Augmentation of regional coronary blood flow by intra-aortic balloon counterpulsation in patients with unstable angina

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ABSTRACT  Intra-aortic balloon counterpulsation is capable of reducing afterload in patients with unstable angina. Whether it is also capable of augmenting coronary blood flow to poststenotic myocardium is controversial. We studied seven patients receiving maximal drug therapy and requiring balloon pumping for unstable angina as balloon volume and assist ratio were altered. All patients had greater than 90% stenosis of the proximal left anterior descending coronary artery. With maximal augmentation (40 cc balloon volume, 1:1 assist ratio) great cardiac vein flow, representing the efflux from the left anterior descending coronary artery bed, rose from a baseline of 52 ± 20 to 67 ± 25 ml/min (mean ± SD, p = .004) and mean aortic diastolic pressure increased from 77 ± 13 to 99 ± 33 mm Hg (p = .004). Increased great cardiac vein flow correlated with increased mean aortic diastolic pressure across changes in balloon volumes (off, 20 cc, 30 cc, and 40 cc) and changes in assist ratio (off, 1:4, 1:2, and 1:1) (p = .02). However, the intermediate balloon volumes produced great cardiac vein flows at an intermediate level between full assist and no assist (p < .05), whereas the intermediate assist ratios did not augment flow. Thus balloon pumping increased flow to a bed fed by collateral vessels or critical stenoses; this increased flow correlated with increased aortic diastolic pressure, indicating probable loss of autoregulatory ability.

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THE BENEFICIAL EFFECTS of intra-aortic balloon counterpulsation (IABC) have been attributed to decreased myocardial oxygen demand via systolic unloading and to increased myocardial oxygen supply via diastolic augmentation of coronary blood flow.1-3 The relative importance of each factor is likely to vary with the hemodynamic setting: Systolic unloading should be the major factor in pump failure with normal or elevated afterload, whereas diastolic augmentation could be a significant factor when ischemia is present. With regard to the latter mechanism, most studies have demonstrated that IABC increases aortic diastolic pressure.4-9 However, if coronary autoregulatory mechanisms are still operating, increases in diastolic aortic pressure would not be expected to augment flow.10, 11 Despite some experimental studies demonstrating that IABC augments coronary blood flow in dogs,8, 12-16 augmentation of coronary flow in man has not been consistently documented; results range from a 10% decrease9 to no change4 to a 40% increase17 with institution of IABC. These disparate findings may be due to the fact that flows were not always measured in coronary beds in which flow was pressure dependent. A direct demonstration of the beneficial diastolic effects of IABC must show that IABC increases coronary flow in proportion to increases in mean aortic diastolic pressure in a coronary bed supplied through a critical stenosis.

We therefore undertook this study to determine whether IABC could increase coronary blood flow to the myocardium perfused by a critically stenosed left anterior descending coronary artery (LAD) in patients with unstable angina refractory to aggressive drug
therapy. Graded levels of aortic diastolic pressure augmentation were produced by alteration of both the balloon displacement volume and the balloon assist ratio. The increases in mean aortic diastolic pressure produced by alteration of displacement volume but not of assist ratio were associated with graded increases in flow from the myocardial region supplied by the LAD.

Methods

Patients. Our patients included all individuals undergoing diagnostic cardiac catheterization with coronary angiography at the Johns Hopkins Hospital between June 1981 and June 1982 who required placement of an intra-aortic balloon because of severe unstable angina pectoris and who consented to the protocol (n = 7). All patients had frequent episodes of angina associated with anterior electrocardiogram (ECG) changes occurring at rest despite maximal drug therapy, which consisted of combinations of β-blockers, nitrates, and calcium antagonists. In each case, IABC provided subjective relief.

Procedure. All studies were performed with patients in the postabsorptive state, and all medications were continued. Informed consent was obtained in each case. After routine coronary angiography and left ventriculography by the Seldinger technique via the femoral artery, a triple-thermistor thermodilution catheter (Wilton Webster Laboratories, Alladena, CA) was placed through a right brachial vein incision and advanced into the coronary sinus. Catheter position was confirmed by fluoroscopy with injection of 2 to 3 ml of meglumine diatrizoate (Renografin-76) into the coronary venous system. In each case the distal sensing thermistor was advanced beyond the junction of the left marginal vein and the coronary sinus so that the flow recorded by this thermistor was entirely from the great cardiac vein.

In the first two patients a fluid-filled catheter connected to a Statham P23Gb pressure transducer was positioned in the ascending aorta for the duration of the study. In the remaining five patients, a micromanometer-tipped catheter with two pressure sensors (Millar Instruments, Houston, TX) was placed retrograde across the aortic valve so that one pressure sensor was in the left ventricle and the other was in the ascending aorta. In these five patients recordings were made on FM tape and subsequently digitized at a rate of 250 Hz on a Data General S/130 computer with a 12 bit analog-to-digital converter. To minimize drift, the micromanometers were immersed for at least 2 hr in saline at body temperature and balanced before insertion.

