The Effect of Intracoronary Injection of Contrast Medium upon Coronary Blood Flow

By Mayer Bassan, M.D., William Ganz, M.D., C.Sc., Harold S. Marcus, M.D., and H. J. C. Swan M.D., Ph.D.

SUMMARY
The changes in coronary blood flow in response to intracoronary injection of 3 ml of 76% Renografin were studied in 47 patients using the thermodilution technique for continuous measurement of coronary sinus blood flow. Within seconds after left coronary injection, an increase in coronary sinus flow began which peaked at an average of 53% above control in 5–10 seconds. There was a corresponding decrease in coronary resistance. Flow returned to control level in almost all patients within one minute of injection.

Twenty-four of 35 patients had no change in coronary sinus flow in response to right coronary injection. This can be explained by the fact that most of the venous flow from the right coronary artery returns in such a way that it cannot be measured by the coronary sinus catheter. Of the eleven patients who did show an increase, seven had angiographically documented right to left collaterals, suggesting that the increase in flow was the result of vasodilatation of the left coronary bed by contrast arriving via the right to left collaterals.

The percent changes in flow and resistance in response to left coronary injection were significantly greater in the 13 normals than in the 34 with obstructive disease of the left coronary artery (P < 0.01). Flow rose 70 ± 27% (mean ± standard deviation) in the normals versus 46 ± 25% in the patients with coronary artery disease, while resistance fell 44 ± 9% versus 33 ± 11%. The differences, however, were not sufficient for these changes to be of value in the assessment of the degree of impairment of the coronary arterial bed in the individual patient.

Additional Indexing Words: Coronary arteriography

Injection of contrast medium into the coronary arteries is a common procedure due to the widespread performance of coronary angiography. Previous authors, using electromagnetic flowprobes, rotameters, or volumetric measurements of coronary sinus flow, have demonstrated large increases in blood flow in human peripheral arteries¹ and canine coronary arteries.² ⁷ The vasodilatation resulting from the hypertonic contrast material caused increases in flow of 50–400%¹ ² ⁷ beginning within seconds after injection. Flow in the dog coronary arteries returned to control within 1–3 minutes after doses proportional to those used in human coronary angiography.³ ⁵ The single study upon human coronary arteries used the Xe¹³³ washout technique for measurement of coronary flow and found by comparison that a 7 ml injection of Renografin 76 caused a relatively modest 35% increase in myocardial blood flow.⁶ This increase was documented at the time of the first measurement, one minute after injection, and persisted at its peak value until at least seven minutes after injection. No difference in response was found between normal subjects and patients with coronary artery disease.

Because of the inability of the Xe¹³³ washout technique to measure changes in blood flow occurring within seconds, and in the face of experimental evidence suggesting that the marked increases in blood flow do occur within seconds, we chose to apply the continuous thermodilution technique⁸ to more accurately define the time course and magnitude of changes in coronary flow resulting from the intracoronary injection of contrast medium. The thermodilution technique for measuring coronary sinus blood flow is able to measure flow continuously and is sensitive to moment-to-moment changes.⁹

Furthermore, we sought to identify differences in response between patients with normal coronary arteries and those with obstructive coronary artery disease, to see if such differences might be of value in assessing the degree of impairment of the coronary arterial bed. Such a possibility has also been suggested by Gould et al.⁷ on the basis of animal studies.

Method
Forty-seven patients were studied during the course of diagnostic right and left heart catheterization and coronary

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Received August 16, 1974; revision accepted for publication October 18, 1974.
arteriography by the Judkins technique. Prior to any diagnostic coronary arterial injections the patients received 0.4 mg of atropine intravenously to prevent contrast-induced bradycardia. A special 7F thermistor catheter was introduced into the coronary sinus for measurement of coronary sinus blood flow by the continuous thermodilution technique. In 28 of the patients the thermistor was positioned close to the ostium to record total coronary sinus blood flow, while in 19 of the patients the catheter was advanced further to record great cardiac vein flow. With flow measurements stable and the patient in the supine position, a 3 ml bolus of 76% Renografin was injected into the left coronary artery over approximately five seconds. Coronary sinus flow was measured continuously until flow returned to control. Following diagnostic left coronary arteriography and an approximately ten-minute pause, the same procedure was repeated for the right coronary artery. Arterial blood pressure and the electrocardiogram were recorded continuously together with flow measurements. Measurements were made on several patients following control injection of 3 ml of 5% dextrose at room temperature. Informed consent was obtained from each patient.

