Differentiation Between Restrictive Cardiomyopathy and Constrictive Pericarditis by Early Diastolic Doppler Myocardial Velocity Gradient at the Posterior Wall

Przemysław Palka, MD; Aleksandra Lange, MD; J. Elisabeth Donnelly, MD; Petros Nihoyannopoulos, MD

Background—The differential diagnosis between restrictive cardiomyopathy (RCM) and constrictive pericarditis (CP) is challenging and, despite combined information from different diagnostic tests, surgical exploration is often necessary.

Methods and Results—A group of 55 subjects (mean age, 63 ± 11 years; 36 men and 19 women) were enrolled in the study; 15 had RCM, 10 had CP, and 30 were age-matched, normal controls. The diagnosis of RCM was supported by a biopsy; in the CP group, the diagnosis was confirmed either surgically or at autopsy. All patients underwent a transthoracic echocardiogram that included the assessment of Doppler myocardial velocity gradient (MVG), as measured from the left ventricular posterior wall during the predetermined phases of the cardiac cycle. MVG was lower (P < 0.01) in RCM patients compared with both CP patients and normal controls during ventricular ejection (2.8 ± 1.2 versus 4.4 ± 1.0 and 4.7 ± 0.8 s⁻¹, respectively) and rapid ventricular filling (1.9 ± 0.8 versus 8.7 ± 1.7 and 3.7 ± 1.4 s⁻¹, respectively). Additionally, during isovolumic relaxation, MVG was positive in RCM patients and negative in both CP patients and normal controls (0.7 ± 0.4 versus −1.0 ± 0.6 and −0.4 ± 0.3 s⁻¹, respectively; P < 0.01). During atrial contraction, MVG was similarly low (P < 0.01) in both RCM and CP patients compared with normal controls (1.6 ± 1.7 and 1.7 ± 1.8 versus 3.8 ± 0.9 s⁻¹, respectively).

Conclusions—Doppler myocardial imaging–derived MVG, as measured from the left ventricular posterior wall in early diastole during both isovolumic relaxation and rapid ventricular filling, allows for the discrimination of RCM from CP.

Key Words: cardiomyopathy • pericarditis • imaging

Several echocardiographic parameters have been proposed as ways to differentiate restrictive cardiomyopathy (RCM) from constrictive pericarditis (CP). These parameters are based on conventional M-mode, 2D images, and Doppler blood-flow patterns. The respiratory variation in transmittal velocity blood flow is the most frequently used parameter to differentiate RCM from CP. However, respiratory variation can also be observed in patients with chronic obstructive airway disease. Also, a considerable percentage of CP patients do not demonstrate respiratory variation in their blood-flow velocities. Oh et al proposed that in this group of patients, additional echocardiographic tests to reduce preload may help unmask or enhance respiratory variation on transmitral Doppler flow. Nevertheless, in some cases, the diagnosis remains equivocal, and other diagnostic tests and/or surgical exploration are required.

Doppler myocardial imaging (DMI) is an echocardiographic technique that has the potential to enhance the diagnostic information available from Doppler blood-flow indices. Pulsed-wave DMI can be used to quantify longitudinal mitral annular motion, which can be useful in the distinction between RCM and CP. Little data exist on the potential role of the myocardial velocity gradient (MVG) in distinguishing RCM from CP. MVG was introduced as a new index of myocardial contraction and relaxation that quantifies the spatial distribution of intramural velocities across the myocardium. Recent studies have shown that MVG is relatively independent of the translational motion of the heart and/or preload alterations. In this study, MVG calculation at the left ventricular (LV) posterior wall was used to quantify myocardial contraction and relaxation in RCM and CP patients to establish whether it can be used in defining these groups.

