Left Ventricular Regional Wall Stress in Dilated Cardiomyopathy

Wataru Hayashida, MD, Toshiaki Kumada, MD, Ryuji Nohara, MD, Hitoshi Tanio, MD, Masashi Kambayashi, MD, Noboru Ishikawa, MD, Yasuyuki Nakamura, MD, Yoshihiro Himura, MD, and Chuichi Kawai, MD

Left ventriculography with simultaneous pressure micromanometry was performed in 11 normal control subjects and 17 patients with dilated cardiomyopathy (DCM). Left ventricular silhouettes in the right anterior oblique projection were divided into eight areas, and regional wall stress was computed by Janz’s method in each area excluding the two most basal areas. Wall stress was higher in DCM patients than in control subjects ($p<0.01$). The percent area changes from end diastole to end systole in each area were lower in DCM patients than in control subjects (mean for six areas, $22\pm14\%$ versus $54\pm9\%$, respectively, $p<0.01$), but the coefficient of variation for the percent area changes in the six areas of the left ventricle in DCM patients was greater than that in control subjects (32±17\% versus 15±4\%, respectively, $p<0.01$), indicating regional differences in hypokinesis. There was a significant negative correlation between end-systolic regional wall stress and percent area change ($r=-0.60$ to $-0.86$, $p<0.05$) in each area. Thus, excessive regional afterload may play an important role in causing regional hypokinesis in DCM. (Circulation 1990;82:2075–2083)

Diffuse hypokinesis of the left ventricular wall motion has been reported in patients with dilated cardiomyopathy (DCM). However, recent studies on DCM with the use of left ventricular cineangiography or radionuclide ventriculography suggest that left ventricular wall motion is not always diffusely hypokinetic and that regional differences in the degree of hypokinesis are frequently present. In clinical settings, patients with segmental wall motion abnormality may have better global left ventricular function and better prognosis than patients with diffuse wall motion abnormality. Thus, the importance of estimating left ventricular regional wall dynamics in patients with DCM has been emphasized.

Because DCM is a degenerative disease of the myocardial tissue, impaired myocardial function may result from histological changes in the myocardium. On one hand, the important role of wall stress in the progression of decompensation was recently suggested in DCM. An increase in wall stress is known to reduce myocardial fiber shortening and increases in left ventricular wall stress have been reported in DCM. Therefore, increased regional wall stress may contribute to the cause of regional wall motion abnormality. However, little is known regarding “regional” wall stress and its effect on “regional” wall motion in different regions of the ventricle in DCM, although Pouleur et al reported a relation between regional wall stress and myocardial relaxation in coronary artery disease.

Recently, Janz proposed a method for estimating regional wall stress, and this method seems to be useful for angiographic data processing. To investigate left ventricular regional wall stress and its relation to regional wall motion abnormalities in DCM, we analyzed left ventricular angiographic data and calculated left ventricular regional wall stress using Janz’s method.

Methods

Subject Population

This study consisted of 11 normal control subjects and 17 patients with DCM. All subjects underwent diagnostic cardiac catheterization. The normal subjects underwent catheterization to evaluate chest discomfort (nine subjects) or electrocardiographic abnormalities in exercise testing (six subjects). None had 1) significant valvular or congenital cardiac disease, 2) history of myocardial infarction, 3) coronary artery lesions (all subjects had normal coronary arteriograms and negative ergonovine tests), or 4) abnormal left ventricular pressure, end-diastolic volume, or ejection fraction. All were diagnosed as having atypical chest pain. The 17
patients with DCM were diagnosed by the criteria of the National Study Group of Idiopathic Cardiomyopathy of Japan19 and the report of the WHO/ISFC Task Force on the definition and classification of cardiomyopathies.20 Left and right ventricular endomyocardial biopsy samples were obtained from all patients with DCM. Biopsy specimens were obtained from the posterior wall of the left ventricle and the right side of the interventricular septum. The histopathological findings included disarrangement and degeneration of myocardial fibers, scarcity of myofibrils, nuclear changes in myocardial fibers, interstitial edema, and fibrosis, which were compatible with DCM.21 None of the patients with DCM had left bundle branch block, mural thrombi, or coronary artery lesions except for one patient with 50% stenosis in the middle portion of the right coronary artery. Only one patient had slight mitral valve prolapse but no mitral regurgitation. Informed consent was obtained from each patient, and no complications occurred as a result of the study.

