Determinants of Reversible Asynergy
The Native Coronary Circulation

By Vidy A. Banka, M.D., Monty M. Bodenheimer, M.D., and Richard H. Helfant, M.D.

SUMMARY
To evaluate the influence of the native coronary circulation on the reversibility of asynergy, ventriculograms before and after sublingual nitroglycerin were performed in 51 patients with coronary artery disease and asynergy. The severity of stenotic lesions and caliber of the distal coronary vessels were determined by comparison with external catheter tip diameter corrected for magnification. Of 42 asynergic zones associated with ≥90% proximal coronary occlusion, 27 (64%) were akinetic or dyskinetic while only 11 of 38 zones (29%) with <90% occlusion showed akinesis (P < 0.005). Twenty-six of the 38 asynergic zones (69%) with <90% occlusion were reversible in contrast to 19 of the 42 zones (45%) with ≥90% occlusion (P < 0.05). Coronary collaterals were observed in 23 of 42 (55%) zones with ≥90% occlusion in contrast to only 11 of 38 zones (29%) with <90% occlusion (P < 0.05). Of the zones with both ≥90% occlusion and collaterals, 74% were reversible, in contrast to only 11% without collaterals (P < 0.001). Of the asynergic zones without collaterals, 63% with <90% occlusion were reversible in contrast to only 11% with ≥90% occlusion (P < 0.001). Pathologic Q waves were associated with 24 of 42 zones (57%) with ≥90% occlusion compared to only nine of the 38 zones (24%) with <90% occlusion (P < 0.01). The presence of Q waves was associated with a significant decrease in the incidence of reversibility regardless of the degree of coronary occlusion. Excluding the asynergic zones with either collaterals or Q waves, 79% with <90% occlusion were reversible in contrast to only 37% with ≥90% coronary occlusion (P < 0.05). In contrast, the caliber of the distal vessel could not be correlated with either the severity of asynergy or the presence of collaterals and was similar in both reversible and irreversible asynergic zones.

In summary, ≥90% proximal stenosis is associated with severe asynergy which is less likely to be reversible compared to asynergy associated with <90% coronary occlusion. In the presence of ≥90% occlusion, coronary collaterals are associated with a significantly higher incidence of reversible asynergy and thus appear to serve a protective function. However, the caliber of the distal vessel per se does not affect the severity or reversibility of asynergy.

RECENT STUDIES have shown that the residual contractile ability of asynergic zones can be detected by performing ventriculography before and after administration of sublingual nitroglycerin,1,6 epinephrine7 or a postextrasystolic beat.8 Asynergic segments which demonstrate improved contraction after nitroglycerin exhibit similar improvement after an aortocoronary bypass grafting to the coronary artery subserving that zone.2,6 A recent study from our laboratory indicated that the presence or absence of pathologic Q waves on the surface electrocardiogram and angiographically demonstrable coronary collaterals in the corresponding asynergic zones as well as anatomic location are important factors in determining the potential for reversibility.9 The present study was undertaken to examine the effect of the severity of the proximal coronary occlusion and the caliber of the distal coronary vessel on the severity of asynergy, its potential for reversibility, and on other determinants of reversibility.

Material and Methods
Studies were performed in 51 patients undergoing cardiac catheterization for evaluation of coronary heart disease. Criteria for admission to the study were 1) asynergy on ventriculography (defined as a localized abnormality of left ventricular contraction); 2) significant (>75%) obstruction of one or more of the three major coronary arteries (left anterior descending, right, and circumflex arteries); 3) absence of other etiologic heart disease determined by cardiac catheterization. All patients were postabsorbent and premedicated with 50 mg nembutal, 50 mg demerol and 0.4 mg atropine.

