Variability in the measurement of regional left ventricular wall motion from contrast angiograms


ABSTRACT Four types of variability affecting quantification of regional wall motion from contrast left ventriculograms (LVgrams) were studied. These included beat-to-beat variability in 24 LVgrams, intraobserver and interobserver variability in 20 LVgrams, and study-to-study variability in serial LVgrams of 21 patients with stable coronary artery disease. Motion was measured at 100 equidistant chords perpendicular to a center line drawn midway between the end-diastolic and end-systolic contours and normalized for heart size. Variability was computed as the absolute difference between observations. Beat-to-beat, intraobserver, and interobserver variability at the 100 chords were similar, averaging 14%, 14%, and 17%, respectively, of the mean motion in 64 patients with normal ventriculograms. Study-to-study variability was significantly higher, averaging 30% of mean normal motion, but was reduced when regional motion was calculated as the mean motion of chords within a region of interest. Variability peaked at the apex. Realignment to correct for cardiac rotation significantly increased variability. Investigators whose methods of wall motion analysis rely on identification of the apex as a landmark should be aware of this source of potential variability and error.


IT HAS LONG BEEN KNOWN that coronary artery stenosis results in abnormal regional left ventricular wall motion.1 Early studies in which wall motion was gauged subjectively were hampered by large interobserver variability that resulted in poor reproducibility of results.2-4 More recently, quantitative methods of measuring regional wall motion have been developed. With these methods, wall motion abnormalities in patients with coronary artery and valvular disease have been measured and related to the site and severity of coronary disease, to the amount of fibrosis in infarcted myocardium, and to the development of congestive heart failure.5-14 The reproducibility or variability in motion measurements by the various quantitative methods, however, has not yet been determined. Knowledge of variability is necessary to gauge the significance of measured abnormalities in wall motion and of changes observed in serial studies performed to assess progression of disease or response to a therapeutic intervention.

Therefore, our study was performed to determine the magnitude of beat-to-beat, interobserver, intraobserver, and study-to-study variability in motion measurement.

Methods and materials

Patient selection. Intraobserver, interobserver, and beat-to-beat variability were studied in the ventriculograms of patients who underwent cardiac catheterization at the University of Washington Hospital between 1976 and 1980 and who were diagnosed as having coronary artery disease. Angiograms were selected for study if they were of good technical quality and were filmed with the patient in the right anterior oblique projection.

Study-to-study variability was examined in 21 patients with stable coronary artery disease. Twelve of these patients had undergone two cardiac catheterizations 18 months apart in a study of the effect of aspirin and dipyridamole on progression of coronary artery stenosis, which was quantified by a method previously described.15 These 12 patients were selected for the study group because (1) in both studies they had a normal sinus beat not following a premature contraction of adequate quality for tracing, (2) none of them had had a myocardial infarction or cardiothoracic surgery or had suffered sudden death in the interim, and (3) none had coronary arteries with lesions that progressed or regressed significantly, i.e., changed from or to a critical stenosis (defined as minimum cross-sectional area of 0.5 mm2 or less), tripled the calculated resistance of conductance across the stenosis, or changed more than 45% in minimum cross-sectional area. The other nine patients in whom study-to-study variability was examined had undergone cardiac catheterization twice to assess progression of symptoms but had no infarction or significant change in coronary artery disease in the interim, change being defined as subjectively assessed progression to or regression from a critical stenosis producing 80%
or more diameter reduction. None of the 21 patients had a change in heart rate of more than 30 beats/min or in ejection fraction of more than 20% in the two studies.

The patients with normal ventriculograms were selected by reviewing the records of all patients who underwent cardiac catheterization at the University of Washington Hospital or Seattle Veterans Administration Hospital between 1975 and 1981 and who were found to have no significant coronary artery stenosis. Significant coronary stenosis was defined as a 50% or more diameter reduction. Patients were excluded if they had valvular or congenital heart disease, a history of myocardial infarction, thoracic surgery, an abnormality of electrical conduction other than first-degree atrioventricular block, or had suffered sudden death. Sixty-four patients comprised the "normal" group, and the values from this group were used to define the normal mean and SD for left ventricular function.

