Hemodynamic Changes Associated with Injection of Angiocardiographic Contrast Medium in Assessment of Valvular Lesions

By Shahbudin H. Rahimtoola, M.B., John P. Duffy, M.D., and H. J. C. Swan, M.B., Ph.D.

INJECTION of large amounts of contrast medium into the circulation for diagnostic angiocardiography has been shown to cause a significant transient increase in cardiac output (18 to 94 per cent), circulating blood volume (10 per cent), and left ventricular end-diastolic and pulmonary artery (PA) pressures. Increases in pulmonary artery, left atrial, and left ventricular end-diastolic pressures have been noted as isolated observations after angiocardiography in patients with heart disease. It is often desirable, during cardiac catheterization, to study the effects of increased cardiac output on the hemodynamics in patients with valvular heart disease.

This study was undertaken to observe the effects of angiocardiography on the dynamics of the left heart in the presence of mitral valve disease and to examine the possibility of utilizing these observations in further evaluation of the status of the mitral valve.

Material and Methods

Table 1 shows the vital statistics of 21 patients in whom cardiac output and PA wedge and left ventricular pressures were measured. Groups 1, 2, and 3 comprise patients with normal, incompetent, and stenotic mitral valves, respectively. There was surgical confirmation of the state of the mitral valve in two, two, and six patients in groups 1, 2, and 3, respectively. There was autopsy confirmation of diagnosis in two patients in group 2.

All patients underwent cardiac catheterization, including angiocardiography, for diagnostic purposes. Left ventricular and PA wedge pressures were measured with cardiac catheters and Statham strain-gauge manometers. The pressures were recorded at the same sensitivities and base lines on photographic paper at a speed of 10 cm./sec. by a galvanometer-oscillograph assembly with a Visicorder (Minneapolis Honeywell Co., Model 1012). The uniform frequency response of the system exceeds 12 cycles per second.

Cardiac output was determined by the indicator-dilution technic according to the method of Hamilton and co-workers. Indocyanine green was injected into the left ventricle; the sampling site was the femoral artery. The systems employed and the technic used have been described in detail elsewhere. In the presence of significant mitral incompetence, cardiac output determined from left ventricular dye curves may be underestimated up to 20 per cent. The time lag of the PA wedge pressure pulse was partially compensated for by transposing this pressure pulse to the left ventricular pressure pulse by a time interval such that the peak of the "v" wave intersected the descending limb of the ventricular pressure pulse at the point of equality; the diastolic filling period was measured from this instant to end-diastole. Three to six pressure pulses were analyzed from each record and the average value was used. Mean pressures were obtained by planimetry. Flow per diastolic second across the mitral valve (in groups 1 and 3) was obtained by dividing the stroke volume by the diastolic filling period.

Procedure

Prior to cardiac catheterization the patients were premedicated with a mixture of meperidine (Demerol), promethazine (Phenergan), and chlorpromazine (Thorazine) according to the method of Moffitt and associates. Before angiocardiography the patient was anesthetized with thiopental (Pentothal), given intravenously, and nitrous oxide and oxygen. Anesthesia was temporarily discontinued for approximately 30 to 60 seconds prior to angiocardiography and the patient was ventilated with 100 per cent oxygen. Angiocardiograms were made with injection of

*Cardio-Green: Hynson, Westcott & Dunning, Baltimore, Maryland.
Table 1

<table>
<thead>
<tr>
<th>Status of mitral valve</th>
<th>No. of cases</th>
<th>Severity of mitral lesions</th>
<th>Age (yr.)</th>
<th>Body surface (M.²)</th>
<th>Associated lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Normal</td>
<td>5</td>
<td></td>
<td>3-44</td>
<td>0.8 – 1.65</td>
<td>Severe aortic valve stenosis, 1 case; possible myocardial disease, 1 case; large ventricular septal defect (Qp/Qs = 3.2, 75% left-to-right shunt), 1 case</td>
</tr>
<tr>
<td>2 Incompetent</td>
<td>8</td>
<td>Severe, 6; moderate, 2</td>
<td>4-65</td>
<td>0.58 – 2.26</td>
<td>Congenital mitral incompetence, 3 cases; ruptured chordae, 1 case; moderate aortic stenosis, 1 case</td>
</tr>
<tr>
<td>3 Stenotic</td>
<td>8</td>
<td>Severe, 5; moderate, 3</td>
<td>34-61</td>
<td>1.5 – 2.02</td>
<td>Trivial mitral regurgitation, 4 cases; mild aortic valve stenosis, 3 cases; severe tricuspid incompetence, 2 cases</td>
</tr>
</tbody>
</table>

69.3 per cent aqueous solution of sodium and methylglucamine diatrizoates (Renovist) into the left ventricle in doses of 1.2 to 1.6 ml./Kg. body weight. Data on flow and pressures were obtained three times during the investigation: study period 1, patient under anesthesia immediately prior to angiocardiography; study period 2, at 2 minutes after angiocardiography while the patient was still under anesthesia; and study period 3, at 4 minutes after angiocardiography.