Right heart catheterization was performed via an antecubital vein cutdown and left heart catheterization was done percutaneously through a femoral artery. Following measurement of left ventricular pressure (using Statham P23Db transducers) and cardiac output (dye dilution method using indocyanine green), left ventriculography (control ventriculogram) was performed in the RAO projection using 30 to 40 cc of meglumine diatrizoate (Renografin-76) injected into the left ventricle. In no case was this performed during or immediately following anginal symptoms. Four patients who developed angina prior to the control ventriculogram and required nitroglycerin were not included in the study. When asynergy was observed, nitroglycerin (gr.)
CORONARY FLOW AND REVERSIBLE ASYNERGY

1/150 sublingual) was administered 15-20 min following the initial ventriculogram. When the characteristic hemodynamic effects of nitroglycerin (TNG) were observed (fall in systolic and end-diastolic pressures and increase in heart rate), the ventriculogram (TNG ventriculogram) was repeated in the same degree of obliquity, using the same amount of contrast material and tube to table-top distance. Selective cine coronary arteriography was then performed in multiple views using the Judkins technique. Cines were taken on a 10 X 6 inch dual-field image intensifier (Siemens) at 64 frames/second using 35 mm Kodak Shellbur film. Hemodynamics were monitored and recorded on an Electronics for Medicine oscillographic recorder.

Ventriculograms were analyzed with respect to location and severity of asynergy. Location was determined according to the anatomic areas of the left ventricle perfused by each of the three major coronary arteries. The anterior wall and apical zone was defined as the "left anterior descending segment," the portion of the inferior wall between the mitral valve and posterior papillary muscle, the "right coronary segment," and the inferior wall between the posterior papillary muscle and the apex taken to be a representative portion of the "circumflex segment." The "circumflex segment" would refer to the area of the left ventricle only in the presence of right dominant coronary circulation.

The severity of the contraction abnormality of each segment was defined as follows: hypokinesis indicated diminished contraction; akinesis referred to absence of contraction and dyskinesis to paradoxical systolic expansion. Since occasional ventricular premature beats were seen in both the control and TNG ventriculograms, analysis for contraction abnormalities was limited to normal sinus beats carefully avoiding premature ventricular contractions and postextrasystolic beats.

A quantitative analysis was performed by superimposing tracings of end-diastolic and end-systolic frames using the cardiac apex to mid-aortic valve as fixed points. Hemiaxes were drawn which trisected the long axis at right angles to it. Each hemiaxis was measured and recorded as a percentage change from end-diastole to ascertain the amount of regional contraction. Qualitatively, an asynergic segment was considered to have responded following nitroglycerin when it either normalized or changed to a lesser degree of severity, e.g., a dyskinetic segment becoming akinetic, an akinetic segment becoming hypokinetic, etc. Quantitatively, an increase of greater than 10% in hemiaxis shortening of the corresponding segment was considered as an index of reversibility. Quantitative ventriculographic analysis correlated closely with the qualitative interpretations.

The severity of coronary occlusions and the caliber of the distal coronary vessels were assessed by comparing the diameter of the opacified coronary vessel with the external diameter of the catheter tip corrected for magnification. Cine coronary arteriograms were projected on a white paper (fig. 1) and the outlines of the catheter tip and each coronary vessel were drawn with a sharp pencil in end-diastolic frames both in right and left anterior oblique views (fig. 1). The outline of each coronary vessel was divided into three equal parts and the average diameter was determined for each third calibrated utilizing the catheter tip diameter corrected for magnification. The severity of the stenotic lesion was assessed by comparing its diameter with the diameter of the vessel immediately proximal to it. The obliquity in which the decrease in diameter was maximal was selected for analysis in each case. "Proximal stenoses" were considered to be those areas of narrowing which involved either the proximal or middle thirds of the left anterior descending and left circumflex arteries. In case of the right coronary artery, any occlusion proximal to the origin of the posterior descending artery was also considered proximal. For the purposes of analysis, the proximal occlusions were divided into 1) \( \geq 90\% \) (subtotal and total occlusions) and 2) \(< 90\% \) (i.e., 75-90\% occlusions).