**Angiography and wall motion analysis.** Coronary angiography was performed with the Judkins technique with hand injections of meglumine diatrizoate (Renograin). Left ventriculograms were performed with a pigtail catheter in the right anterior oblique position with a power injection of 40 to 70 ml meglumine diatrizoate at 12 to 20 ml/sec, and were recorded on 35 mm cine film. During ventriculography a timing strip recorded the electrocardiogram and marked the timing of each cine frame. A grid filmed at the level of the patient's heart was used to correct for distortion and magnification. In the laboratory, the cine film images were projected and the frame containing the earliest well-opacified sinus beat not following a premature ventricular contraction was selected for study. The end-diastolic endocardial contour was hand-traced from the frame nearest the peak of the R wave on the electrocardiogram. The end-systolic contour was traced from the frame at which, by visual inspection, the left ventricular volume reached a minimum. The end-diastolic and end-systolic contours were entered into a PDP 11/45 computer with the use of an X-Y digitizer. Further processing of data was performed with specially written programs.

A center line was constructed by the computer midway between the end-diastolic and end-systolic contours (figure 1, A). One hundred equidistant chords were drawn perpendicular to the center line, extending from the end-diastolic to the end-systolic contour (figure 1, B). The length of each chord was the motion of the corresponding point on the left ventricular contour. To adjust for differences in heart size, the shortening fraction (SF) at each chord was calculated as

\[ SF = \frac{\text{Chord length (cm)}}{\text{End-diastolic perimeter (cm)}} \times 100 \]

This normalization factor, the perimeter of the left ventricular contour traced from the angiogram, was selected for the following reasons. First, a linear measure was needed to yield a linear equivalent of the ejection fraction and to eliminate the need to correct for magnification; second, this factor reflected the size of the heart; and third, normalization by the end-diastolic perimeter resulted in a lower SD for the motion value in patients with no coronary artery disease and in increased ability of regional wall motion measurements to distinguish the wall motion in these patients from that in patients with coronary artery disease. Since it is a ratio, the shortening fraction is expressed in dimensionless SF units.

**Variability studies.** To determine intraobserver variability, the ventriculograms of 20 patients with coronary artery disease were traced twice by the same experienced technician. A minimum of 7 days lapse between tracings of the same ventriculogram to ensure that the memory of the first tracing would not influence the second tracing.

To determine interobserver variability, the 20 ventriculograms used for the intraobserver variability study were traced by different experienced technicians. In measuring interobserver and intraobserver variability the same angiographic frames were traced in both studies.

Beat-to-beat variability was determined from 24 ventriculograms in which two normal sinus beats were sufficiently well opacified to be traced. In 23 of the 24 patients two consecutive beats were traced, and in one patient beats 3 and 6 were traced. For this part of the study the beats were traced by the same observer on the same or on consecutive days for consistency.

Study-to-study variability was measured in the 21 patients with stable coronary artery disease. Two patients had isolated stenosis of the left anterior descending coronary artery (LAD), nine patients had isolated stenosis of the right coronary artery (RCA), and eight patients had both. As in the beat-to-beat variability study, the same observer traced both ventriculograms of each patient consecutively so that each pair would be interpreted consistently.

Variability was calculated as the SDs of the two observations and the two were compared by one-way analysis of variance.

**Effect of realignment on variability.** Realignment was performed to correct for overall rotational motion of the heart. With the use of previously digitized end-diastolic and end-systolic contours, the computer drew a long axis from the middle of the aortic valve to the apex, defined as the point furthest from the midaortic valve. The long axes of the two contours were superimposed, while keeping the distance between the midpoints of the aortic valve in the two contours constant. The angle through which the long axis was rotated during superimposition was determined and the variability in this rotational angle between and within observers, between beats, and between serial studies, was calculated as the absolute difference between observations.

Motion at each of the 100 chords was then measured by the center line method described above. Interobserver, intraobserver, beat-to-beat, and study-to-beat variability were calculated as for nonrealigned data. The significance of differences between the variability of realigned vs nonrealigned data were assessed by paired t-test.