Cardiac Catheterization

Diagnostic cardiac catheterization was performed through the percutaneous femoral approach with the subjects in the fasting state, 30 minutes after oral premedication with 5 mg diazepam. All other medications were withheld at least 24 hours before cardiac catheterization. All subjects were in normal sinus rhythm. First, right heart catheterization was performed using a Swan-Ganz catheter (7F). Cardiac output was measured by the thermodilution method. Left heart catheterization was then conducted by use of a high-fidelity catheter-tipped transducer with side holes (8F, Millar Instruments, Houston).22 Before measurement, a gain amplitude of 100 mm Hg for the catheter-tipped transducer was matched to that for a fluid-filled pressure transducer. Any baseline shift of the catheter-tipped transducer signal was corrected by simultaneous pressure recordings from the catheter-tipped transducer and the fluid-filled transducer. After aortic and left ventricular pressures were obtained, left ventriculography was performed. Coronary angiography was conducted by the Judkins technique after left ventriculography. In patients with DCM, endomyocardial biopsy was also performed after coronary angiography.

Ventriculographic Image Acquisition

Biplane left ventriculography was performed (while subjects held their breaths at end inspiration) in the 30° right anterior oblique (RAO) and the 60° left anterior oblique (LAO) projections at 60 frames/sec; 35–45 ml nonionic contrast solution was injected at the rate of 10–15 ml/sec. With a Millar"s catheter-tipped transducer with side holes, left ventricular pressure was recorded simultaneously on an Electronics for Medicine VR-12 (Pleasantville, N.Y.) and on a magnetic tape recorder with cine markers during left ventriculography. Magnification and peripheral distortions of ventriculographic images were corrected by using a calibration grid positioned at the level of the left ventricle.

Left ventricular endocardial and epicardial surfaces in the RAO projection were digitized manually frame by frame in one cardiac cycle. The end-diastolic frame was determined as the frame closest to the beginning of the rise of left ventricular pressure where the first derivative of left ventricular pressure (dP/dt) became zero. The end-systolic frame was determined as the frame closest to the time of 20 msec preceding the left ventricular peak negative dP/dt.23 Determination of the epicardial surface was sometimes difficult because of its poor contrast to the surroundings, especially in the anterobasal portion of the ventricle. Therefore, we selected subjects whose left ventricular endocardial and epicardial surfaces could be completely and easily distinguished. Ectopic beats and postextrasystole beats were excluded. Patients with a marked, abrupt fall in the left ventricular pressure due to negative intrathoracic pressure during inspiration were also excluded. Thus, only patients with normal beats and stable left ventricular pressure during left ventriculography were selected for the analysis of left ventricular wall stress in the present study. No patients had pericardial effusion, thickening of the pericardium, or marked right ventricular hypertrophy that may obscure the epicardial surface of the left ventricular wall in the RAO projection. We also reviewed the LAO projection cine films, and we found that there were no remarkable rotatory changes along the long axis of the left ventricle that significantly affected the quantitative analysis of wall motion in the RAO projection. The intraobserver variability of the ventriculographic data acquisition was 4.2%, and the interobserver variability between the two independent observers was 5.4% with regard to digitized areas, indicating good reproducibility of the measurement.