The average caliber of the distal vessel was also determined in eight patients of comparable age and body surface area with normal ventriculograms and coronary arteriograms. The normal distal right coronary, left anterior descending, and circumflex measured \( 2.32 \pm 0.58 \) (SD), \( 1.86 \pm 0.29 \) (SD) and \( 1.92 \pm 0.52 \) (SD) millimeters respectively. The distal vessel was considered to be narrowed when its diameter was reduced by 20% compared to the normal group. Thus a diameter of \( \leq 1.16 \) mm for right coronary, \( 1.28 \) mm for left anterior descending, and \( 0.88 \) mm for left circumflex was considered abnormal. To normalize for individual variation in vessel diameter, the ratio of the caliber of the distal vessel with the vessel proximal to the stenosis was also examined.

Angiographic criteria for the presence of coronary collateral vessels were as follows: 1) direct visualization of accessory blood vessels either filling the distal segment of an occluded or severely stenotic vessel or subserving the area of myocardium that would ordinarily be supplied by the severely stenotic vessel; and 2) visualization of a coronary artery after injection of contrast material into the collateral vessel. Twelve lead electrocardiograms, performed routinely on all patients were analyzed for the presence of pathologic Q waves prior to cardiac catheterization by a staff cardiologist without knowledge of the patient. Q waves \( \geq 0.04 \) seconds duration were considered pathologic. The presence of a Q wave in lead III unaccompanied by a similar Q in aVR was not considered pathologic. Q waves in leads II, III and aVF were considered to correspond to an asynergic right coronary or circumflex segment while Q waves in leads I, aVL, V1-V4 were considered to correspond anatomically to the left anterior descending segment. Statistical data were derived using the Chi-square method.

Results

Since each ventriculogram was divided into three zones, a total of 153 segments were analyzed. One hundred twenty-two of these were subserved by coronary arteries showing \( \geq 75\% \) proximal stenosis. Of the 50 zones with \( \geq 90\% \) occlusion, 42 (84\%) showed asynergy and eight (16\%) were normal while 34 (47\%) of the 72 zones with \(< 90\% \) occlusion demonstrated normal contraction and 38 (53\%) were asynergic.

Of 80 asynergic zones, 42 were hypokinetic, 34 akinetic, and four dyskinetic. Because the number of dyskinetic segments was small and all were unresponsive to nitroglycerin, they were included in the akinetic group for purposes of statistical analysis.

I. Severity of Proximal Coronary Occlusion

A. Correlation with severity of asynergy. Table 1 demonstrates the relationship between the
severity of proximal coronary occlusion and severity of asynergy. Of the 42 asynergic zones associated with $\geq 90\%$ proximal coronary occlusion, 27 (64\%) were akinetic or dyskinetic (23 akinetic, 4 dyskinetic) and only 15 (36\%) were hypokinetic. In contrast, only 11 of the 38 zones (29\%) with $< 90\%$ occlusion showed akinesis, none dyskinesis, and 71\% exhibited hypokinesis ($P < 0.005$).

B. Correlation with Pathologic Q Waves. Pathologic Q waves were associated with 24 of the 42 (57\%) asynergic zones with $\geq 90\%$ coronary occlusion compared to only nine of the 38 zones (23.7\%) with $< 90\%$ occlusion ($P < 0.01$) (table 1).

C. Correlation with Coronary Collaterals. Table 1 demonstrates the correlation of proximal coronary occlusion with the presence of angiographically demonstrable collaterals. Twenty-three of the 42 zones (55\%) with $\geq 90\%$ occlusion were associated with coronary collaterals in contrast to only 11 of the 38 zones (29\%) with $< 90\%$ occlusion ($P < 0.05$).

D. Correlation with Reversibility of Asynergy. The

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**Table 1**

<table>
<thead>
<tr>
<th>Severity of stenosis</th>
<th>A (Severity of asynergy)</th>
<th>B (Pathologic Q waves)</th>
<th>C (Coronary collaterals)</th>
<th>D (Reversibility of asynergy)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Akinesis</td>
<td>Hypokinesis</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>$\geq 90%$</td>
<td>27 (64%)</td>
<td>15 (36%)</td>
<td>24 (57%)</td>
<td>18 (43%)</td>
</tr>
<tr>
<td>$&lt; 90%$</td>
<td>11 (29%)</td>
<td>27 (71%)</td>
<td>9 (23.7%)</td>
<td>29 (76.3%)</td>
</tr>
<tr>
<td>$P &lt; 0.005$</td>
<td></td>
<td></td>
<td>$P &lt; 0.01$</td>
<td></td>
</tr>
</tbody>
</table>