**Variability in regional wall motion.** For the purpose of assessing the relationship between coronary artery disease and ventricular function, we measured wall motion in the region supplied by the coronary artery being studied. The measurement of motion in regions of the ventricle has been shown to better separate patients without those with coronary artery disease than measurement of motion at individual chords. Normal motion, however, varies in magnitude in different regions of the ventricle (figure 1, B). To make comparisons between different regions the values for motion must be comparable. Therefore, we converted the SFs into units of normal SDs from the normal group mean (figure 1, C). To do this, the means and SDs for motion at each chord, designated \( M_1, M_2, \ldots, M_{100}, SD_1, SD_2, \ldots, SD_{100} \), were calculated in the coronary artery disease patients. Then, for each chord, with a shortening fraction SF, the standardized value \( Z_i \) was calculated as

\[ Z_i = \frac{(SF_i - M_i)}{SD_i} \]

where \( Z \) is expressed in SDs. This standardization enables comparisons between different regions of the same heart and between different hearts.

The region of the ventricular wall in which motion was affected by stenosis of each coronary artery was defined in 62 patients with isolated significant stenosis of the LAD and 46 patients with isolated stenosis of the RCA who had no history of thoracotomy or congenital or valvular heart disease. Myocardial infarction was present in 32 of the LAD stenosis patients and in 21 of the RCA stenosis patients. The LAD and RCA regions were
defined as those in which the motion of patients with isolated LAD or RCA stenosis was significantly hypokinetic (p < .05, one-way analysis of variance) compared with motion in the normal group (figure 2). The LAD territory extended from chord 10 to 66, numbering clockwise from the anterior aortic valve, and the RCA territory extended from chord 51 to 80. In patients with stenosis of both the LAD and RCA, the overlap region was arbitrarily halved, and the LAD and RCA territories were assigned chords 10 to 58 and 59 to 80, respectively. In normal patients there were small regional deviations from normal motion that we considered to be "noise" in the motion measurement. To eliminate this noise motion was measured only in the most severely hypokinetic chords in the LAD and RCA territories. That is, the computer selected the region within the LAD or RCA territory in which the length was set at 50% of the length of the artery territory and that yielded the most severely hypokinetic value for the mean motion of chords within the region. Thus, in patients with single-vessel LAD disease, for example, the length of the region was 28 chords. The mean motion of chords within each hypokinetic region was calculated and used as the measure of regional wall motion abnormality.

**Results**

**Normal motion.** In the normal group of 64 patients the SFs of individual chords averaged 3.80 units, ranging

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**FIGURE 1.** Center line method of analyzing regional left ventricular wall motion. A. End-diastolic and end-systolic endocardial contours with the center line drawn midway between the contours. B. One hundred chords were constructed perpendicular to and evenly spaced along the center line. The chords were numbered consecutively beginning at the anterior edge of the aortic valve and proceeding clockwise around the circumference of the left ventricle. The length of each chord is the extent of motion of the corresponding point on the ventricular contour. C. Wall motion in a patient (solid line) is compared with the normal group mean ± SD for motion at each chord. D. Wall motion of the same patient (solid line) plotted in SDs from the normal mean (horizontal dashed line). This patient had right coronary artery occlusion, inferior hypokinesia and, anterior hyperkinesia.
Variability in measuring motion of individual chords. Variability in the measurement of changes between beats in the same ventriculogram averaged 0.51 ± 0.25 SF (SD) units and ranged between 0.32 and 0.90 SF units (figure 3), with the peak variability occurring at the apex. When compared with the magnitude of normal motion at each chord, beat-to-beat variability averaged 14.2 ± 7.6% of normal mean motion (range, 7.9% to 28.5%; figure 4), and was highest at the apex. The end-diastolic volume fell from 75 ± 23 to 74 ± 23 ml/m² (p < .05) between successive beats, the end-systolic volume (29 ± 19 to 29 ± 19 ml) did not change, and the ejection fraction fell (63.5 ± 11.7% to 62.3 ± 11.3%, p < .02).

