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. (Circulation. 2000;102:655-662.)

Key Words: cardiomyopathy • pericarditis • imaging

Several echocardiographic parameters have been proposed as ways to differentiate restrictive cardiomyopathy (RCM) from constrictive pericarditis (CP).¹ These parameters are based on conventional M-mode,²,³ 2D images,⁴ and Doppler blood-flow patterns.⁵⁻⁹ The respiratory variation in transmittal velocity blood flow is the most frequently used parameter to differentiate RCM from CP.⁵,⁶ However, respiratory variation can also be observed in patients with chronic obstructive airway disease.¹⁰ Also, a considerable percentage of CP patients do not demonstrate respiratory variation in their blood-flow velocities.⁶ Oh et al¹¹ 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.¹²,¹³

Doppler myocardial imaging (DMI) is an echocardiographic technique that has the potential to enhance the diagnostic information available from Doppler blood-flow indices.¹⁴⁻¹⁹ Pulsed-wave DMI can be used to quantify longitudinal mitral annular motion, which can be useful in the distinction between RCM and CP.¹⁴ 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.²⁰⁻²⁴ Recent studies have shown that MVG is relatively independent of the translational motion of the heart²⁵ and/or preload alterations.²⁶ 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-
protocol at the following institutions: Victoria Hospital, Kirkcaldy; Western General Hospital and Royal Infirmary, Edinburgh; and Hammersmith Hospital, London, UK. The study group was formed prospectively and in a nonselective manner from all referrals of patients with unexplained right-sided heart failure between January 1994 and December 1998. The diagnosis of RCM or CP was based on clinical assessment and the results of the following diagnostic tests: echocardiogram, cardiac catheterization, MRI, and/or CT scan. All 15 patients with RCM underwent a biopsy, which confirmed amyloidosis in 12 patients. In patients with CP, the diagnosis was confirmed at surgery (n=8) or autopsy (n=2). In 4 patients, CP was described as idiopathic; it was described as postpericardiotomy in 4, as postradiotherapy in 1, and as neoplastic pericardial infiltration in 1. All 15 RCM and 7 of the 10 CP patients had no evidence of coronary artery disease. The remaining 3 CP patients who had previous open heart surgery due to coronary artery disease had not had a myocardial infarction and/or reversible ischemia on the interposterior LV wall. Pericardial thickness (≥4 mm) or pericardial calcification was shown in 4 of the 5 CP patients in whom a CT scan was performed.

Table 1. Clinical Characteristics of Study Subjects

<table>
<thead>
<tr>
<th>Age, y</th>
<th>RCM (n=15)</th>
<th>CP (n=10)</th>
<th>Normal (n=30)</th>
</tr>
</thead>
<tbody>
<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.

Doppler Myocardial Imaging

The system used in this study has been previously described. 20,28 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 (RVF), 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. 17,20,28 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. 20-26,28 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. 20,28 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%. 11 Multivariate regression analysis was performed to

Table 2. Conventional Echocardiographic and Digitized M-Mode Data of Study Subjects

<table>
<thead>
<tr>
<th>LV Wall Thickness, cm</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, s⁻¹</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 thickening, s⁻¹</td>
<td>-5.4±2.3*</td>
<td>-7.6±2.4</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±0.62†</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-

<table>
<thead>
<tr>
<th>TABLE 3. Doppler MVG Measurements in the Study Groups</th>
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<tbody>
<tr>
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<tr>
<td>--------------------------</td>
</tr>
<tr>
<td>VE-MVG, s⁻¹</td>
</tr>
<tr>
<td>IR-MVG, s⁻¹</td>
</tr>
<tr>
<td>RVF-MVG, s⁻¹</td>
</tr>
<tr>
<td>AC-MVG, s⁻¹</td>
</tr>
</tbody>
</table>

*\( P < 0.01 \) compared with CP patients or normal subjects; †\( P < 0.01 \) compared with normal subjects (ANOVA).

Analysis was of subjects in sinus rhythm only; patients with atrial fibrillation were rejected. VE-MVG in RCM patients (n=13) was lower compared with CP patients (n=7) and normal subjects (3.0±1.2 vs 4.8±0.9 and 4.7±0.8 s⁻¹, respectively; \( P < 0.01 \)). IR-MVG was positive in RCM patients compared with CP patients and normal subjects (0.8±0.4 vs −1.0±0.6 and −0.4±0.3 s⁻¹, respectively; \( P < 0.01 \)). RVF-MVG was lower in RCM patients compared with CP patients and normal subjects (2.1±0.7 vs 8.2±1.6 and 3.7±1.4 s⁻¹, respectively; \( P < 0.01 \)).