Regional Wall Motion Analysis

A long axis of the left ventricular silhouette was determined by joining a line from the midpoint of the aortic valve plane to the farthest portion of the apex. The left ventricular cavity was divided into eight areas by the long axis and three perpendicular short axes at equal intervals (Figure 1). The area method may underestimate wall motion of the posterobasal regions that contain the mitral valve plane. Therefore, the two basal areas (areas 1 and 8) were excluded.17 Each area was computerized and smoothed by the method of Savitzky and Golay.24 The difference between the smoothed and the raw values was 3.8% in the present study. Percent area change was derived as follows: Percent area change is equal to (end-diastolic area minus end-systolic area) multiplied by 100 divided by end-diastolic area. To evaluate the degree of regional difference in percent area change, coefficient of variation (CV) of the percent area changes was derived in each subject as follows: CV(%) is equal to standard deviation divided by mean value of percent area change.
multiplied by 100. As a parameter for shortening velocity, the first derivative of area (dA/dt) in an absolute value that was normalized by end-diastolic area was calculated and plotted against regional wall stress.

**Regional Wall Stress Computation**

We used the modified Janz's method to estimate regional wall stress in six areas (Figure 1). In each area, a line (L1) was joined between two intersecting points where two neighboring short axes crossed the endocardial surface. Then, the second line (L2) was joined perpendicularly to L1 at each of these intersecting points, and the third line (L3) was joined between two intersecting points where the two L2s crossed the epicardial surface. The cavity area (Ac) was defined as the area surrounded by the long axis, L1, and two neighboring L2s. The wall area (Aw) was defined as the area surrounded by L1, two neighboring L2s, and L3. Regional wall stress was calculated by multiplying the left ventricular pressure by the ratio of cavity area to wall area. The calculated stress values were smoothed using the same technique as for the area calculation described above. The long axis of the ventricular silhouette in the RAO projection may not be an axis of symmetry of the ventricle. We reviewed the biplane data, and reconstructed the three-dimensional "true" ventricular long axis from the two projected long axes of the RAO and LAO ventricular silhouettes. The angle of deviation between the "true" ventricular long axis and the RAO plane was proved to be relatively small (mean angle: control subjects, 4.7° and DCM patients, 4.1°). Therefore, we considered that the long axis in the RAO projection approximately represented the axis of symmetry of the ventricle. Regional mean wall thickness was derived as a mean for the distance between epicardial and endocardial contours of each area.

**Statistical Analysis**

Values are expressed as mean±SD. The statistical comparison was performed with an analysis of variance. Linear regression analysis was used to assess the relation between end-systolic regional wall stress and percent area change in each area. A probability value less than 0.05 was considered significant.

**Results**

Hemodynamic and volumetric parameters are summarized in Table 1. In DCM patients, cardiac index and ejection fraction were lower than those in control subjects, and left ventricular end-diastolic pressure, end-diastolic volume, and end-systolic volume were greater than those in control subjects. There were no significant differences in age, heart rate, and left ventricular peak systolic pressure between control subjects and DCM patients.

**Figure 1. Illustration of methods.** Left ventricular cavity was divided into eight areas by one long axis and three perpendicular short axes at equal intervals. Two most basal areas were excluded. Representative example of calculating regional wall: Regional wall stress=P×(Ac3/Aw3), where P is left ventricular pressure, and Ac3 and Aw3 are area 3 cavity area and wall area, respectively. A1 to A8 are regional areas. L1, L2, and L3 are lines joined for the determination of cavity and wall areas. See text for details.
Table 2. Regional Wall Stress, Area Change, and Wall Thickness

<table>
<thead>
<tr>
<th>Area</th>
<th>Control (n=11)</th>
<th>DCM (n=17)</th>
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<tr>
<td></td>
<td>Stress (kdyn/cm²)</td>
<td>Area change (%)</td>
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<tr>
<td></td>
<td>ED</td>
<td>ES</td>
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<tr>
<td>2</td>
<td>38±17</td>
<td>143±42</td>
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<td>174±70</td>
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<td>7</td>
<td>47±22</td>
<td>213±74</td>
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Coefficient of variation 15±4 32±17

DCM, dilated cardiomyopathy; ED, end diastole; ES, end systole; wall thickness, regional mean wall thickness; stress, regional wall stress; r, correlation coefficient of the relation between ES regional wall stress and percent area change in each area of DCM; coefficient of variation, coefficient of variation for percent area change values of six areas of the left ventricle.