Results

Figure 1 demonstrates that, after angiocardiography, increased flow was accompanied by increased PA wedge pressures in a case from each group whereas a gradient at end-diastole was present only in group 3 (mitral stenosis). The patient in group 3, shown in this figure, represents the most severe case of mitral stenosis in this study. The patient in group 2 had a decrease in stroke volume at the 4-minute interval but the heart rate had increased, and the mean flow per diastolic second remained elevated. The increases in flow, pressures, and gradients after angiocardiography for groups 1, 2, and 3 are shown in table 2. Patients in group 3 had a significantly greater increase in the mean PA wedge and "v" wave pressures and mean diastolic and end-diastolic gradients compared to those of the other two groups. Three of the patients with normal mitral valve (group 1) did not have a normal left ventricle, and this may account for the large increases in PA wedge pressures in this group.

The PA wedge-left ventricle end-diastolic gradient was positive both before and after angiocardiography only in patients with mitral stenosis (fig. 2, left panel). This gradient was

![Figure 1](http://circ.ahajournals.org/)
Table 2

Increases in Flow, Pulmonary Artery Wedge Pressure and Diastolic Gradients Across the Mitral Valve after Angiocardiography*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1, normal mitral valve</th>
<th>Group 2, mitral incompetence</th>
<th>Group 3, mitral stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac output (liters/min.)</td>
<td>2.0 ± 1.6 (0.7–4.1)</td>
<td>1.1 ± 1.0 (0.1–3.5)</td>
<td>1.1 ± 0.9 (0.2–2.8)</td>
</tr>
<tr>
<td>Flow per diastolic second (ml.)</td>
<td>92.7 ± 78 (34–157)</td>
<td>.  .  .</td>
<td>58.9 ± 50.5 (20–173)</td>
</tr>
<tr>
<td>Mean PA wedge pressure (mm. Hg)</td>
<td>7.6 ± 4.2 (3.0–12.0)</td>
<td>6.3 ± 3.7 (0–12.0)</td>
<td>12.4 ± 6.3 (4.0–23.0)</td>
</tr>
<tr>
<td>“v” Wave of PA wedge pressure (mm. Hg)</td>
<td>7.2 ± 5.1 (7.0–13.0)</td>
<td>8.8 ± 5.2 (2.0–18.0)</td>
<td>19.6 ± 8.9 (9.0–36.0)</td>
</tr>
<tr>
<td>Pressure gradient: PA wedge—left ventricle mean diastolic (mm. Hg)</td>
<td>2.2 ± 2.4 (−2.0 to +6.0)</td>
<td>2.9 ± 2.6 (−2.0 to +6.0)</td>
<td>10.1 ± 3.9 (5.0–17.0)</td>
</tr>
<tr>
<td>Pressure gradient: PA wedge—left ventricle end diastolic (mm. Hg)</td>
<td>−2.2 ± 1.7 (0 to −6.0)</td>
<td>−1.5 ± 2.8 (0 to −8.0)</td>
<td>9.0 ± 2.6 (5.0–14.0)</td>
</tr>
</tbody>
</table>

*Data shown as mean ± SD with range in parentheses.
†No calculations possible.

significantly increased after angiocardiography. Four patients with a small initial gradient (1 to 5 mm. Hg) had a large increase of the gradient. In two of these four patients the diagnosis has been confirmed surgically. Included among the patients with normal mitral valve was one who had a ventricular septal defect with 75 per cent left-to-right shunt (Qp/Qs = 3.2) and a huge pulmonary and mitral valve flow; yet, despite tachycardia (and a short diastolic filling time), there was no gradient at end diastole. The patients with mitral incompetence had significant incompetence and must have had large mitral valve diastolic flows (combination of systemic flow plus regurgitant flow) but none showed a gradient at end-diastole.

There was a moderate to large mean diastolic gradient initially in five of eight patients with mitral stenosis and this increased significantly in all (fig. 2, right panel). Three patients with mitral stenosis had small gradients initially and could not be separated from patients in groups 1 and 2. They had increases of gradient after angiocardiography and two of these could be separated from patients in groups 1 and 2. The mean diastolic gradients in groups 1 and 2 both before and after angiocardiography were probably due to inadequate compensation for the time lag of the

Figure 2

Effect of angiocardiography on PA wedge-left ventricle end-diastolic (left panel) and PA wedge-left ventricle mean diastolic (right panel) gradients for patients with normal (group 1), incompetent (group 2), and stenotic mitral valves (group 3).
PA wedge pressure pulse (resulting in an overlap with mitral stenosis values of one case in the postangiographic observations).

In a hydraulic system with a fixed obstruction to nonpulsatile flow, the square root of the gradient and the mean flow across the obstruction are directly related.7 Within the limitations of applying this directly to the intact human heart, it can be seen from figure 3 that the postangiographic increases of gradient in mitral stenosis are related to increased flow. Figure 4 demonstrates that, in three patients from group 2 and three from group 3, PA wedge pressure was normal (normal mean ± 2 SD = 12 ± 4 mm. Hg)8 initially but was clearly abnormal after angiocardiography.

