (solid bars) and SD for comparison. Also see Fig 3 abbreviations.

Figure 8. Example of regional filling curves obtained in the short-axis view in a patient with a 75% stenosis of the mid left anterior descending coronary artery. When compared with the normal profiles (dashed bands), diastolic endocardial motion is substantially delayed in the anteroseptal and septal left ventricular segments. Also see Figs 1 and 3 abbreviations.
Our study was designed to determine whether regional quantitative analysis of Color Kinesis images could provide (1) information additional to Doppler indices of global LV diastolic function, particularly in patients with concentric hypertrophy and normalized mitral inflow profiles and (2) objective characterization of regional diastolic LV wall motion.

**Quantitative Analysis of End-diastolic Color Kinesis Images**

To compare mitral flow Doppler-derived indices with Color Kinesis data, we limited the analysis of the latter to the period of LV filling. Color Kinesis images provide real-time information on the timing and magnitude of diastolic endocardial displacement. Using segmental analysis of these images, we calculated various parameters of regional diastolic endocardial motion. The segmentation schemes used (Fig 1) were similar to those recommended by the American Society of Echocardiography. To facilitate the comparison between LV inflow Doppler and Color Kinesis findings, regional diastolic fractional area change was displayed as a function of time. Interpolation allowed intersubject comparisons of diastolic endocardial motion profiles irrespective of the duration of LV filling. These time histograms had two distinct peaks, one in early diastole corresponding to the period of rapid LV filling and a second one in late diastole reflecting the atrial contribution toward LV filling (Figs 3, 4, and 5).

To evaluate the temporal patterns of diastolic endocardial motion on a regional basis, segmental fractional area change was also displayed as time curves. The percentage of total endocardial motion completed at 50% of the LV filling period was computed for each segment and used to objectively assess regional diastolic asynchrony during rapid LV filling. Delayed diastolic endocardial motion was identified by comparing individual curves obtained in hypertensive patients with reference profiles obtained in normal subjects (Figs 7 and 8).

**Assessment of Global LV Diastolic Function**

As expected, both the isovolumic relaxation and early deceleration times were prolonged and the VT1e/VT1a ratio reduced in patients with LV hypertrophy when compared with age-matched control subjects (Table 1), reflecting impaired LV relaxation and compliance. However, normal subjects and patients with LV hypertrophy had similar E/A ratios, time to half LV filling, pulmonary vein S/D ratios, and peak reversal flow velocities during atrial contraction (Table 1). The latter findings differ from those reported in previous studies in which reduced E/A ratios and augmented S/D ratios were reported in patients with cardiac hypertrophy as a result of increased dependence on atrial systolic filling. These discrepancies might reflect differences in age, loading conditions, and heart rates, which are known to affect both mitral and pulmonary vein flow velocity profiles. In our study, however, no differences in heart rate or age were present between patients with LV hypertrophy and control subjects. Because it is now well established that Doppler flow profiles change with the progression of LV hypertrophy, differences in both the severity and duration of hypertensive heart disease were presumably responsible for the inability of the Doppler indices to differentiate between hypertensive and normal subjects.

In contrast, the analysis of Color Kinesis images, which provides information on LV diastolic properties by quantifying endocardial motion, separated patients with LV hypertrophy from control subjects. Although the magnitude of diastolic fractional area change was not significantly different between hypertensive and normal subjects, LV filling was delayed in patients with concentric hypertrophy, as evidenced by the increased endocardial motion during late diastole (Fig 3). This finding was confirmed by a decreased peak1/peak2 ratio in patients with cardiac hypertrophy, in agreement with decreased Doppler VT1e/VT1a ratio (Table 1) and with previous studies based on radionuclide techniques and acoustic quantification. In contrast, mean filling time obtained from Color Kinesis was prolonged, whereas the time to half LV filling derived from Doppler was similar in patients with hypertrophy and control subjects (Table 1).