Methods

A group of 55 subjects (aged 63 ± 11 years; 36 men and 19 women) was enrolled in this study; subjects consisted of 15 RCM patients, 10 CP patients, and 30 age-matched, normal controls (Table 1). Subjects were recruited from the Departments of Cardiology and Rheumatol-
TABLE 1. Clinical Characteristics of Study Subjects

<table>
<thead>
<tr>
<th>Parameter</th>
<th>RCM (n=15)</th>
<th>CP (n=10)</th>
<th>Normal (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>54±14</td>
<td>57±14</td>
<td>58±8</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>9 (60)</td>
<td>7 (70)</td>
<td>20 (67)</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>81±18*</td>
<td>75±14</td>
<td>67±11</td>
</tr>
<tr>
<td>Sinus rhythm, n (%)</td>
<td>12 (80)</td>
<td>7 (70)</td>
<td>30 (100)</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>112±13†</td>
<td>109±18†</td>
<td>131±8</td>
</tr>
<tr>
<td>NYHA class</td>
<td>2.9±0.4</td>
<td>3.1±0.5</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as mean±SD or n (%). BP indicates blood pressure; NYHA, New York Heart Association.
*P<0.05 compared with normal subjects; †P<0.01 compared with normal subjects (ANOVA).

Protocol

Each subject underwent a standard echocardiographic and DMI study of the LV posterior wall using an Acuson ultrasound scanner (XP/10, Aspen).

Standard echocardiography consisted of M-mode, 2D, and Doppler blood-flow measurements. The parameters measured at end-diastole were interventricular septum, LV posterior wall, and LV diameter; at end-systole, we measured the left atrium. The M-mode of the LV posterior wall was digitized, and then the normalized peak diameter; at end-systole, we measured the left atrium. The M-mode DMI images of the LV posterior wall were obtained at 5 to 10 minutes were used for off-line analysis of images. None of the patients was excluded from the study on the basis of DMI image quality.

Doppler Myocardial Imaging

The system used in this study has been previously described. M-mode DMI images of the LV posterior wall were obtained at end-expiration and were digitally downloaded to the image capture system for MVG off-line analysis. Peak MVG values were determined in systole during early ventricular ejection (VE), in early diastole during isovolumic relaxation (IR) and rapid ventricular filling (R VF), and in late diastole during atrial contraction (AC). These phases were defined using the combined information derived from M-mode images taken at the tips of mitral valve leaflets with visible valve openings and the simultaneously recorded ECG and phonocardiogram. To obtain M-mode DMI images, the echocardiographic examination was extended by 2 to 3 minutes. Another 5 to 10 minutes were used for off-line analysis of images. None of the patients was excluded from the study on the basis of DMI image quality.

Doppler MVG was defined as the slope of linear regression of the myocardial velocity estimates along each M-mode scan line throughout the thickness of the myocardium. Myocardial velocity estimates were calculated automatically in each pixel of each M-mode scan. Positive or negative MVG indicated a faster motion of either a subendocardial or a subepicardial layer, respectively. To calculate peak MVG in the predefined phases of the cardiac cycle, a plot graph of MVG changes over time was drawn using computer software.

Interobserver and intraobserver variability for MVG were assessed in our previous work. Both interobserver and intraobserver variability were low, at 0.1±0.2 and 0.2±0.2 s⁻¹, respectively.

Statistics

Data are expressed as mean±SD. ANOVA with Scheffe’s F adjustment for multiple comparisons was used to assess the differences between each group. The degree of respiratory variation in peak E-wave velocity was calculated as follows: [(peak E-wave in expiration)−(peak E-wave in inspiration)]/(peak E-wave in expiration)]×100%. Multivariate regression analysis was performed to account for the effects of other variables.

Table 2.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>RCM</th>
<th>CP</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV wall thickness, cm</td>
<td>1.3±0.3†</td>
<td>1.0±0.2</td>
<td>0.9±0.1</td>
</tr>
<tr>
<td>LV diameter, cm</td>
<td>4.3±0.5*</td>
<td>4.5±0.5</td>
<td>4.8±0.6</td>
</tr>
<tr>
<td>Left atrial diameter, cm</td>
<td>4.1±0.7†</td>
<td>4.2±0.4†</td>
<td>3.2±0.4</td>
</tr>
<tr>
<td>Peak rate of posterior wall thickening</td>
<td>4.5±1.8</td>
<td>4.8±1.8</td>
<td>5.6±1.5</td>
</tr>
<tr>
<td>Peak rate of posterior wall thinning</td>
<td>−5.4±2.3*</td>
<td>−7.6±2.5</td>
<td>−7.8±2.0</td>
</tr>
<tr>
<td>Peak E-wave, m/s</td>
<td>1.03±0.25†</td>
<td>0.96±0.27†</td>
<td>0.59±0.10</td>
</tr>
<tr>
<td>Peak A-wave, m/s</td>
<td>0.55±0.21</td>
<td>0.42±0.22</td>
<td>0.58±0.10</td>
</tr>
<tr>
<td>E/A ratio</td>
<td>2.21±0.82†</td>
<td>2.61±1.20†</td>
<td>1.05±0.23</td>
</tr>
<tr>
<td>E-wave deceleration time, ms</td>
<td>111±13†</td>
<td>114±11†</td>
<td>195±14</td>
</tr>
<tr>
<td>IR time, ms</td>
<td>54±12†</td>
<td>48±13†</td>
<td>90±8</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>58±7</td>
<td>56±7</td>
<td>59±4</td>
</tr>
</tbody>
</table>

