Changes in Left Ventricular Wall Motion After Coronary Artery Bypass Surgery: Signal or Noise?

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SUMMARY We evaluated changes in ventricular wall motion after surgery by comparing smoothed, filtered measurements of regional percent shortening (RPS) from right anterior oblique ventriculograms in 37 patients before and after surgery. After surgery there was a significant \((p < 0.05)\) decrease in the number of regions with hypokinetic wall motion. The distribution of RPS values was also different \((p < 0.005)\). However, the mean value of RPS for the surgery group as a whole was not significantly altered. These data were contrasted with RPS data from 11 control patients, who were each studied twice but did not have surgical intervention. Similar analysis of the control group did not show any significant change between studies in the number of hypokinetic regions, and the distributions of RPS for the first and second angiograms were not different. We found a 10.3% absolute mean change in repeated measurements of RPS in the control group.

We conclude that significant changes occurred after surgery that were not evident in the control group, and the amount of variability in repeated measurements of RPS suggests that analysis should be applied to group rather than individual data.

QUANTITATIVE ANALYSIS of ventricular angiograms has been used to assess changes in ventricular wall motion after coronary bypass grafting. Such investigations have addressed several pitfalls related to pre- and postoperative comparisons of ventriculographic data: (1) Postoperative ventriculograms should be obtained sufficiently late after surgery so that effects attributed to increased postoperative catecholamine levels could be excluded.1-5 (2) Postoperative ventriculograms should be obtained from a patient population that is not biased by an excessive proportion of patients with recurring symptoms. (3) Regional wall motion should be analyzed because regional function may change even if global function does not.6-9

Because random variation has been observed in serial comparisons of ventricular function in the absence of any therapeutic intervention,2, 8-11 this additional issue should be considered. Because the magnitude of this variability appears to be substantial, conclusions about postoperative changes may be susceptible to errors caused by regression toward the mean.12 This type of error can result when there is sufficient variability in the data and when only initially abnormal segments are analyzed. In such circumstances, it is difficult to know whether improvement in an initially depressed region is the therapeutic benefit of coronary surgery or simply follows from the fact that with measurements that are not highly reproducible, there is a very slight chance that the same region would be classified abnormally low twice in a row.

We performed this study to evaluate the effects of coronary artery surgery on left ventricular wall motion after considering the effects of variability upon the actual measurements themselves. First, we studied differences between measurements of wall motion obtained from ventriculograms in 11 patients who had no significant medical or surgical intervention between the two ventriculograms. Then, we analyzed differences in measurements of wall motion from ventriculograms performed on 37 patients before and after coronary artery bypass surgery. Trends in the surgical group were compared with the presence or absence of such trends in the control group. Statistical tests that would not be influenced by regression toward the mean were used.

Methods

Patient Populations

The control group consisted of 11 patients with coronary artery disease who had neither a significant change in clinical status nor a surgical intervention between the ventriculographic studies. The repeat studies were performed either because the initial coronary arteriograms were technically unsatisfactory or the patient chose not to have surgery and later changed his mind. In addition to the lack of historical evidence of a change in the patient's clinical course, we also checked to ensure that none of these patients sustained a documented myocardial infarction or a noticeable change in their resting ECGs between the left ventriculographic studies. Two of the 11 patients had prior coronary artery surgery, but both angiograms used in this study were obtained more than 6 months after surgery. The interval between studies in this group was 1-9 months (mean 4.4 months).

The surgical population was selected by reviewing

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preoperative and postoperative ventriculograms of 216 patients randomly selected from a group of 729 patients who agreed before surgery to undergo postoperative ventriculography regardless of the presence or absence of postoperative symptoms. Thirty-seven patients had adequate preoperative and postoperative ventriculographic data (normal sinus beats occurring at least two beats after an ectopic beat and complete ventricular opacification throughout the cardiac cycle). When the study group was compared with the larger group of patients in whom postoperative ventriculograms were obtained, there was no difference in the presence or absence of symptoms after surgery. There were 35 men and two women in this subgroup, mean age 58 years (range 37-74 years). Twenty-four (65%) patients had documented myocardial infarction before surgery. The interval between surgery and the postoperative angiogram was 5-19 months (mean 7 months). No patient in either group had evidence of valvular disease.

Data Acquisition

Ventriculography was performed before coronary angiography. Digitalis, diuretics, nitrates and propranolol were discontinued at least 24 hours before catheterization. Single-plane, 30° right anterior oblique ventriculograms were recorded on cine film at 60 frames/sec. One observer traced frame-by-frame contours of the ventriculographic silhouettes throughout systole and diastole for each beat that was analyzed. To minimize subjective bias in the tracing of the postoperative ventriculogram for a patient, outlines were obtained in preoperative and postoperative batches, with the patient order randomized in each batch. Heart rate and left ventricular end-diastolic pressure (LVEDP) were measured immediately before ventriculography.