**Characterization of LV Filling Profiles**

Progression of hypertensive heart disease modifies LV diastolic properties, which in turn results in gradual alterations of mitral flow Doppler patterns, from abnormal relaxation (group 1) to normalized (group 2) and finally restrictive (group 3) profiles. Interestingly, the pulmonary vein flow S/D ratio as well as the time to half LV filling progressively decreased from group 1 to group 3, whereas the E/A ratio exhibited opposite changes (Table 2). These findings suggest that the proportion of LV filling that depends on atrial contraction is limited in hypertensive patients with advanced LV hypertrophy. As previously reported, hypertensive patients with normalized mitral flow velocity profiles and age-matched control subjects had similar patterns of pulmonary venous flow velocities (Table 2). Consequently, none of the conventionally used Doppler indices identified global diastolic dysfunction in our patients with LV hypertrophy and normalized mitral flow velocity patterns.

In these patients, Color Kinesis time histograms depicted a decreased early peak, whereas the late peak of diastolic fractional area change was augmented, resulting in diminished peak1/peak2 ratios with prolonged mean LV filling times (Table 3). Similar findings were noted in patients with abnormal relaxation (Figs 4 and 5), in agreement with previous studies. In contrast, patients with restrictive mitral flow Doppler patterns exhibited a markedly increased peak1/peak2 ratio (Figs 4 and 5) with short mean filling times (Table 3). Thus Color Kinesis time histograms depicted two distinct abnormal patterns: (1) a reduced contribution of rapid LV filling compensated by augmented atrial contraction in patients with either abnormal relaxation or normalized mitral Doppler profiles and (2) a predominant rapid filling and impaired left atrial emptying observed in patients with restrictive LV inflow velocity profiles.

Color Kinesis time histograms were abnormal in group 2 patients, whereas Doppler indices were similar to those obtained in age-matched control subjects. In addition, mean filling time obtained from Color Kinesis images was prolonged in these patients (Table 3), whereas the time to half LV filling failed to separate group 2 patients from control subjects (Table 2). This discrepancy between instantaneous variations in LV
inflow velocities and diastolic fractional area change can be explained as follows. First, using quantitative evaluation of mitral flow propagation along the LV long axis with color M-mode Doppler, Takatsuji et al. have recently demonstrated that LV filling flow propagation is rapidly attenuated despite increased early transmural velocities in patients with normalized Doppler profiles. This finding was explained by the marked increase in ventricular pressure immediately after mitral valve opening secondary to reduced LV compliance, which might stall the driving force of LV filling near the mitral orifice. Second, it has been demonstrated that mitral flow velocity does not have a flat spatial profile. Third, blood flow entering the left ventricle appears to be oriented differently in early versus late diastole. Finally, the mitral annulus cross-sectional area has been shown not only to gradually increase as diastole progresses but also to change in shape.

**Assessment of Regional Diastolic Function**

Nonuniformity in temporal and regional distribution of load and inactivation has been described as a major factor influencing LV relaxation. These local diastolic disturbances can be identified as deviations of endocardial motion from normal patterns, which are also nonuniform to a certain degree. Accordingly, we used segmental analysis of end-diastolic Color Kinesis images to characterize diastolic wall motion asynchrony in patients with concentric LV hypertrophy and in normal subjects for comparison. In patients with cardiac hypertrophy, regional endocardial motion occurred proportionally later in diastole in all LV segments when compared with control subjects. This was reflected by the smaller percentage of total diastolic fractional area change completed within the first half of the LV filling period. In normal subjects, diastolic endocardial motion was relatively uniform in all segments. In agreement with previous studies in which increased diastolic wall motion nonuniformity in patients with cardiac hypertrophy has been reported in association with impaired global LV relaxation, our patients exhibited diastolic wall motion asynchrony evidenced by delayed endocardial motion in 32% of LV segments (Fig 7). Diastolic wall motion asynchrony may be related to various mechanisms, such as heterogeneous myocardial hypertrophy resulting in regional differences in wall stress, localized foci of interstitial fibrosis, and nonuniform inactivation secondary to the loss of contractile elements and normal intercellular connections. Consequently, increased diastolic wall motion nonuniformity may result in uncoordinated and consequently prolonged LV filling in patients with cardiac hypertrophy. Although in our study, patients with diastolic wall motion asynchrony had normal systolic function, nonuniformity in systolic wall motion not detectable by conventional visual interpretation of two-dimensional echocardiograms may have contributed to the regional diastolic abnormalities. Bonow et al. have reported that only 15% of patients with cardiac hypertrophy and preserved systolic function exhibited homogeneous LV filling when evaluated with radionuclide angiography. Similarly, in our study, only 3 of 25 patients (12%) with LV hypertrophy and preserved systolic function had no evidence of diastolic asynchrony.