*P<0.05; †P<0.01 compared with normal subjects (by ANOVA).
evaluate the relation between the MVG and other echocardiographic variables. Linear regression analysis was performed to present the relationship between VE-MVG and LV posterior wall thickness in RCM patients. P<0.05 was considered significant.

Results

Standard Echocardiography

The RCM group had a greater LV wall thickness (44%) and a smaller LV diameter (−10%) compared with age-matched normal controls (Table 2). The pericardium was calcified/thickened in 6 CP patients, and interventricular septal motion with a “respiratory bounce” was seen in 8 CP patients. When compared with normal subjects, RCM and CP patients had greater left atrial diameters (28% and 31%, respectively), higher peak E-waves (75% and 63%), higher E/A ratios (110% and 149%), shorter E-wave decelerations (−46% and −44%), and shorter isovolumetric relaxation times (−40% and −47%).

In the CP group, the mean peak E-wave was 0.96±0.27 m/s in expiration and 0.69±0.18 m/s in inspiration; the mean respiratory variation in this group was 38±17% (range, 10% to 68%). In 8 of the 10 CP patients, respiratory variations were >25%, and the peak E-wave decreased from 1.06±0.20 m/s (range, 0.77 to 1.41 m/s) in expiration to 0.74±0.16 m/s (range, 0.50 to 1.00 m/s) in inspiration. In the remaining 2 CP patients, respiratory variations in the peak E-wave were <25% (10% and 15%).

In hepatic venous flow by pulsed-wave Doppler, a constriction pattern with a >25% decrease in diastolic forward flow and/or prominent late diastolic flow reversal after the onset of expiration was observed in 8 CP patients (7 of 8 with a concomitant characteristic pattern of transmural inflow and one with an inconclusive pattern of transmural inflow). The diagnosis of CP as based on combined information from all Doppler blood-flow recordings was inconclusive in 1 of the 10 CP patients studied.

**Digitized M-Mode**

No differences existed between the RCM and CP groups in the measurement of the peak rate of systolic wall thickening and diastolic wall thinning. However, the peak rate of wall thinning was lower in the RCM group than in normal subjects (−31%).

**MVG**

VE-MVG was lower in the RCM group when compared with both the CP group (−36%) and normal controls (−40%). In all groups, VE-MVG was positive, indicating that during the LV posterior wall thickening, the subendocardium was mov-
ing faster than the subepicardium (Table 3 and Figure 1). For all groups, the IR-MVG was relatively low compared with either the VE-MVG or RVF-MVG. IR-MVG differed between the RCM group and both the CP group and normal controls. The absolute value of IR-MVG was 75% higher for RCM patients and 150% higher for CP patients than in normal controls. During the IR, the analyzed myocardium was coded as blue, indicating that the movement was away from the center of the LV. In the RCM group, IR-MVG was positive, indicating that the subendocardium was moving faster than the subepicardium. Conversely, in both CP patients and normal controls, the IR-MVG was negative, indicating that outward movement was mainly due to subepicardial motion. The RVF-MVG was lower in RCM patients compared with both CP patients (278%) and normal controls (249%); RVF-MVG was higher in CP patients than in normal controls (135%). In all groups, RVF-MVG was positive, indicating that the LV posterior wall was thinning due to a faster motion of the subendocardium rather than the subepicardium.