A radial coordinate system was superimposed on each ventriculographic contour. From a reference point (defined as the midpoint of the long axis from the apex to the midpoint of the aortic valve plane), radii were drawn to the endocardial border at 5° increments around the contour. Radii intersecting the ventriculographic silhouette in regions corresponding to the aortic and mitral valve planes were excluded from further analysis.

To reduce random variation and redundancy in the data, we averaged the values for five contiguous radii corresponding to a 20° arc, or region, on the endocardial border. Thus, we obtained averaged radii for three regions on the inferior wall (80-150°), two regions at the apex (155-200°), and six regions on the anterior wall (205-345°) (fig. 1).

Ventricular volume was calculated for each silhouette by applying Simpson's rule. Because the magnitude of change in radial length is sensitive to the definition of end-diastolic and end-systolic, the frame-by-frame sequence of volume data was then smoothed with a nine-point parabolic filter (fig. 2). End-diastolic and end-systolic contours were selected as the frames with the maximum and minimum smoothed volumes, respectively. We calculated ejection fraction in the usual manner (ejection fraction = 1 - end-systolic volume/end-diastolic volume). Similarly, we smoothed the time sequence of values for regional radial lengths. Using the end-diastolic and endsystolic frames selected for the ejection fraction calculation, we calculated the percent shortening for each region (RPS) (percent shortening = 1 - end-systolic length/end-diastolic length).

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\text{FIGURE 1. The radial reference system used to identify endocardial segments at 5° increments on a left ventricular silhouette. Shown are the 11 regions generated by averaging five contiguous radii. For the region between 330° and 345°, only four radial lengths were used. The area between 345° and 80° was not analyzed because it corresponded to the location of the mitral and aortic valves.}
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\text{FIGURE 2. The time sequence of left ventricular volume measurements throughout systole and diastole. Shown are the parabolically smoothed values (points) generated by using a nine-point filter on the original data (open circles).}
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The distributions of values of RPS were plotted for each set of angiograms in each patient group. Separate plots for regions on the anterior, apical and inferior walls were also obtained. The distributions in these histograms were smoothed with a low-pass filter to remove high-frequency noise without disturbing the underlying shape of the distribution. Then we used a Kolmogorov-Smirnov test to test the null hypothesis that there was no significant difference between distributions of RPS values for each group. For the control patients, this comparison was between the distributions of RPS obtained on the first and second left ventriculographic studies. For the surgical group, the comparison was between the distributions obtained on the preoperative and postoperative ventriculograms.

To characterize regional motion of the surgery and control patients as normal or abnormal, we used values of RPS obtained in a similar manner from 32 normal patients. The normal patients were studied to evaluate chest discomfort syndromes and had no electrocardiographic, hemodynamic or angiographic evidence of heart disease. For each region of the ventricle shown in figure 1, threshold values 2 standard deviations above and below the mean normal value of regional percent shortening were obtained. These thresholds were used to classify regional wall motion in the control and surgery populations as hyperkinetic, normal or hypokinetic. We evaluated changes in classification between the two ventriculograms for each group by the McNemar test using the null hypothesis that no significant change occurred in the total number of hyperkinetic, normal and hypokinetic regions between studies. Essentially, the McNemar test compares the number of abnormal regions that become normal to the number of normal regions that become abnormal. In the presence of random variability and absence of a systematic effect, these two numbers should be nearly equal.

To determine if changes in regional wall motion might be associated with changes in global parameters, the significance of differences in heart rate, end-diastolic pressure and ejection fraction between study groups was evaluated using Welch's adaptation (for the case of unequal variances) of the conventional t test.

**Results**

**Control Patients**

The mean ± sd for heart rate, ejection fraction and LVEDP for each group are listed in Table 1. The significant levels were obtained using a paired t test to evaluate changes between the first and second angiograms within each group. For the control group, no significant changes were noted between the two studies for any global variable. Although the means did not change, there was an average absolute study to study change of 9 beats/min in heart rate and 3.5 mm Hg in LVEDP.

Figure 3A presents the distributions of RPS in the control patients. In this case, the Kolmogorov-Smirnov test indicated that there was no significant difference between these two distributions. Fourteen of 22 regions that had abnormally low values of RPS on the initial angiogram were classified as normal on the second angiogram (fig. 4A). On the other hand, 18 of 92 regions initially classified as normal were classified as hypokinetic on the second angiogram. Using the McNemar's test, we found that these changes in classification were not significant. None of the regions originally classified as hyperkinetic showed a change in classification on the second study, while two of the normal regions were reclassified as hyperkinetic. Because of the small numbers involved, McNemar's test was not performed on these data.