Regional diastolic LV filling abnormalities are sensitive early signs of myocardial ischemia and may occur when systolic function is still preserved. Thus characterization of regional LV diastolic endocardial motion with the use of Color Kinesis appears to be of potential value for the detection of myocardial ischemia. In this study, patients with nonsignificant coronary artery stenosis had an index of asynchrony similar to that observed in normal subjects. In contrast, patients with coronary artery disease exhibited significantly increased regional diastolic wall motion heterogeneity. As opposed to patients with LV hypertrophy in whom segmental diastolic abnormalities were identified without predominance of specific regions, in patients with coronary artery disease, delayed endocardial diastolic motion was specific to myocardial segments perfused by narrowed epicardial coronary arteries. Absence of delayed endocardial motion in certain LV segments supplied by narrowed epicardial coronary arteries may be explained by the absence of significant myocardial ischemia at rest in these myocardial regions. Further studies are needed to determine whether characterization of regional diastolic endocardial motion with the use of Color Kinesis may help to noninvasively assess myocardial ischemia during stress testing.

Several diagnostic methods such as contrast or radionuclide ventriculography have been used to quantify regional diastolic function by generating regional diastolic volume–time curves. Color Kinesis has several advantages over these modalities. First, Color Kinesis does not require exposure to radiation and can therefore be used readily for serial assessment of regional diastolic function. Second, with the use of Color Kinesis, it is possible to quantify regional diastolic endocardial motion on line.

**Limitations**

Color Kinesis has several limitations, such as its dependence on image quality and operator-dependent gain settings. Color Kinesis does not allow color encoding of the entire LV filling sequence in patients with heart rate <55 bpm because the diastolic color scale currently has only 19 hues. In addition, the low temporal resolution of Color Kinesis (30 frames/s) may not allow accurate enough definition of endocardial motion at high heart rates. For all these reasons, almost one third of our screened patients were not suitable for adequate Color Kinesis studies. Further studies are needed to determine the feasibility and value of quantitative analysis of diastolic Color Kinesis images in nonselected patients with LV hypertrophy or ischemic heart disease. Some of these limitations could be overcome by using higher frame-rate imaging in conjunction with an extended color scale and automated gain settings. Because Color Kinesis is designed to color-encode endocardial motion, it is not suited for the assessment of the isovolumic relaxation period. In addition, because coronary angiograms were not obtained in our patients with LV hypertrophy, the possibility of underlying coronary artery disease in these patients could not be ruled out. Finally, in our study, patients with LV hypertrophy and a restrictive filling pattern constituted a small group. Accordingly, our results need to be confirmed in a larger population.

**Conclusions**

In this study, quantitative analysis of Color Kinesis images was used to (1) identify diastolic dysfunction in patients with concentric cardiac hypertrophy, with normalized mitral inflow Doppler profiles and (2) characterize and quantify diastolic wall motion asynchrony in patients with cardiac hypertrophy and in patients with coronary artery disease. Our results demonstrate that quantitative analysis of Color Kinesis images enables
objective evaluation of global as well as regional LV filling properties. As such, this methodology promises to be valuable in the clinical assessment of diastolic function in a large variety of heart diseases and in the evaluation of therapeutic interventions on regional LV diastolic properties.

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