*Asynery assessed by number of asynergic zones. Numbers = number of asynergic zones.*

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*Circulation, Volume 52, November 1975*
effect of the proximal coronary occlusion on reversibility of asynergic zones is shown in Table 1D. Twenty-six of the 38 zones (69%) with < 90% coronary occlusion were reversible in contrast to only 19 of the 42 zones (45%) with ≥ 90% occlusion (P < 0.05).

E. Correlation with Reversibility in Presence or Absence of Collaterals and Q Waves.

i) Proximal coronary occlusion and collaterals. Table 2 shows the correlation of the severity of proximal coronary occlusion with reversibility of asynergy in the presence or absence of angiographically demonstrable coronary collaterals. Seventeen of the 23 (74%) asynergic zones with both ≥ 90% occlusion and coronary collaterals were reversible in contrast to only two of the 19 (11%) with ≥ 90% occlusion but without collaterals (P < 0.001). However, in the asynergic zones associated with < 90% coronary occlusion, there was no statistically significant difference in the reversibility of zones with or without collaterals. When asynergic zones without collaterals were compared, 17 of the 27 (63%) zones with < 90% occlusion were reversible, in contrast to only two of the 19 (11%) with ≥ 90% occlusion (P < 0.001).

ii) Proximal Coronary Occlusion and Pathologic Q Waves. The correlation of severity of proximal coronary occlusion with reversibility of asynergy in the presence or absence of pathologic Q waves is shown in Table 3. Thirteen of the 18 (72%) asynergic zones with ≥ 90% coronary occlusion but without Q waves were reversible in contrast to six of the 24 (25%) zones with Q waves (P < 0.005). Similarly, 22 of the 28 (79%) zones with < 90% coronary occlusion but without Q waves were reversible in contrast to only four of the ten (40%) zones with Q waves (P < 0.025). In the presence of pathologic Q waves, ≥ 90% occlusion was associated with a somewhat higher but statistically insignificant decrease in reversibility when compared to the findings in patients with < 90% occlusion.

iii) Proximal coronary occlusion without collaterals and Q waves. Figure 2 demonstrates the correlation of severity of proximal coronary occlusion with reversibility of asynergy in those zones which were associated with neither coronary collaterals nor pathologic Q waves. There were only 27 asynergic zones in this group. Fifteen of the 19 (79%) with < 90% coronary occlusion were reversible in contrast to only three of eight (37%) with ≥ 90% coronary occlusion (P < 0.05).

Table 2

Reversibility of Asynergy: Correlation with Severity of Proximal Coronary Occlusion in the Presence or Absence of Coronary Collaterals

<table>
<thead>
<tr>
<th>Asynergy</th>
<th>≥ 90% coronary occlusion</th>
<th>&lt;90% coronary occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Collat</td>
<td>No collat</td>
</tr>
<tr>
<td>Reversible</td>
<td>17 (74%)</td>
<td>2 (11%)</td>
</tr>
<tr>
<td>Irreversible</td>
<td>6 (20%)</td>
<td>17 (89%)</td>
</tr>
</tbody>
</table>

Numbers = number of asynergic zones. Collat. = collaterals.

Table 3

Reversibility of Asynergy: Correlation with Severity of Proximal Coronary Occlusion in the Presence or Absence of Pathological Q Waves

<table>
<thead>
<tr>
<th>Asynergy</th>
<th>≥ 90% coronary occlusion</th>
<th>&lt;90% coronary occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Q</td>
<td>No Q</td>
</tr>
<tr>
<td>Reversible</td>
<td>6 (25%)</td>
<td>13 (72%)</td>
</tr>
<tr>
<td>Irreversible</td>
<td>18 (75%)</td>
<td>5 (28%)</td>
</tr>
</tbody>
</table>

Number = number of asynergic zones. Q and No Q = presence and absence of Q wave.

