The Effect of Intraaortic Balloon Counterpulsation on Regional Myocardial Blood Flow and Oxygen Consumption in the Presence of Coronary Artery Stenosis in Patients with Unstable Angina

David O. Williams, M.D., Kenneth S. Korr, M.D., Henry Gewirtz, M.D., and Albert S. Most, M.D.

SUMMARY To determine whether a reduction in myocardial oxygen demand or an increase in coronary blood flow or both are responsible for the salutary effect of intraaortic balloon counterpulsation (IABP) in relieving medically refractory angina, we assessed these variables in six patients in whom IABP was required for relief of myocardial ischemia. IABP decreased the rate-pressure product and aortic end-diastolic pressure, and the peak systolic aortic pressure and regional myocardial oxygen consumption declined in all but one patient. Peak and mean aortic diastolic pressures increased. Changes in regional coronary blood flow paralleled changes in peak systolic aortic pressure ($r = 0.92, p < 0.007$). Thus, relief of angina during IABP could not be ascribed to an increase in regional coronary blood flow. Reduction of myocardial oxygen consumption is the most likely mechanism by which IABP relieves myocardial ischemia in patients with unstable angina pectoris.

INTRAORTIC balloon counterpulsation (IABP) can alleviate manifestations of myocardial ischemia in patients with recurrent angina pectoris that cannot be controlled by conventional medical therapy. The frequency and intensity of anginal episodes are reduced, electrocardiographic and metabolic evidence of ischemia and left ventricular contractile function are improved, and refractory ventricular ectopic activity may resolve completely. The use of IABP allows such unstable patients to undergo coronary artery bypass surgery with lower mortality and perioperative infarction rates than otherwise expected.

The mechanism by which IABP relieves myocardial ischemia is unclear. Possible explanations include enhancement of coronary blood flow through obstructed or collateral coronary vessels, reduction in myocardial oxygen demand, or both. An increase in coronary blood flow during IABP might be anticipated because marked augmentation of diastolic blood pressure is a fundamental and consistent effect of this intervention. Nevertheless, data reported regarding the coronary blood flow response are inconsistent. An important limiting factor in assessing the coronary hemodynamic effect of IABP in patients with coronary artery disease has been the difficulty in measuring regional rather than global left ventricular myocardial blood flow.

An investigation from our laboratory using a fixed, high-grade coronary stenosis in the awake pig indicates that coronary blood flow to ischemic myocardium does not consistently increase with IABP. Rather, regional blood flow distal to the stenosis tends to decrease in association with the observed reduction in myocardial oxygen demand that results from IABP.

Accordingly, the results of our animal study suggest the hypothesis that IABP lessens myocardial ischemia primarily by reducing myocardial oxygen demand rather than by increasing oxygen supply. The objective of the present investigation was to test this hypothesis in patients with medically refractory unstable angina pectoris.

Methods

The patients were carefully selected to include only those with high-grade left anterior descending stenosis and objective evidence of anterior wall ischemia to permit regional assessment of coronary blood flow and myocardial metabolism in the area of myocardium responsible for the clinical syndrome. Nine patients were identified as being suitable candidates for investigation. The thermocouple catheter could not be properly positioned in two patients and satisfactory diastolic augmentation was not achieved in one patient. The remaining six patients constitute the study group. There were four males and two females, ages 48–71 years (mean 62 years). All patients had recurrent chest discomfort in the hospital despite conventional treatment with bedrest, oxygen, long-acting nitrates and propranolol. Further, ST-segment depression, T-wave inversion, or both were observed in leads 1, aV1, or V4, or V3, or V2, or V1, during chest pain in each patient. In four patients, IABP completely relieved these ischemic episodes, and in two reduced their severity. All patients underwent cardiac catheterization with left ventricular and coronary cineangiography. Each patient had high-grade (76–100% arterial diameter reduction) left main or left anterior descending coronary artery narrowing that was not reversed by nitroglycerin.