Results
Of the 47 patients, 13 proved to have normal left coronary artery systems, while 34 had one or more significant (> 75% obstructive) lesions of the left system. Only one patient had isolated left circumflex disease, and he was in the group whose total coronary sinus blood flow was measured.

Left Coronary Artery Injection
All 47 patients demonstrated a marked and characteristic response to the left coronary bolus of contrast medium. Within a few seconds an increase in coronary sinus blood flow was noted, which reached its peak between 5 and 10 seconds after injection. The maximum increase in flow averaged 53% above control. The flow returned to its control value within 60 seconds in almost all patients. Figure 1 shows the record of a typical response. The left coronary injection of contrast medium induced small decreases in mean arterial pressure, averaging 5 mm Hg. There was also a small decrease in heart rate of 2–3 beats/min on the average.

For analysis, patients were divided into subgroups, depending upon whether coronary sinus or great cardiac vein blood flow was measured and whether the left coronary arterial system was normal or exhibited significant obstructive disease. Tables 1 and 2 list the changes in coronary sinus blood flow and coronary resistance (calculated as the ratio of mean arterial blood pressure and coronary sinus blood flow).

All groups showed a marked increase in blood flow and fall in resistance in response to the contrast injection. Of interest is the fact that while flow and resistance at rest were similar for patients with normal and abnormal left coronary systems, the percentage increase in flow and decrease in coronary resistance was significantly greater in the normal coronary bed. Average change in blood flow for the 13 normals was 70 ± 27% (mean ± standard deviation) vs 46 ± 25% for the 34 abnormals (P < 0.01). Differences in resistance were −44 ± 9% vs −33 ± 11% (P = 0.001).

There were no changes in coronary blood flow measured in response to injection of 3 ml room temperature 5% dextrose.

Right Coronary Artery Injection
Thirty-five patients had right coronary artery injections during continuous coronary sinus or great cardiac vein flow measurement. Twenty-four patients showed no change in flow. Eleven patients, however, showed an increase in coronary venous flow, many with a response similar to that during left coronary artery injection. Seven of these eleven (64%) had

Figure 1
Increase in coronary sinus blood flow (CSBF) from 111 ml/min to 216 ml/min eight seconds after injection of 3 ml of 76% Renografin into the left coronary artery. Flow returns to control approximately 45 seconds after injection. Changes in the T waves of the ECG follow a similar time course. One second time lines. CABP = catheter tip blood pressure.
Table 1

Maximum Changes in Coronary Blood Flow Rate

<table>
<thead>
<tr>
<th>Coronary sinus flow group</th>
<th>Great cardiac vein flow group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normals (N = 6)</td>
</tr>
<tr>
<td>Control flow (cc/min)</td>
<td>132 ± 71*</td>
</tr>
<tr>
<td>Flow after contrast (cc/min)</td>
<td>214 ± 80</td>
</tr>
<tr>
<td>Significance of change</td>
<td>P &lt; .001</td>
</tr>
<tr>
<td>Mean percent change</td>
<td>70 ± 18</td>
</tr>
<tr>
<td>Significance (normals vs CAD)</td>
<td>P &lt; .01</td>
</tr>
</tbody>
</table>

*Mean ± sd.

Abbreviation: CAD = coronary artery disease.