We found substantial variability in individual measurements of RPS, although the distributions for the entire group were not different between the two ventriculograms. Figure 5 is a histogram of the measured change in RPS for 121 regions in the 11 control patients. The mean change in RPS (−0.33%) for the control group as a whole was not significantly different from zero, but the mean absolute change was 10.3%. The standard deviation of this distribution was 13.0%, indicating that approximately one-third of the regions had changes in RPS greater than that value. Using a chi-square test, we found that regions with increased RPS in the second angiogram were associated (p < 0.02) with patients in which the heart rate also increased and vice versa. We also found that regions with increased RPS in the second ventriculogram were significantly (p < 0.001) related to patients with decreased LVEDP and vice versa. However, changes in heart rate and changes in LVEDP were independent of each other.

**Surgical Group**

The mean values for ejection fraction, heart rate and LVEDP before and after surgery in the surgery group are presented in Table 1. Ejection fraction did not change significantly, but heart rate increased and end-diastolic pressure decreased significantly after surgery. The mean absolute change in heart rate was 14 beats/min and the mean absolute change in LVEDP was 3.7 mm Hg.

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<th>TABLE 1. Measurements of Global Variables for the Two Study Groups</th>
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Values are mean ± sd.

Abbreviation: LVEDP = left ventricular end-diastolic pressure.
In the group as a whole, 89 of 94 grafts (95%) were patent at the follow-up study. The occluded grafts occurred in five patients with additional functioning grafts. Two surgical patients had documented perioperative infarcts and one patient had a documented infarction approximately 2 months after surgery but before the follow-up angiogram. Two of the occluded grafts occurred in patients who sustained a myocardial infarction between ventriculographic studies.

Figure 3B presents the preoperative and postoperative distribution of RPS for all segments in the surgical group before and after surgery. In contrast to the findings in the control population, the Kolmogorov-Smirnov test indicated that these two distributions were significantly different (p < 0.005). Figure 4B illustrates the change in pre- and postoperative classification of regional wall motion. Fifty-seven of 107 regions classified as hypokinetic before surgery were normal after surgery, whereas 30 of 276 regions classified as normal before surgery were classified as hypokinetic after surgery. Again, in contrast to the findings for the control group, these changes in classification were significant (p < 0.005, McNemar's test). Of the 24 regions classified as hyperkinetic before surgery, 19 were classified as normal after surgery, whereas 12 regions classified as normal before surgery were classified as hyperkinetic after surgery. These changes were not significant.

The increase in the number of normal regions after surgery comes primarily from the inferior and anterior walls. Figure 6 shows the distributions of RPS before and after surgery for different areas of the ventricular chamber. The Kolmogorov-Smirnov test indicates that, for the inferior and anterior walls, the postoperative distributions of RPS were significantly (p < 0.05) different from the preoperative distributions. However, at the apex, the hypothesis that the distributions were similar could not be rejected.

The mean change in RPS (0.11%) for the surgical group as a whole was not significantly different from zero. However, as in the control group, there was considerable variability in repeated measurements of RPS; the mean absolute change was 10.9%. Using a chi-square test, we found relationships between changes in RPS and changes in heart rate and LVEDP that were similar to those in the control group. Increased contraction was dependent upon increased

**Figure 3.** Superimposed histograms represent distributions of regional percent shortening for all regions of the ventricle for 11 patients examined during a mean interval of 4 months with no surgical intervention between studies, and 37 patients examined before and a mean of 7 months after surgery. The solid line represents the first or preoperative examination. The dashed line represents the second or postoperative study. The p values were obtained using a Kolmogorov-Smirnov test.

**Figure 4.** The number of regions classified as as hypokinetic, normal and hyperkinetic, based on the initial angigrams and follow-up. The number of regions changing from one classification to another is shown by the arrows between groupings.
heart rate ($p < 0.01$) and decreased LVEDP ($p < 0.02$), although changes in heart rate were independent of changes in LVEDP.

We wondered if perioperative infarction and/or the presence of occluded grafts could have influenced the results of the McNemar's test. Therefore, we subdivided the surgical patients into two subsets: those with patent grafts and no complications (31 patients) and those with occluded grafts and/or perioperative or early postoperative infarction (six patients). After identifying these subsets, we performed a McNemar's test for the hypokinetic regions. In the case of uncomplicated surgical patients, 51 abnormal regions became normal and 25 normal regions became normal ($p < 0.01$). For the complicated surgical patients, six abnormal regions became normal and five normal regions became abnormal. These changes for patients with an occluded graft or intrastudy infarction were not shown to be significant by McNemar's test.

The differences in changes of regional ventricular function between the surgical and control groups do not appear to correlate with changes in global physiologic measurements (table 1). Using the Welch test, the mean changes between angiograms in ejection fraction and LVEDP were not shown to be different in the surgery and control groups. The study to study change in heart rate was significant ($p < 0.05$) between the two groups.