The effects of IABP on systemic hemodynamics, regional coronary blood flow and myocardial metabolism were evaluated at least 20 minutes after routine angiography. A venotomy was performed in either a right or left antecubital vein. A #7F thermocouple catheter (Wilton-Webster Laboratories) was intro-

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duced and positioned in the coronary sinus under fluoroscopic guidance. The catheter was advanced into the great cardiac vein (GCV) to the point of entry of the anterior interventricular vein. This location was determined by injecting radiographic contrast material through the flow catheter and demonstrating reflux into the anterior interventricular vein (fig. 1). The position of the catheter tip in relation to a bony thoracic landmark or to an ink mark on the video monitor screen was noted to assure constant catheter position. Ability to withdraw blood through the catheter in this location was also confirmed.

With the balloon pump rate at 1:1 (On), aortic pressure, the ECG and GCV flow were recorded. Systemic arterial and GCV blood samples were obtained for oxygen content determination. The balloon pump frequency was then reduced to 1:8 (Off) and maintained at this rate. Blood samples and flows were obtained 5 minutes thereafter. After 10 minutes of 1:8 pumping, the sequence was reversed. Aortic pressure, flow and blood samples were first obtained during 1:8 pumping and then again after 5 minutes of 1:1 pumping. To detect any effect of the sequence of IABP (that is, either initiation or cessation), the two sets of pumping values at 1:1 and 1:8 were compared. No significant difference was observed. The respective means of these values were then determined so that each patient contributed one pair of values to the analysis.

Intravascular pressures, GCV flow and the ECG were recorded simultaneously on a multichannel recorder (Hewlett-Packard model 8890A). Pressures were obtained through polyurethane fluid-filled catheters attached to Statham (P23Db) transducers. Oxygen content was analyzed using a Lex-O2-Con Analyzer (Lexington Instruments). Aortic pressure was analyzed as peak systolic, peak diastolic, mean diastolic and end-diastolic pressures. Diastole was defined as commencing with the dicrotic notch of the aortic pressure trace and ending at the onset of rapid rise in pressure due to left ventricular ejection. The maximal pressure during this interval was identified as peak diastolic pressure. The mean diastolic pressure was obtained by dividing the area under the diastolic pressure curve by the duration of diastole. The rate-pressure product, an index of myocardial oxygen demand, was calculated as a product of peak systolic aortic blood pressure and heart rate. Regional myocardial oxygen consumption was determined as the product of GCV flow and the difference in oxygen content of the paired arterial and GCV blood samples. IABP was performed using 40-ml balloons and a console capable of variable pumping frequencies (Avco Medical Products).

The hypothesis that no true difference existed in the variables that were measured or calculated during IABP at 1:1 compared with IABP at 1:8 was tested by a t test for paired observations. The least-squares method was used to evaluate the relationship of changes in GCV blood flow (dependent variable) to changes in other variables. Differences were considered significant when p was less than 0.05. All values are expressed as mean ± se.

**Results**

The effects of IABP on systemic hemodynamics are shown in table 1. The most pronounced changes occurred in aortic diastolic blood pressure and in rate-
pressure product. IABP increased peak aortic diastolic pressure (95 ± 13 to 149 ± 23 mm Hg, \( p = 0.001 \)) and mean aortic diastolic pressure (82 ± 12 to 96 ± 13 mm Hg, \( p = 0.006 \)). Significant decreases were observed in rate-pressure product (10.7 ± 2.6 to 10.2 ± 2.6 × 10^7 mm Hg/min, \( p = 0.022 \)) and aortic end-diastolic pressure (71 ± 12 to 56 ± 15 mm Hg, \( p = 0.011 \)). No significant changes were noted in heart rate or systolic aortic pressure, although systolic aortic pressure declined in all but one patient.

The effects of IABP on regional coronary dynamics and myocardial oxygen use are shown in table 2 and figure 2. IABP reduced GCV flow from 78 ± 11 to 69 ± 8 ml/min (\( p = 0.048 \)). Flow increased in the only patient (JC) in whom systolic aortic pressure increased. Thus, changes in GCV flow paralleled changes in systolic aortic pressure in each patient. Regional myocardial oxygen consumption was also reduced during IABP in five of six patients (\( p = 0.061 \)). No significant changes were observed in arteriovenous oxygen difference or oxygen extraction.

The correlations between changes in GCV flow as a function of changes in the various systemic hemodynamic variables are shown in table 3. GCV flow correlated significantly with peak systolic aortic blood pressure (\( r = 0.92, p = 0.007 \)) and rate-pressure product (\( r = 0.91, p = 0.008 \)).