Figure 2

Correlation of severity of proximal coronary occlusion with reversibility of asynergic zones without coronary collaterals and pathologic Q waves. Numbers within the bars indicate the number of asynergic zones.
II. Caliber of the Distal Coronary Artery

A. Correlation with Severity of Asynergy. Thirty of the 38 zones (48%) associated with a normal caliber distal vessel were akinetic while 32 of 42 (52%) were hypokinetic. Similarly, eight of the 18 (44%) asynergic zones associated with reduced caliber distal vessel were akinetic and ten (56%) were hypokinetic (table 4).

B. Correlation with pathologic Q waves. Pathologic Q waves were associated with only 21 of the 62 (34%) asynergic zones with normal caliber of the distal vessel in contrast to 12 of the 18 (67%) zones in which the distal vessel caliber was reduced (P < 0.02) (table 4B).

C. Correlation with Coronary Collaterals. Table 4C demonstrates that a reduced caliber distal vessel is associated with a somewhat higher incidence of collaterals although this did not achieve statistical significance.

D. Correlation with Reversibility of Asynergy. There was no correlation between the reversibility of asynergic zones and the caliber of the distal vessel (table 4D). Table 5 demonstrates that the caliber of the distal vessel was similar in both reversible and irreversible asynergic zones.

When the caliber of the distal vessel was normalized for individual variation, the ratio of the diameter of the distal vessel to that of the vessel proximal to the stenosis for reversible and irreversible asynergic zones was not significantly different (0.52 ± 0.04 for reversible and 0.45 ± 0.03 for irreversible).

Discussion
Since the severity of a proximal coronary occlusion is the major determinant of blood flow to the area of the left ventricle it subserves, it would be expected that a higher degree of obstruction would render the dependent areas of myocardium more severely asynergic than lesser degrees of occlusion. The present study indicates that two thirds of the asynergic zones associated with ≥ 90% coronary occlusion showed akinesis or dyskinesis in contrast to less than one third with < 90% coronary occlusion (table 1A). Conversely, 71% of the zones with < 90% occlusion were hypokinetic while only 36% with ≥ 90% occlusion exhibited hypokinesis (table 1A).

The potential reversibility of an asynergic zone is a function of the degree to which the contraction abnormality is due to chronically ischemic viable myocardium as opposed to the presence of irreversible fibrosis. In this regard, recent studies have shown that areas of asynergy which do not demonstrate residual contractile ability ventriculographically usually exhibit severe degrees of fibrosis at the time of open heart surgery. In addition, it has previously been observed that the more severe degrees of asynergy are less likely to demonstrate residual contractile ability. The present study indicates that the degree of coronary occlusion directly affects the reversibility of the corresponding asynergic zone. More than two-thirds of the zones with < 90% coronary occlusion were reversible in contrast to less than half with ≥ 90% occlusion (table 1D). The potential reversibility of asynergic zones is influenced by the presence of pathologic Q waves and angiographically demonstrable coronary collaterals. When segments without either collaterals or Q waves were considered in the present study, 79% of the zones with < 90% occlusion were found reversible in contrast to only 37% with ≥ 90% coronary occlusion (figure 2). Therefore, these findings quantitatively substantiate the importance of the severity of the coronary occlusion in determining both the severity and potential for reversibility of the corresponding asynergic zones. The methods used in this study to assess the severity of coronary occlusion are limited by several factors. An angiographic assessment of coronary obstruction has inherent limitations of X-ray distortion and magnification factors, and in addition, represents an anatomic assessment which does not provide data regarding actual blood flow. Although occasional discrepancies between the interpretation of the coronary arteriogram and the findings at postmortem examination or coronary artery surgery are generally recognized, studies have shown a good over-all correlation. An attempt was made to overcome these methodological difficulties by using an object of known external dimension, i.e., the coronary catheter tip diameter, to calculate the magnification factor. Although the catheter may not be in the same plane as