Table 2

Maximum Changes in Coronary Resistance

<table>
<thead>
<tr>
<th>Coronary sinus flow group</th>
<th>Great cardiac vein flow group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normals (N = 6)</td>
</tr>
<tr>
<td>Resistance (mm Hg/ml/min)</td>
<td>.83 ± .23*</td>
</tr>
<tr>
<td>Control</td>
<td>.47 ± .11</td>
</tr>
<tr>
<td>After contrast</td>
<td>P &lt; .001</td>
</tr>
<tr>
<td>Significance of change</td>
<td>−.42 ± 8</td>
</tr>
<tr>
<td>Mean percent change</td>
<td>P &lt; .02</td>
</tr>
</tbody>
</table>

*Mean ± sd.

Abbreviation: CAD = coronary artery disease.

significant filling of the left coronary artery system via collaterals from the right coronary artery. By comparison, of the 24 patients with no change in coronary venous flow, only three (13%) had right-to-left collaterals. The difference in response between the two groups is significant (P < 0.01).

Figure 2 shows an increase in coronary sinus flow from 73 ml/min to 113 ml/min after right coronary injection in a patient with a left anterior descending coronary artery totally occluded at its origin and retrograde filling of the whole left anterior descending to the obstruction by collaterals from the right coronary artery. Figure 3 shows the typical lack of response to right coronary injection in a patient with no right-to-left collaterals.

Discussion

Marked increases in human coronary blood flow — beginning within seconds and ending within one minute — caused by a direct vasodilating effect of contrast material have been demonstrated. These findings are in agreement with animal data. We used a 3 ml injection of contrast, smaller than that used in routine arteriographic injections and smaller than the 7 ml used by Kloster et al. The cause of the difference between our findings and those of Kloster et al., who found a marked increase in flow as long as seven minutes after injection, is unclear. The difference may be related to the different methods of coronary blood flow measurement rather than to the amount of contrast injected, since we studied an additional four patients with coronary artery disease following a 7 ml injection and found that flow had returned to control within one minute in all. We did not see the transient decrease in coronary flow described by some in animals immediately following injection.

It is not surprising that most of our patients showed no change in coronary sinus flow in response to right
coronary artery injection. Under normal circumstances, the contribution of the right coronary artery to coronary sinus flow is small and enters so close to the ostium that it may be missed during measurement. A number of patients did, however, show an increase in flow, and most of these had significant right-to-left collaterals visible on coronary angiography. In these cases, the measured increase in flow was presumably caused by contrast reaching the left coronary bed via the right-to-left collaterals.

We found that the increase in flow in patients with occlusive disease of the left coronary artery system was significantly smaller than that in patients with unobstructed vessels, despite the fact that resting flows were similar. This is in agreement with the demonstration by Gould et al. in dogs that the hyperemic response to intracoronary contrast is a provocative test which can reveal the hemodynamic significance of obstructive lesions not severe enough to produce changes in resting flow. The differences we found between normal and obstructed vessels, while statistically significant, were not large enough or consistent enough to serve as a basis for the independent assessment of the hemodynamic significance of angiographically demonstrated lesions in a given patient.

Our inability to achieve a clear-cut separation between normals and patients with coronary artery disease relates at least in part to the fact that coronary sinus blood flow reflects the flow in the obstructed as well as the unobstructed arteries, whereas Gould et al. were able to measure the flow in the constricted artery selectively. It is possible, however, that larger doses of contrast material might increase the flow in normals disproportionately more and thus lead to better separation from patients with occlusive coronary artery disease. In any case, information obtained from studies of coronary sinus blood flow can relate to global restriction of the left coronary artery bed only. Assessment of the functional significance of lesions in single coronary arteries will require measuring regional distribution of flow, for instance by myocardial imaging, or measuring flow in single vessels, for instance by videodensitometry.

Acknowledgment

We are indebted to Juliana Schwarz for outstanding technical assistance.

References

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M Bassan, W Ganz, H S Marcus and H J Swan

Circulation. 1975;51:442-445
doi: 10.1161/01.CIR.51.3.442

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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