**Discussion**

The objective of this investigation was to gain additional insight into the mechanisms by which IABP relieves myocardial ischemia in patients with medically refractory unstable angina. Accomplishing this goal necessitated measurement of both oxygen delivery to and oxygen consumption of potentially ischemic myocardium that was judged responsible for the unstable angina syndrome. We used the thermodilution technique to measure coronary blood flow because it allows the measurement of regional flow and serial changes in flow and is applicable to man.\(^{30}\) When advanced far into the GCV, the thermodilution catheter can selectively sample blood from myocardium in the distribution of the left anterior descending coronary artery.\(^{30}\) For this reason, only IABP patients with left anterior descending coronary stenosis and electrocardiographic evidence of anterior wall ischemia were selected for evaluation.

IABP substantially increased peak and mean aortic diastolic pressures. As in experimental\(^{19}, 20, 25\) and clinical studies,\(^{28}\) coronary blood flow in our patients did not increase as might be anticipated from augmenting diastolic pressure in the aorta. Rather, changes in coronary blood flow closely paralleled the changes in aortic

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**Table 2. Effect of Intraaortic Balloon Counterpulsation on Coronary Circulation and Myocardial Oxygen Use**

<table>
<thead>
<tr>
<th>Pt</th>
<th>GCV flow (ml/min)</th>
<th>A-VO(_2) (vol%)</th>
<th>Myocardial O(_2) consumption (ml O(_2)/min)</th>
<th>O(_2) extraction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Off</td>
<td>On</td>
<td>Off</td>
<td>On</td>
</tr>
<tr>
<td>RC</td>
<td>82</td>
<td>69</td>
<td>11.6</td>
<td>11.3</td>
</tr>
<tr>
<td>JM</td>
<td>74</td>
<td>64</td>
<td>9.3</td>
<td>9.3</td>
</tr>
<tr>
<td>JC</td>
<td>72</td>
<td>77</td>
<td>9.2</td>
<td>9.1</td>
</tr>
<tr>
<td>MW</td>
<td>61</td>
<td>58</td>
<td>9.0</td>
<td>8.9</td>
</tr>
<tr>
<td>RV</td>
<td>92</td>
<td>78</td>
<td>12.7</td>
<td>11.7</td>
</tr>
<tr>
<td>MM</td>
<td>84</td>
<td>68</td>
<td>12.9</td>
<td>12.6</td>
</tr>
<tr>
<td>Mean</td>
<td>78</td>
<td>69</td>
<td>10.8</td>
<td>10.5</td>
</tr>
<tr>
<td>± SD</td>
<td>±11</td>
<td>±8</td>
<td>±1.8</td>
<td>±1.6</td>
</tr>
</tbody>
</table>

\( p = 0.048 \), \( p = 0.203 \), \( p = 0.061 \), \( p = 0.571 \)

**Abbreviations:** GCV = great cardiac vein; A-VO\(_2\) = arteriovenous oxygen difference.

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**Figure 2.** Great cardiac vein flow (\( T_m \)GCV) before (left, frequency 1:8) and after (right) sustained (frequency 1:1) intraaortic balloon counterpulsation (IABP) in patient RV. IABP augments diastolic aortic pressure, reduces peak aortic systolic pressure (arrow) and decreases (upward deflection) GCV flow. \( T_m = \) temperature of indicator; \( A_o = \) aortic pressure; \( L V = \) left ventricular pressure.

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**Table 3. Relationship Between Change in Great Cardiac Vein Flow and Systemic Hemodynamic Variables**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Absolute change</th>
<th>% change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( r )</td>
<td>( p )</td>
</tr>
<tr>
<td>Peak aortic systolic pressure</td>
<td>0.92</td>
<td>0.007</td>
</tr>
<tr>
<td>Peak aortic diastolic pressure</td>
<td>0.45</td>
<td>0.40</td>
</tr>
<tr>
<td>Mean aortic diastolic pressure</td>
<td>0.10</td>
<td>0.86</td>
</tr>
<tr>
<td>Rate-pressure product</td>
<td>0.91</td>
<td>0.008</td>
</tr>
</tbody>
</table>
systolic pressure and rate-pressure product that resulted from IABP. In each patient, the directional changes in coronary flow and aortic systolic blood pressure were the same; when analyzed, the correlation was significant and close. The arteriovenous oxygen difference and myocardial oxygen extraction in the distribution of the left anterior descending coronary artery were unchanged during IABP, which suggests that changes in flow were proportional to changes in oxygen demand. These results are consonant with those in the awake pig subjected to artificial stenosis.