*p<0.01 vs. control subject; †p<0.05 vs. control subject.

Percent Area Change

Percent area change in each area was significantly reduced in DCM patients compared with that in the control subjects (Table 2). Values for percent area change ranged from 38% to 71% (54±9%) in control subjects and from 0.5% to 50% (22±14%, p<0.01 versus control subjects) in DCM patients. Among the six areas of the ventricle, there were no significant differences in the mean value for percent area change in control subjects and in DCM patients (Table 2). However, the coefficient of variation of percent area changes was significantly higher in the DCM than in control group (32±17% versus 15±4%, p<0.01, Table 2), indicating considerable variations in regional hypokinesis in DCM.

Regional Wall Stress and End-Systolic Stress-Shortening Relation

Representative tracings of regional stress of anterior (area 2) and inferior (area 6) walls in a control subject and a DCM patient are shown in Figure 2, with left ventricular pressure tracings. Regional wall stress is higher in the DCM patient than in the control subject at a given level of left ventricular pressure (Figure 2, Table 2), and the elevated wall stress tends to be sustained during late systole in DCM patients. Wall thickness was less in the DCM than in the control group for each area and was least in the apical area for both the DCM and the control groups (Table 2). Wall thickening was also decreased in DCM patients.

Figure 3 shows the regional wall stress-area loops for one cardiac cycle in the same control subject and DCM patient as in Figure 2. Stress-area loops for the DCM patient were positioned upward and to the right of those for the control subject. Linear relations were observed between regional wall stress and area during late phase of systolic period. The slope of the best-fitted regression line was obtained as an index to
Regional wall stress–area relations for one cardiac cycle in the same control subject and patient as in Figure 2. Linear relations were found between stress and area during the late phase of systolic period, and slopes (s) for best-fitted regression lines of these relations were calculated in each case. Slope (s) for the dilated cardiomyopathy (DCM) patient was less steep than that for the control subject in each area, suggesting decreased regional myocardial contractility.

In areas 2 and 6, this slope was less steep in the DCM patient than in the control subject.

Instantaneous regional wall stress–shortening velocity relations during systole (from end diastole to end systole) for the same control subject and DCM patient as in Figure 2 are shown in Figure 4. In the DCM patient, dA/dt was markedly reduced throughout systole; during early ejection period, dA/dt did not increase (area 6) or even decreased (area 2).

Although there were considerable variations in percent area change, a significant negative correla-

![Figure 3](image)

**FIGURE 3.** Regional wall stress–area relations for one cardiac cycle in the same control subject and patient as in Figure 2. Linear relations were found between stress and area during the late phase of systolic period, and slopes (s) for best-fitted regression lines of these relations were calculated in each case. Slope (s) for the dilated cardiomyopathy (DCM) patient was less steep than that for the control subject in each area, suggesting decreased regional myocardial contractility.

![Figure 4](image)

**FIGURE 4.** Instantaneous regional wall stress–velocity relations during systole (end diastole to end systole) in the same control subject and patient as in Figure 2. First derivative of area (dA/dt) as an absolute value, which was normalized by end-diastolic area (EDA), was plotted against wall stress. In the dilated cardiomyopathy (DCM) patient, dA/dt was markedly reduced. Onset of ejection is indicated by arrowheads. Regional shortening velocity did not increase during early ejection in the DCM patient, suggesting decreased regional myocardial performance.
tion was observed between end-systolic regional wall stress and percent area change in each area in the DCM patients \((r = -0.60\) to \(-0.86, p<0.05, \text{Table 2})\). Representative examples of the end-systolic regional wall stress–percent area change relation in areas 2 and 6 are shown in Figure 5. Areas in the control subjects were positioned upward and to the left of this relation.