The magnitudes of interobserver and intraobserver variability were similar and did not differ significantly at any chord. Both interobserver and intraobserver variability were also similar to beat-to-beat variability (figures 3 and 4). Significant differences were found at 14 chords: beat-to-beat variability was lower than interobserver variability at 6 chords in the anterior wall and at 4 chords in the inferior wall of the left ventricle, and was higher than intraobserver variability at 4 chords near the apex. Intraobserver variability averaged 0.53 ± 0.39 SF units (range 0.21 to 0.85) When compared with the magnitude of normal motion, variability ranged from 7.9% to 25.1% (mean 14.0 ± 10.4%) and was highest at the apex. Interobserver

A. LAD Stenosis

B. RCA Stenosis

FIGURE 2. Wall motion in patients with isolated stenosis of the LAD or RCA compared with the mean motion of the normal group (dashed line). A. In 62 patients with LAD stenosis, hypokinesis was significant between chords 10 and 66. B. In 46 patients with RCA stenosis, hypokinesis was significant between chords 51 and 80.
variability averaged 0.66 ± 0.32 SF units (range 0.32 to 1.00) or 17.4 ± 8.1% of normal motion (range 12.1% to 24.6%). Interobserver variability was highest at the anterobasal region of the left ventricle.

Variability from study to study was considerably higher than between different observations in the same study (figures 3 and 4), even though heart rate, ejection fraction, and end-diastolic volume were similar in the two studies (table 1). Variability averaged 1.06 ± 0.42 SF units (range 0.64 to 1.99) or 30.1 ± 13.3% of normal motion (range 16.3% to 77.3%). As in the beat-to-beat and intraobserver variability studies, peak variability occurred at the apex. Study-to-study variability was significantly higher than interobserver variability at 35 chords, than intraobserver variability at 59 chords, and than beat-to-beat variability at 86 chords.

Variability after realignment to correct for cardiac rotation. Suboptimal visualization of the endocardial border may be one explanation for the high variability at the apex. However, beat-to-beat and study-to-study variability may also be due to slight changes in the rotation of the heart within the chest. Therefore, the angle of cardiac rotation and its variability were determined, and variability in motion measurement was calculated after realigning to correct for rotation.

Intraobserver, interobserver, and beat-to-beat variability in rotational angle were similar at 1.9 ± 1.5, 1.7 ± 1.5, and 1.9 ± 2.7 degrees, respectively. Study-to-study variability was 3.4 ± 2.5 degrees, a value significantly higher than that obtained for each of the other three comparisons (p < .05, one-way analysis of variance), indicating that some study-to-study variability is due to changes in cardiac rotation and that this is separate from variability in identifying and tracing the endocardial contour.

However, after realignment, intraobserver, interobserver, beat-to-beat, and study-to-study variability in

<p>| TABLE 1 | Hemodynamic measurements in serial studies of stable patients |</p>
<table>
<thead>
<tr>
<th>Study 1</th>
<th>Study 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>End-diastolic volume (ml/m²)</td>
<td>81 ± 27</td>
</tr>
<tr>
<td>End-systolic volume (ml/m²)</td>
<td>36 ± 19</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>57 ± 11</td>
</tr>
<tr>
<td>RR interval (sec)</td>
<td>0.97 ± 0.28</td>
</tr>
</tbody>
</table>

FIGURE 3. Variability in measurement of wall motion at 100 chords around the ventricle was greater between serial studies of the same patient than between different observations or beats in the same study. Motion was normalized for heart size by dividing by end-diastolic perimeter and was expressed in SF units.

FIGURE 4. Variability in measurement of wall motion was highest at the apex, but fairly uniform elsewhere in the ventricle, when compared with the magnitude of normal motion at each chord. Here beat-to-beat, intraobserver, interobserver, and study-to-study variability are plotted as a percentage of mean normal motion.
measuring regional wall motion increased at 80%, 66%, 92%, and 72% of chords, respectively, compared with the variability of nonrealigned data (figure 5). The increases were significant at multiple chords along the anterior and inferior walls. Study-to-study variability increased significantly at the fewest chords, and even decreased significantly at 3 apical chords. These data suggest that realignment to correct for cardiac rotation produced reduction in apical variability, but at the cost of extensive significant increases in variability along the anterior and inferior walls.