Most clinical investigations of the effect of IABP on coronary dynamics have been limited to patients with cardiogenic shock. Measuring total coronary sinus flow by the iodine-131 antipyrine technique, Mueller et al. noted an increase in coronary blood flow during IABP, but their patients were hypotensive before IABP. Experimental studies have shown that the response of coronary blood flow to IABP may depend on the blood pressure at the time IABP is initiated. Thus, in normotensive dogs, coronary blood flow tends to decline during IABP, whereas flow may increase significantly when IABP is initiated in the hypotensive, failing, flow-limited preparation.

Leinbach and co-workers observed variable changes in coronary blood flow during IABP in patients initially instrumented because of cardiovascular collapse. Again, global rather than regional blood flow was measured. Systolic blood pressure declined in all but one patient, and diastolic blood pressure was uniformly increased. Coronary blood flow decreased in seven, was unchanged in three and increased in four. One of the patients in whom flow increased had been hypotensive. Further, the authors acknowledge the difficulty in accurately assessing changes in flow when sampling total coronary blood flow from combined areas of normal, ischemic and infarcted myocardium.

Each patient in the present study had relief of recurrent angina after the initiation of IABP. Although our observations were not made during active ischemia, they suggest that relief of angina during IABP cannot be ascribed to an absolute increase in coronary blood flow. Myocardial oxygen consumption, however, declined in all but one patient; consistent declines in myocardial oxygen consumption have also been observed in the open-chest dog, and in the awake pig with artificial coronary stenosis. Thus, reduction of myocardial oxygen demand is most likely the mechanism by which IABP relieves ischemia.

Acknowledgment

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Two-dimensional Echocardiography in Experimental Coronary Stenosis

I. Sensitivity and Specificity in Detecting Transient Myocardial Dyskinesis: Comparison with Sonomicrometers

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SUMMARY The purpose of this study was to assess the sensitivity and specificity of two-dimensional echocardiography in detecting ischemia-induced transient myocardial dyskinesis. We prepared an open-chest dog model of severe coronary stenosis (90% reduction of circumflex coronary artery diameter) and induced ischemia by acutely raising myocardial oxygen requirements with i.v. isoproterenol and acute aortic constriction. The changes observed with echocardiography were compared with those obtained by intramyocardial sonomicrometers placed side by side or in an endocardial-epicardial orientation. Ischemia was defined as systolic wall expansion or thinning on sonomicrometers and two-dimensional echocardiography. We found complete agreement between sonomicrometers and two-dimensional echocardiography in all control tracings and after ischemia was induced; whenever dyskinesis occurred it was seen by both techniques. Although there was qualitative agreement between echocardiographic and sonomicrometric techniques, there were quantitative differences in the assessment of wall thickening. Such differences may be related to malalignment of the sonomicrometers, echocardiographic resolution limitations or other technical factors. We conclude that two-dimensional echocardiography is a sensitive and specific technique for detecting transient myocardial ischemia, and therefore should be useful for demonstrating exercise-induced ischemia in patients with coronary artery disease.

TWO-DIMENSIONAL echocardiography can demonstrate resting cardiac wall motion abnormalities after clinical and experimental myocardial infarction.1-12 However, coronary artery disease in the absence of myocardial infarction may not be associated with resting abnormalities. Instead, contraction abnormalities may occur only transiently, such as during stress-induced ischemia. Whether two-dimensional echocardiography is sensitive and specific in demonstrating contraction abnormalities during transient ischemia has not been established.

The goal of this investigation was to determine the sensitivity and specificity of two-dimensional echocardiography in detecting transient ischemia in coronary stenosis. Therefore, we compared the ability of two-dimensional echocardiography to detect ischemia-induced contraction abnormalities with an independent standard, ultrasonic sonomicrometers, in a canine model of severe coronary stenosis.

Methods

Model of Coronary Stenosis

Ten dogs that weighed 20–35 kg were anesthetized with i.v. chloralose (100 mg/kg) and urethane (1000
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