**Discussion**

Impairment of left ventricular systolic function and dilatation of the ventricle are characteristic features of DCM. The present findings that the cardiac index and ejection fraction were significantly reduced and left ventricular end-diastolic volume was greater in patients with DCM than in normal subjects (Table 1) is consistent with previous results. The reduced systolic function despite the increased preload suggests decreased contractility of the left ventricle. In addition to the decrease in overall systolic function, regional wall motion evaluated by percent area change was also decreased, and the coefficient of variation of percent area change was significantly higher in DCM patients than in the normal control subjects (Table 2). Thus, in DCM, considerable variations occur in regional hypokinesis, and this is supported by previous findings.

Several mechanisms for the regional wall motion abnormality in DCM have been proposed. First, some patients with DCM have left ventricular mural thrombus or left bundle branch block, both of which may cause regional wall motion abnormalities. But, we did not include patients with such abnormalities. Second, in DCM autopsy and endomyocardial biopsy results have proved the presence of interstitial fibrosis in the left ventricle, and the severity of interstitial fibrosis correlates with the degree of left ventricular dysfunction. In addition, a degenerative change of the myocardial cell itself can also lead to left ventricular dysfunction. Therefore, histological changes of myocardial tissue should involve wall motion abnormality in our cases.

Third, afterload reduction by vasodilators can improve left ventricular pump function in DCM; the improvement is primarily due to the decrease in left ventricular wall stress. The present data showed that wall stress in DCM patients is significantly increased in the entire left ventricular wall and that percent area change correlated inversely to end-systolic regional wall stress in each area of the left ventricle (Figure 5). An inverse relation between fiber shortening and stress is established, and hence, the increase in regional afterload, which could cause afterload mismatch, may account for the hypokinetic wall motion in DCM. Important determinants of the increase in end-systolic regional wall stress are both the depressed contractility of myocardium and the changes in left ventricular geometry. Depressed contractility of left ventricular wall may be caused by the impaired contractile property of individual myocardial fiber and the decrease of the number of fibers. In a whole left ventricle, the slope of the late systolic stress–volume relation is reported to be proportional to that of the end-systolic pressure–volume relation (end-systolic elastance), and the decrease in the slope reflects the decrease in myocardial contractility. As shown in Figure 3, linear relations, similar to the result of Pouleur et al., were observed between regional wall stress and area in a control subject and a DCM patient, and the slope of the relation in a DCM patient was less steep than that in a control subject. In addition, regional shortening velocity was markedly reduced throughout systole in the DCM patient, and the stress-velocity loop was located below and to the right of that in the normal control subject (Figure 4), which is consistent with observations by Gault et al., who suggested the decreased contractility in DCM. Furthermore, re-
regional shortening velocity did not increase (or decreased in some regions) during early ejection in DCM, suggesting that myocardium could not generate enough force to accelerate the shortening velocity against increasing wall stress. Acceleration of the initial impulse of the ventricular force and ejection fraction in the early one-third ejection phase are reduced when ventricular function is impaired. Thus, these data support the present findings that strongly suggest that regional myocardial contractility is reduced at least in some of the regions with hypokinesis. The changes in left ventricular geometry observed in our DCM patients can be characterized as a cavity dilatation that was disproportionate to wall thickness (Table 2), which resulted in an increase in wall stress. Despite evidence for the depressed contractility in DCM, developed systolic tension and regional work were not decreased in some regions of the left ventricle (area 2, Figure 3). This may indicate preserved myocardium in such regions. In fact, papillary muscles from the failing human heart show an ability to generate isometric tension to the same level as those from normal heart. Thus, from these findings, one can speculate that remodeling of the left ventricle produces excessive afterload, which results in the decrease of regional wall motion, which is regional afterload mismatch.