**Variability in measuring regional motion.** Study-to-study variability in regional wall motion was 0.84 ± 0.65 SDs in the LAD territory, and 0.60 ± 0.40 SD in the RCA territory. For comparison, study-to-study variability was also calculated for the 100 chords in units of SDs from normal. As would be predicted mathematically (see Appendix), the average variability of individual chords was greater than the variability of mean chord motion in the region of interest (figure 6).

**Discussion**

The assessment of any new method of measurement should include evaluation of its accuracy as well as of its usefulness as a tool. In measuring left ventricular wall motion from contrast angiograms, accuracy cannot be determined because there is no accepted method for tracking endocardial motion in man. In fact, due to endocardial infolding during systole it is impossible to establish a one-to-one correspondence between points on the endocardial contour at end-diastole and points on the end-systolic contour. Therefore, the methods used to analyze wall motion actually model rather than measure the contraction of the left ventricle. For these reasons, the reliability of motion measurement must be evaluated by determining the reproducibility, rather than the accuracy, of results.

In this study we found that the magnitude of variability was least between different beats traced by the same observer and between repeated studies by the same observer, slightly higher between studies by different observers, and highest between serial studies on stable patients even though tracings were by the same observer.

Beat-to-beat variability could have been caused by contrast-induced vasodilation, which lowers end-systolic volume, but studies have shown that a significant change from the preinjection volume does not occur until the seventh beat after injection. Beat-to-beat variability can also be due to an inadvertent Valsalva maneuver by the patient, which may have occurred in our study and caused the decrease in end-diastolic volume. A third possible cause is intraobserver variability.

In measuring interobserver and intraobserver variability, the same angiographic frames for end-diastole and end-systole were traced in both studies. Thus, our variability data are measurements of the reproducibility in identifying and tracing the endocardial contour from a projected contrast ventriculogram. However, in the beat-to-beat and study-to-study comparisons, the selection of the end-systolic frame may account for some variability because the time of minimum calculated volume may not correspond exactly to end ejection, defined as aortic valve closure, due to sensitivity to slight variations in measuring cavity area. Indeed, full assessment of regional wall motion abnormality requires frame-by-frame analysis because of the asynchrony in the regional contraction that is normally present and accentuated by coronary artery disease.

Beat-to-beat, study-to-study, and intraobserver variability were higher at the apex than elsewhere on the ventricular contour. This may be due to difficulty in visualizing the apex, which is occasionally more poorly opacified than the base, rather than intrinsic variability in apical motion, since studies in which other imaging modalities, such as radionuclide angiography or two-dimensional echocardiography, were used have not measured a higher ratio of SD to mean at the apex than elsewhere in the left ventricles of normal patients. Since the magnitude of motion at the apex is low and variability there is high, the reliability of motion measurement is poorer there than in the other regions of the ventricle. This may influence the results when wall motion is measured by methods that rely on identification of the apex to construct their coordinate systems. Also, motion at the apical region must be almost dyskinetic to be considered abnormal. In contrast, interobserver variability was significantly higher at the anterobasal wall, probably because this region is often obscured by rib margins or by a partially opacified coronary artery.

Another reason for the increased variability in apex measurements may be change in rotation of the heart between different beats and between serial studies. However, when the end-diastolic and end-systolic endocardial contours were realigned to correct for this overall cardiac motion, variability increased significantly over a large region of the anterior and inferior walls. Realignment decreased variability significantly at only 3 chords at the apex in the study-to-study comparison, even though it had the greatest variability in rotational angle. This suggests that variability in cardi-
FIGURE 5. For legend see opposite page.
ac rotation is responsible for some of the study-to-
study variability in motion at the apex. However, due
to the uncertainty in identifying and tracing the apical
to the long contour, with the resulting variability in constructing
the long axis and hence in determining the angle of
rotation, realignment increased the magnitude of in-
traobserver and interobserver variability along extensive sections of the anterior and inferior walls. These
data reinforce the conclusion that the apex is an unre-
liable landmark and that its use as one adversely affects
the reproducibility of motion measurements.