**Discussion**

Injection of contrast medium for angiocardiography causes a transient increase in cardiac output, heart rate, and stroke volume. The increase in cardiac output is caused by the volume of fluid injected, by systemic vasodilatation due to the effects of the contrast material on the peripheral vessels, and by an increase of blood volume due to the hyperosmotic nature of the contrast medium.1 In general, patients with mitral valve disease have a similar increase in cardiac output; in some there is no significant change. The increases in heart rate and stroke volume are very variable from patient to patient among those with mitral valve disease.

The PA wedge pressure, if technically satisfactory, reflects left atrial pressure. It is a damped, delayed version of the left atrial contour with the addition of artifact due to the motions and impacts on the wedged catheter imparted by the beating heart.9 It has been widely used to represent the left atrial pressure.10, 11 The delay averages 0.05 second10 but is very variable. We have only been able to correct partially for this delay; this might be the reason for the apparent mean diastolic gradients between PA wedge and left ventricular pressures in groups 1 and 2.

The increased circulatory blood volume after angiocardiography is probably the major determinant of the increased left ventricular end-diastolic pressure. In the absence of obstruction to left ventricular inflow, this

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**Figure 3**

*Relationship of the mean mitral diastolic flow to the square root of the PA wedge-left ventricle mean diastolic gradient before and after angiocardiography in patients with mitral stenosis.*

*Figure 4*

*Effect of angiocardiography on mean PA wedge pressure in patients with mitral incompetence (left panel) and with mitral stenosis (right panel). The high normal value is drawn in.*8

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results in an increase in the left atrial and PA wedge pressures. In addition, in mitral incompetence, giant "v" waves may be produced (these reached values of 59 and 65 mm. Hg in two of our patients). This is probably the result of the regurgitant volume entering a left atrium already distended and on the steep part of its pressure-volume curve. In the presence of mitral valve obstruction, the increase of PA wedge pressure is largely due to the increased flow across the stenotic valve (fig. 3). The pulmonary artery pressure would be expected to be correspondingly increased under these circumstances.

This increased flow is particularly useful for diagnosis in patients with small gradients initially (three in group 3) or with normal PA wedge pressures (three each in groups 2 and 3), since they developed significant gradients and increased PA wedge pressures, respectively, to an extent such that they could be differentiated from normal. The incompetent and stenotic valves were clearly differentiated from each other by the diastolic gradients.

After angiocardiography the mean PA wedge pressures were increased to high values—in four of eight patients with mitral stenosis and in one with mitral incompetence it was 35 mm. Hg or higher. This is above the value that normally may induce pulmonary edema but the fact that clinical pulmonary edema did not occur is probably due to a combination of three factors. First, the plasma osmolality is increased by an average of 9 per cent, therefore, a higher intravascular pressure would be needed to cause exudation of fluid. The osmolality is maximal at 2 minutes after angiocardiography and decreases rapidly over the next 5 to 8 minutes, after which there is a slower decrease and, even at 30 minutes, there is a significant residual increment over the base line. (The PA wedge pressure in these patients also decreases rapidly and approaches base line values at about 15 to 20 minutes.) Second, the duration of increased pressure and the initial status of the patient are apparently important. It has been shown that, in patients who do not have orthopnea at rest (all of our patients were in this category) exercise produces PA wedge pressure in the pulmonary edema range for 3 minutes without actual pulmonary edema developing. The total amount of time needed for pulmonary edema to develop in this group is not known. Furthermore, it must be remembered that contrast medium in the circulatory system is constantly being excreted by the kidneys and its effects are relatively short lived. Third, in patients with long-standing mitral disease (all but one of our patients) pathologic changes develop in the pulmonary vessels and interstitial tissue, which would hinder the development of pulmonary edema.

The circulatory changes attending the injection of angiocardiographic contrast medium provide a good opportunity for examination of the effects, on a diseased mitral valve, of higher flow rates. Exercise studies have been widely used in assessment of valvular heart disease. Exercise increases cardiac output by an increase in the heart rate and, to a lesser extent, by an increase of stroke volume whereas, after angiocardiography, both heart rate and stroke volume are increased. Exercise studies are difficult to perform in a diagnostic cardiovascular laboratory, particularly with children and uncooperative or anesthetized persons; the hemodynamic effects of angiocardiographic contrast medium provide a simple means of obtaining similar information.

Summary

Measurements of flow and pressures related to the left heart were made on 21 patients immediately prior to and at intervals of 2 and 4 minutes after angiocardiography. These patients had normal mitral valves (group 1), mitral incompetence (group 2), or mitral stenosis (group 3). There was an increase in left ventricular end-diastolic pressure accompanied by an increase in "pulmonary artery wedge" (PA wedge) pressure in all patients. Patients with mitral valve disease generally develop higher PA wedge pressures; those with mitral stenosis develop, in addition, significantly increased mean diastolic
and end-diastolic gradients across the mitral valve.

These increased gradients in mitral stenosis are due to increased flow across the mitral valve, which results from a combination of increased cardiac output and decreased diastolic filling time. Diagnostic angiocardiography affords an opportunity of observing the effects of valve lesions at a higher flow rate and is particularly useful in those patients with normal PA wedge pressure and small gradients initially.

References


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