Some limitations should be mentioned in the present study. First, Janz's method was derived with the assumptions of 1) neglecting shear stress, inertial forces, and other surface pressure, and 2) uniform wall thickness for a reference region. This method provides no information on the contributions of elastic, viscous, hydrostatic, and contractile components of stress, and it does not characterize the variation of stress through the wall. Therefore, the calculated stress value is considered to be an average value at some point within the wall and may not estimate the actual tension that is generated in the direction of the dominant fiber. In four of our 17 DCM patients, the estimated wall stress during diastole was greater than the end-systolic wall stress in the control subjects (Figure 2). The distribution of stresses across the ventricular wall is not uniform, and circumferential wall stress is reported to be maximal at the midwall or endocardium, where the imposed stress may be greater than the average stress estimated. High levels of stress may be expected to interrupt coronary perfusion of the ventricular wall. However, coronary flow has been reported to be generally normal at rest in DCM, and none of our coronary cineangiograms showed any interruption of the washout of contrast medium injected into the coronary arteries, suggesting that the calculated wall stress may not be correct. Both marked dilatation of the cavity and thinning of the ventricular wall in DCM may lead to much greater values for the ratio of cavity area to wall area in the equation of Janz compared with actual differences between end-systolic pressures in the control subjects and the diastolic pressure in DCM patients.

Therefore, at present, we cannot fully exclude the overestimation of wall stress by Janz's method.

Another possible explanation is as follows. The calculated circumferential wall stress may have approximated the true stress, but myocardial perfusion may still have been maintained despite the high diastolic stress. The essential differences between end systole and end diastole are differences of ventricular pressure and wall thickness, and these differences remain even if the wall stress is identical in both phases. During systole, left ventricular intramyocardial pressure (which is determined primarily by the ventricular pressure) is greater and ventricular wall thickness increases, with both of these changes having a compressive effect on the intramyocardial vessels and interrupting coronary perfusion. During diastole, on the other hand, the intramyocardial pressure is lower, the left ventricular wall is relaxed, and the wall is thinner. In such a situation, the diastolic wall stress is determined primarily by the passive stress-strain relation that reflects myocardial diastolic properties, that is, wall stiffness or compliance. An increase in circumferential wall stress will cause changes in the strain acting in a circumferential direction in the ventricle and lead to secondary deformation or the myocardial tissues that may impose compressive forces on the coronary vessels. In DCM, however, the degenerative changes of the myocardium result in a marked increase in passive myocardial stiffness, which causes the stress-strain curve to become steeper. As a result, the myocardial strain or deformation becomes smaller relative to the greater increment in wall stress. Hence, in DCM, the compressive forces on the intramyocardial coronary vessels may not be so strong as might be expected from high wall stress so that coronary perfusion is preserved during diastole. One experimental study has shown that myocardial blood flow was not decreased in the failing left ventricle, although the diastolic circumferential wall stress seems to be higher than in the normal ventricle. This hypothesis, however, requires further confirmation. Despite these limitations, the validity of Janz's method has been confirmed by a comparison with finite element models, and regional stress values calculated by this method distinguished ischemic regions from the normal regions in a recent study in coronary artery disease. In addition, the simplified form of the equation is useful for various applications. Therefore, this method is considered to be warranted in clinical investigations. Second, there is no precise method for the analysis of left ventricular wall motion at present. In clinical practice, however, a simple, but reliable, method for regional wall motion analysis is required, and the area method has been proposed to be best for this purpose. Therefore, this method was used in the present study.

Analysis of left ventricular regional wall motion combined with that of regional wall stress has impor-
tant clinical implications. One of the regional wall motion abnormality in DCM seems to be due to regional afterload mismatch. Therefore, regional function in the hypokinetic areas where excessive wall stress is imposed is expected to be improved by vasodilators.

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**KEY WORDS**  • dilated cardiomyopathy  • regional wall stress  • regional wall motion  • afterload mismatch
Left ventricular regional wall stress in dilated cardiomyopathy.

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Circulation. 1990;82:2075-2083
doi: 10.1161/01.CIR.82.6.2075

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1990 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/82/6/2075

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