<table>
<thead>
<tr>
<th>A. Severity of Asynergy</th>
<th>B. Pathologic Q waves</th>
<th>C. Collaterals</th>
<th>D. Reversibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Akinetic</td>
<td>Hypokinetic</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Normal</td>
<td>30 (48%)</td>
<td>32 (52%)</td>
<td>21 (34%)</td>
</tr>
<tr>
<td>Reduced</td>
<td>8 (44%)</td>
<td>10 (56%)</td>
<td>12 (67%)</td>
</tr>
</tbody>
</table>

Numbers = number of asynergic zones.
the distal opacified coronary artery, the involved error of measurement should be minimal. However, the diameter of the coronary artery distal to the stenosis may occasionally appear smaller on the angiogram than is observed at the time of surgery, presumably due to low perfusion pressure. The limitations of single plane ventriculogram for assessment of asynergy are well recognized.2,9 Although the right anterior oblique view used in this study serves well for most areas of left ventricular dysfunction, it provides no information regarding the contraction abnormalities of the posterolateral wall and the interventricular septum.

The presence of pathologic Q waves on the surface electrocardiogram is generally recognized to be indicative of transmural myocardial infarction17 and correlates well with the presence of scar tissue in the corresponding zones of the left ventricle at autopsy.22 Recent studies from our laboratory have indicated that about three-fourths of patients with pathologic Q waves electrocardiographically show corresponding severe asynergy ventriculographically23 which is associated with a high incidence of irreversible asynergy.9 The present study indicated that more than one-half of of the asynergic zones having corresponding pathologic Q waves are associated with \( \geq 90\% \) coronary occlusion in contrast to less than one-fourth with \(< 90\% \) occlusion (table 1B). It is thus clear that total or subtotal coronary occlusion often leads to frank infarction and therefore these lesions are more frequently associated with more severe degrees of asynergy which tend to be irreversible (table 3). However, once the presence of a critical degree of scar tissue (as depicted by pathologic Q waves) exists, there is no significant difference in the reversibility of asynergic zones associated with \( \geq 90\% \) or \(< 90\% \) coronary occlusion (table 3).

The caliber of the coronary vessel distal to the major obstruction is an important factor in assessing the feasibility of coronary bypass surgery.18,34 The functional importance of the distal vessel per se has not been previously studied. The findings of the present study indicate that the caliber of the distal vessel per se bears no significant relationship to either the severity and potential for reversibility of asynergy or the incidence of coronary collaterals. As shown in table 5, the caliber of the distal vessel is similar in both reversible as well as irreversible asynergic zones and does not appear to be a determinant of reversibility. This observation is not surprising since the caliber of the distal vessel represents an anatomical and not a functional parameter and as previously discussed, the blood flow to the asynergic zone is determined primarily by the severity of the proximal occlusion. It was interesting, however, that reduced caliber of the distal vessel was associated with pathologic Q waves in 67% of asynergic zones (table 4B).

The coronary collateral circulation represents an additional source of blood supply to compromised areas of the left ventricle. The relationship of collaterals and asynergy has been of considerable interest.9,16,25,28 Previous studies have indicated that collaterals do not protect a patient from the actual development of asynergy.16,26,28 However, a recent study from our laboratory has shown that the presence of angiographically demonstrable collaterals does favorably affect the potential for reversibility of an asynergic zone.9 In the present study, coronary collaterals were observed in more than half of the asynergic zones with \( \geq 90\% \) coronary occlusion compared to less than one-third with \(< 90\% \) occlusion (table 1). In addition, 74% of the asynergic zones with both \( \geq 90\% \) coronary occlusion and coronary collaterals were reversible in contrast to only 11% with the same degree of coronary occlusion but without angiographically demonstrable collaterals (table 2). However, in the asynergic zones with \(< 90\% \) coronary occlusion, the presence or absence of collaterals did not affect the incidence of reversibility (table 2). These findings indicate that in the presence of severe obstruction of the native coronary circulation, angiographically demonstrable collaterals appear to provide an important additional source of blood flow necessary to maintain the potential functional viability of the jeopardized myocardium. With lesser degrees of coronary occlusion, the contribution of collateral flow to maintenance of potential viability appears to be less critical.

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References


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