**Discussion**

We found limited but significant improvement in regional ventricular contraction in the patients who underwent coronary artery bypass surgery. These changes were not found in patients in the control group. We also found substantial variability in sequential measurements of RPS in individual ventricles. This variability made assessment of changes in a specific patient extremely difficult.

Quantitative and qualitative studies of preoperative vs postoperative comparisons of regional wall motion have produced disparate results. The variability in repeated measurements could contribute to this disagreement. First, factors such as sympathetic stimulation (and enhanced contractility) in the early postoperative period imply that the timing of the postoperative ventriculogram may influence the results of preoperative vs postoperative comparisons. Second, analyzing unreproducible data when improvement is only expected in abnormally low regions is a problem. Because our ventriculograms were obtained late after surgery, our concerns in this study focused on the latter problem. In this instance, imprecise data must be analyzed in such a way that the tendency of data to regress toward the mean does not influence the outcome of the data analysis.

The magnitude of the problem of regression toward the mean is illustrated in figure 4B. Fifty-three percent (57 of 107) of the abnormally low regions in the surgical group crossed a threshold set at 2 standard deviations below the normal mean. This magnitude of improvement could be interpreted to be a result of surgery, and if a paired $t$ test is performed on the pre-
postoperative changes of the 107 presurgically hypokinetic regions, one might conclude that there is significant improvement ($p < 0.001$).

The contradictory nature of this approach becomes evident if the control group (no surgery between angiograms) is also analyzed using a paired $t$ test on the initially abnormal regions. In this instance (fig. 4A), 63% (14 of 22) of the hypokinetic regions in the first ventriculograms improved. A paired $t$ test of the changes from the first to the second angiogram shows an even greater significance ($p < 0.001$) than that in the surgical group. This conclusion is contradictory because there were more abnormal regions found in the second angiogram than in the first despite statistical evidence that the abnormal regions improved.

This paradox is resolved because the mean absolute change in RPS for the control group is 10.3%. Such variability could easily push borderline regions back and forth across a threshold value. If a region were abnormal by chance the first time, it is highly unlikely that it would be classified abnormal on the second measurement. The use of thresholds to classify normal and abnormal measurements limits interpretation of our data. A region close to the threshold value but with little actual change in function could easily change classification if measurements are imprecise. Alternatively, a poorly functioning region could improve substantially without crossing a threshold.

We and others\textsuperscript{4-6} believe that it is inadvisable to evaluate specific patients because of the difficulty of reducing noise in the individual measurements. Our efforts to reduce noise in this study included filtering and smoothing contour sequences throughout a heartbeat. These procedures should reduce errors due to incorrect definition of end-diastole and end-systole\textsuperscript{17, 28} as well as contour-to-contour noise. When single frames are traced at points subjectively judged to be end-diastole and end-systole, even greater variability could result. Still another source of error results from interobserver variability in tracing ventriculographic contours.\textsuperscript{27, 28} To minimize this error, one observer traced all the ventriculographic contours.

We suspect that some of the variability comes from repositioning errors and physiologic changes. There were significant study-to-study changes in heart rate and LVEDP in the surgical group but not in the control group. In both surgical and control groups there was a dependence between changes in RPS and changes in heart rate and LVEDP. Controlling for these changes to reduce variability in an individual patient is a formidable task.

However, because the noise process affects the measurements of the first and second angiograms of the control and surgical groups in a similar manner, one can circumvent problems due to variability by looking at the group distributions as a whole. In the absence of any systematic effect, one would expect the “before” and “after” distributions to have a similar number of abnormal regions even if the same regions were not classified abnormal each time. If, in addition to the random variation, there is also an underlying trend, then the distributions would not be expected to be similar. Such a trend could explain why, in the absence of significant differences in the control population, there were 25% fewer abnormal (hypokinetic) regions (107 vs 80) after bypass grafting. These findings, based upon group analysis of the surgical and control groups, appear to be more consistent with what might be expected than those obtained when analyzing only initially abnormal regions. In agreement with some earlier quantitative studies,\textsuperscript{4-7, 20} we found significant improvement for a subgroup of patients with patent grafts.

The possible amount of improvement in a comparative study is determined to some extent by the mix of patients. In our case, 26.3% (107 of 407) of all regions were abnormal before surgery. Because 65% of the patients had documented infarctions, it is not known what fraction of the abnormal regions represent areas of scar tissue and which regions could be revascularized. Therefore our overall finding that 6% (27 of 407) of all regions changed classification from hypokinetic to normal may reflect on our study population.

We concluded that despite substantial variability in measurements of ventricular function, one can see group effects in a surgical but not in a control population. The duration of the observed improvement in regional motion and the relationship of such improvement to longer life expectancy have not been investigated. Moreover, analysis of changes in individual patients cannot be reliably performed unless the variability in measurements of regional wall motion can be substantially reduced.

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