![Figure 1.](http://circ.ahajournals.org/)

Figure 1. Comparison of Doppler MVG measurements between the study groups. MVG was taken (A) during VE, (B) during IR and RVF, and (C) during AC. ● indicates patients with sinus rhythm; ○, patients with atrial fibrillation, *\( P < 0.01 \) compared with CP or normal subjects; †\( P < 0.01 \) compared with normal subjects, by ANOVA.
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 (78%) and normal controls (49%); 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-
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myocardial or endocardial disease.33 In this study, Doppler
versely, in RCM, the LV wall is resistant to stretch due to
properties of the myocardium.19 Garcia et al 14 conducted the first
study to measure mitral annulus longitu-
dinal velocities to differentiate RCM from CP. Although
pulsed-wave DMI study to measure mitral annulus longitu-

Figure 3. Schematic diagram of early diastolic pattern of MVG
in RCM patients, CP patients, and normal subjects. Both
phases IR and RVF consist of outward motions with negative
velocities. The sign of the MVG depends on the relative fastness
of 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 5 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 interaction29 and a dissociation of intrathoracic-intracardiac pressure changes with respiration,5,6,30 both CP and RCM may have similar clinical manifestations, which are related to decreased LV compliance.31 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.32 Conversely, in RCM, the LV wall is resistant to stretch due to myocardial or endocardial disease.33 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.19 Garcia et al14 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.14 A different approach was undertaken to quantify color DMI images by our group and others.16–26,28

Findings
Conventional echocardiographic assessment allowed us to
establish the correct diagnosis in all RCM and CP patients.1–6
The evaluation of respiratory variations of Doppler blood-
flow velocities alone were inconclusive in 2 patients for
transmitral velocity pattern and in 2 patients for hepatic vein
flow. For the entire study group, the information from both
transmitral and hepatic vein Doppler blood flow assisted the
diagnosis of CP in all but one patient. This is in agreement
with Oh et al,6 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 agree-
ment with previously published data.2 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 measure-
ments 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 transmyocardial veloci-
ties 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.33,34 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-in-
tracardiac 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 thinning. Although
this was observed in all study patients, the magnitude of
IR-MVG was relatively low compared with other analyzed

Figure 3. Schematic diagram of early diastolic pattern of MVG in RCM patients, CP patients, and normal subjects. Both phases IR and RVF consist of outward motions with negative velocities. The sign of the MVG depends on the relative fastness of subendocardial or subepicardial velocities; it is positive if subendocardial velocities move faster and negative in the opposite scenario.

Graph showing the relationship between transmitral peak E-wave, E-wave deceleration time, and RVF-MVG.
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,29,34 reduces late diastolic blood inflow to the LV,35 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

**Figure 4.** The relationship between LV posterior wall thickness and MVG as measured during (A) VE, (B) IR, (C) RVF, and (D) AC. A shows a linear regression analysis for the RCM group ($r=-0.75; P<0.001$). Dotted lines indicate the 95% predictive interval.

**Figure 5.** The relationship between RVF-MVG and (A) peak E-wave and (B) E-wave deceleration time.
TABLE 4. The Role of Doppler MVG in Distinguishing Different Myocardial/Pericardial Disease

<table>
<thead>
<tr>
<th></th>
<th>VE(+)</th>
<th>IR(−/+</th>
<th>RVF(+)</th>
<th>AC(+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic cardiomyopathy</td>
<td>↓</td>
<td>No data</td>
<td>↓</td>
<td>No data</td>
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<tr>
<td>Dilated cardiomyopathy</td>
<td>↓</td>
<td>↓</td>
<td>N</td>
<td>↑/↓</td>
</tr>
<tr>
<td>“Young” hypertrophic cardiomyopathy</td>
<td>↓</td>
<td>No data</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>“Old” hypertrophic cardiomyopathy</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>RCM</td>
<td>↑</td>
<td>(+)</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>CP</td>
<td>N</td>
<td>↑</td>
<td>(−)</td>
<td>↑</td>
</tr>
</tbody>
</table>

N indicates normal; ↓, decrease in MVG compared with normals; ↑, increase in MVG compared with normals; (+), positive MVG; (−), negative MVG; “Old,” 46–70 years; and “Young,” 18–45 years.

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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Circulation. 2000;102:655-662
doi: 10.1161/01.CIR.102.6.655
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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