There are many possible explanations for the higher
variability between serial study results. In our stable
patients the severity of coronary artery stenosis, heart
rate, end-diastolic volume, and ejection fraction did
don't differ significantly between the two studies, and
none had evidence of myocardial infarction in the in-
term. However, other variables such as film quality, position of patients, heart rate, hydration, blood pres-
sure, level of sympathetic stimulation, silent focal in-
farctions, development of collaterals or hypertrophy,
drug therapy, and heart size may differ between stud-
ies. In addition, a transient ischemic episode, perhaps
due to a platelet clot or coronary artery spasm even
hours before catheterization, may result in persistent
regional dysfunction. The severity of disease may
also affect the variability of repeated measurements of
left ventricular function. Our results underline the
importance of assessing the significance of changes in
regional function measured during serial studies, such
as before and after an event or a therapeutic interven-
tion, along with changes in a control group. Also,
evaluation of changes in individual patients should be
done cautiously.27

Jeppson et al.27 discussed the problem of regression
toward the mean, the tendency for improvement to
appear on follow-up study due to statistical unlikeli-
hood that the same sample will show severe abnor-
mality more than once. We avoid this problem by com-
paring motion in the most abnormally contracting region
in the first study with motion in the most abnormally
contracting region in the second study, keeping the
length of the region constant. The location of the re-
gion varied in our stable patients by only 5 ± 7 chords,
but the lack of anatomic landmarks in the left ventricle
makes it impossible to assign the same chord number
to a hypokinetic region in both studies anyway. This
method of computing regional motion by averaging the
standardized motion of chords in the region of inter-
est enables comparisons between different regions of the
same heart and between different hearts.

Our results agree with those of most earlier studies
of variability in measuring regional motion. Chaitman
et al.2 also found that intraobserver variability is less
than that between observers. Clayton et al.28 found that
variability was least between beats, moderate between

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observers, and highest between serial studies. Sigel et al.29 found significant interobserver and intraobserver variability most frequently at the apex, but they also reported that the magnitude of variability depended on the method used to analyze wall motion. Only McAnulty et al.30 found almost no significant variability between observers, but they measured the circumference of the aokinetic region rather than extent of contraction.

In summary, we have measured the variability in the measurement of regional wall motion from contrast ventriculograms. Our results show that study-to-study variability is significantly greater than interobserver, intraobserver, and beat-to-beat variability. Variability at the apex is high, in part because of variability in cardiac rotation. However, realignment increases variability because the apex is an unreliable landmark. Motion measurements by methods that require identification of the apex as a landmark may be adversely affected.

References

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Appendix

The following is elementary but is included for the sake of clarity and completeness.

Theorem: Let \( \hat{y} = \frac{1}{k} \sum \gamma_i \) and \( \hat{x} = \frac{1}{k} \sum \chi_i \)

Then \( | \hat{x} - \hat{y} | \leq \frac{1}{k} \sum | \chi_i - \gamma_i | \)

where \( \chi_i \) is the motion measured in the first of the serial studies at each chord \( i \), \( \gamma_i \) is the motion measured at each chord \( i \) in the second study, \( |x - y| \) is the study-to-study variability in motion, \( k \) is the number of chords in the region of interest, the
expression to the left of the inequality is the variability in regional motion, and the expression to the right is the mean variability of the individual chords in the region of interest.

\[ k \cdot |\hat{x} - \hat{y}| \leq k \cdot \left( \sum_{i=1}^{k} |x_i - y_i| \right) \]  

(2)

**Proof:**

\[ k \cdot |\hat{x} - \hat{y}| = \left| \sum_{i=1}^{k} (x_i - y_i) \right| \]  

(1)

\[ \Sigma (x_i - y_i) \leq \sum_{i=1}^{k} |x_i - y_i| \]  

(3)

However \[ \Sigma (x_i - y_i) \leq \sum_{i=1}^{k} |x_i - y_i| \]  

(3)

Dividing both sides by \( k \) yields the result. Since there are cases in which \( x_i < y_i \).

Substituting (3) and (4) into (2) yields

\[ k \cdot |\bar{x} - \bar{y}| \leq k \cdot \left( \sum_{i=1}^{k} |x_i - y_i| \right) \]

(2)

where

\[ \sum_{i=1}^{k} |x_i - y_i| = k \left( \frac{1}{k} \cdot \sum_{i=1}^{k} |x_i - y_i| \right) \]  

(4)
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