Examples of MVG analysis in RCM and CP patients (with and without marked respiratory variation on transmitral Doppler blood flow) are shown in Figure 2. Figure 3 shows the differences in early diastolic MVG changes in the study groups.

Multivariate Regression Analysis of MVG

Systole

In RCM patients, VE-MVG was dependent on LV posterior wall thickness but was independent of other echocardiographic and clinical variables. Figure 4A shows a correlation between LV posterior wall thickness and VE-MVG (for RCM group, \( r = -0.75; P < 0.001 \)).

Diastole

All diastolic MVGs (IR-MVG, RVF-MVG, and AC-MVG) were independent of other echocardiographic variables, including transmitral Doppler blood-flow indices, LV dimension, and the degree of LV posterior wall thickness (Figures 4B through 4D). Also, IR-MVG and RVF-MVG were inde-
myocardial or endocardial disease. In this study, Doppler
versely, in RCM, the LV wall is resistant to stretch due to
erties of the myocardium. Garcia et al. conducted the first
MVG was used to quantify structural/functional myocardial
velocities. The sign of the MVG depends on the relative fastness
subendocardial or subepicardial velocities; it is positive if
subendocardial velocities move faster and negative in the oppo-
site scenario.

dependent of age, heart rate, and systolic blood pressure. Figure
shows a relation between the transmitral peak E-wave, E-wave deceleration time, and RVF-MVG.

Discussion
The results of this study indicate that the assessment of
myocardial contraction and relaxation using Doppler MVG at the
LV posterior wall may be helpful in distinguishing RCM from CP.

Although in CP patients there is an increase in ventricular interaction and a dissociation of intrathoracic-intracardiac pressure changes with respiration, both CP and RCM may have similar clinical manifestations, which are related to decreased LV compliance. However, the mechanism leading to the decrease in chamber compliance is different. In CP, decreased ventricular compliance is due to an increase in pericardial restraint, which is related to the pathological process of pericardial scarring and/or calcification. Conversely, in RCM, the LV wall is resistant to stretch due to myocardial or endocardial disease. In this study, Doppler MVG was used to quantify structural/functional myocardial status by following the hypothesis that DMI has the potential to quantify changes in the intrinsic mechanical elastic properties of the myocardium. Garcia et al. conducted the first pulsed-wave DMI study to measure mitral annulus longitudinal velocities to differentiate RCM from CP. Although pulsed-wave DMI records myocardial motion as reflected by annulus motion, it has some important limitations, including the angulation of the ultrasound beam and the potential effect of LV contractile function and cavity size/shape on mitral annulus velocities. A different approach was undertaken to quantify color DMI images by our group and others.

Findings
Conventional echocardiographic assessment allowed us to
establish the correct diagnosis in all RCM and CP patients. The evaluation of respiratory variations of Doppler blood-flow velocities alone were inconclusive in 2 patients for transmitial velocity pattern and in 2 patients for hepatic vein flow. For the entire study group, the information from both transmitial and hepatic vein Doppler blood flow assisted the diagnosis of CP in all but one patient. This is in agreement with Oh et al., who found that characteristic respiratory variations of Doppler blood-flow velocities are present in ~88% of CP patients.

Our results from digitized M-mode images are in agreement with previously published data. Although the peak rate of wall thinning was reduced in RCM patients compared with normal subjects, the data did not allow for a clear distinction between RCM and CP.

Both VE-MVG and RVF-MVG were reduced in RCM patients compared with both CP patients and normal subjects. Although VE-MVG was reduced by 36% in RCM patients compared with CP patients, an overlap in MVG measurements still occurred; this overlap did not allow for a clear-cut distinction between RCM and CP. In addition, this reduction of VE-MVG in RCM was dependent on LV hypertrophy. The most striking difference between RCM patients and both CP patients and normal controls was observed during RVF; at this time, no overlap between the study groups occurred. In RCM patients, the RVF-MVG was 78% lower than that measured in CP patients and ~50% lower than that in normal controls. Also, IR-MVG differed between RCM patients and both CP patients and normal subjects. The absolute value of IR-MVG was 75% higher in RCM patients and 150% higher in CP patients compared with normal subjects. Both IR-MVG and RVF-MVG were independent of the degree of LV hypertrophy. Thus, even in the absence of LV hypertrophy in RCM patients, RVF-MVG was lower in the RCM group than in the CP group.

Low VE-MVG and RVF-MVG in the RCM group indicate a pathological uniform distribution of transmoyocardial velocities between the endocardium and epicardium. We believe that the observed clear reduction in both VE-MVG and RVF-MVG in the RCM group results from fibrotic and/or infiltrative processes involving the subendocardium and/or myocardium. This process of structural and functional myocardial changes is typical for RCM rather than CP.

High IR-MVG and RVF-MVG in CP patients may be explained by the increased dissociation of intrathoracic-intracardiac pressure changes during end-respiration.

In all study subjects, the LV posterior wall was thickening during VE and thinning during RVF; in both these time periods, wall thickening and thinning was generated by a faster movement of the subendocardial layer. The situation was different in early diastole during IR. In all study groups, the IR period was coded blue, indicating that the wall movement was away from the center of the LV. We found that during this time period, MVG was positive in RCM patients, indicating that the LV posterior wall was thickening due to faster subendocardial velocities. In both CP patients and normal subjects, the IR period was also coded blue, but the MVG was negative, which indicates a faster movement of the subepicardial layer, causing wall thickening. Although this was observed in all study patients, the magnitude of IR-MVG was relatively low compared with other analyzed
AC-MVG was reduced by 50% in both the RCM group and CP group. Thus, the analysis of MVG in late diastole was not helpful in differentiating RCM from CP. We speculate that the increase in LV end-diastolic pressure, which is well documented in both RCM and CP, reduces late diastolic blood inflow to the LV, which will reduce AC-MVG.

Table 4 summarizes our results in light of already published data on the role of MVG in the differentiation of myocardial/pericardial disorders.

Limitations
In this study, we do not have a patient in whom the diagnosis of CP or RCM was not made by standard echocardiography alone. However, a standard echocardiographic study is technically demanding and involves complex measurements taken from several acoustic windows. No single conventional echocardiographic parameter could have been used to make the diagnosis. The measurement of MVG, taken as a single diagnostic index, allowed for the differentiation of CP from RCM in all patients. The DMI study was technically simple, and it was not time consuming. We did not routinely perform periods; therefore, a study in a larger patient population is needed to fully investigate this observation.

AC-MVG was reduced by >50% in both the RCM group and CP group. Thus, the analysis of MVG in late diastole was not helpful in differentiating RCM from CP. We speculate that the increase in LV end-diastolic pressure, which is well documented in both RCM and CP, reduces late diastolic blood inflow to the LV, which will reduce AC-MVG.

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preload reduction to unmask Doppler respiratory variation.\textsuperscript{10} However, a recent study by Shimizu et al\textsuperscript{26} showed that MVG is relatively independent of loading conditions. Therefore, we can assume that MVG measurements should be similar to those obtained with preload reduction.

Our study group consisted of 6 subjects (24%) in atrial fibrillation, and the influence of missing atrial function might be an important underscoring factor for blood-flow recordings or MVG calculation. However, MVG did not differ between patients in sinus rhythm and those in atrial fibrillation. Therefore, we assume that MVG can be of clinical value in the differentiation of CP from RCM in patients in both sinus rhythm and atrial fibrillation.

RCM patients had a lower New York Heart Association class than CP patients, which suggests that the latter group had a higher left atrial pressure. This could lead to an earlier mitral valve opening and/or an increase in RVF-MVG in CP patients. However, in this study, invasive measurements of LV diastolic function were not performed to verify this hypothesis. Although our patients had no evidence of LV posterior wall ischemia, some data suggest that ischemia may reduce MVG, as was observed in the RCM group in this study.\textsuperscript{22} We did not include patients with combined constrictive/restrictive disease\textsuperscript{12,31,36}; however, we believe that in this group of patients, MVG would also be reduced after myocardial infiltration.

**Conclusions**

This study confirmed the hypothesis that direct evaluation of structural/functional myocardial status by DMI-derived MVG calculation at the LV posterior wall is helpful in distinguishing restrictive from constrictive physiology. It seems that the measurement of early diastolic MVG is an accurate echocardiographic parameter that differentiates patients with RCM from those with CP.

**References**


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