Throughout the study, balloon inflation and deflation were set so that inflation began at the diastolic notch and deflation began at midisovolumetric systole. After all catheters were in place, the balloon assist ratio and displacement volume were systematically altered in the following manner: 3 min each at 40 cc 1:1, 40 cc 1:2, 40 cc 1:4, off, 40 cc 1:1, 30 cc 1:1, 20 cc 1:1, off, and 40 cc 1:1. During the final minute at each setting, great cardiac vein flow was determined by continuous infusion of 5% dextrose in water at room temperature and a constant rate of 0.9 ml/sec for approximately 20 sec with a Viamonte/Hobbs power injector (Angiomat 3000; Liebel-Flarsheim Co., Cincinnati, OH) according to methods previously described. Ascending aortic pressures (and, in the last five patients, left ventricular pressures) were recorded simultaneously.

Data analysis. All coronary angiograms were reviewed by two independent cardiologists. Great cardiac vein flows were determined independently by two of the authors without knowledge of the balloon settings, as previously described. For each patient the repeated measurements at settings of „40 cc 1:1” and „off” were averaged. In all but two instances, repeat measurements varied by less than 7%. For the two patients in whom fluid-filled catheters were used, mean aortic systolic and diastolic pressures were determined by manual digitization of the pressure tracings for the „40 cc 1:1” and „off” settings with a Hewlett-Packard digitizing table connected to an HP-9810A desktop computer. In the remaining five patients, mean systolic and diastolic pressures were determined for each setting from the computer-digitized data; systole was defined as beginning with the upstroke of the aortic tracing and ending with the nadir of the diastolic notch. Mean systolic and diastolic pressures for at least 3 nonconsecutive beats were averaged for each balloon volume; for the 1:2 and 1:4 assist ratios, data from three nonconsecutive sets of 2 and 4 sequential beats were averaged.

The significance of the hemodynamic changes across all balloon volumes and all assist ratios was assessed independently by analysis of variance with repeated measures. Subsequently, the significance of the individual data derived at the intermediate levels of displacement volume and assist ratio was determined with both Fisher’s least significant difference test and Duncan’s multiple range test. Differences and correlations were considered significant if p < .05. Data are presented as mean ± SD.

The relationship between great cardiac vein flow and mean aortic diastolic pressure was assessed by linear regression analysis of the data at all balloon volumes and assist ratios for each patient separately. To test the overall significance of the relationship between great cardiac vein flow and mean aortic diastolic pressure, we applied the Student’s t test to the aggregate of the slopes of the regression lines.

Results

Patient characteristics (Table 1). Four of the seven patients were men, and the mean age was 58 (range 48 to 69). Two patients (Nos. 3 and 6) had recently suffered anterior subendocardial myocardial infarctions and two (Nos. 4 and 7) had suffered transmural anterior infarctions manifested by Q waves on the ECG; however, all had anterior wall ECG changes with pain. All patients had greater than 90% narrowing in the proximal LAD; angiographically visible collateral vessels supplying the LAD territory were present in five patients and filled the distal LAD in all cases where total occlusion was noted.

Great cardiac vein flow. Great cardiac vein flow, representing the venous efflux from the LAD territory, increased from 52 ± 20 ml/min with the balloon off to 67 ± 25 ml/min at maximal augmentation (40 cc balloon volume, 1:1 assist; see figure 1).

As the balloon volume was progressively decreased from 40 to 30 to 20 to 0 cc while assist ratio was maintained constant at 1:1, there was a significant decrease in mean great cardiac vein flow (p = .002, Table 2A). Similarly, as the assist ratio was progressively decreased from 1:1 to 1:2 to 1:4 to 0 while balloon volume was maintained constant at 40 cc, there was a significant decrease in mean great cardiac flow (p = .001, Table 2B). The multiple comparison tests revealed that the flows at the intermediate levels of bal-
locomotion displacement (20 and 30 cc) did not differ from each other but differed significantly both from the \( p \) with the balloon off and from the flows during full balloon support (\( p < .05 \)). In contrast, flows at the intermediate assist ratios (1:4 and 1:2) did not differ significantly from great cardiac vein flows obtained with the balloon off.

**Pressures.** Balloon counterpulsation produced a graded decrease in mean aortic systolic pressure and a graded increase in mean aortic diastolic pressure (tables 3A and 3B) with progressive increases in either balloon volume or assist ratio. Maximal augmentation raised mean aortic diastolic pressure from 77 ± 13 to 99 ± 33 mm Hg (\( p = .004 \), paired t test) and decreased mean systolic pressure from 102 ± 21 to 92 ± 21 mm Hg (\( p = .01 \), paired t test). Maximal augmentation also produced a reduction in mean left ventricular pressure (table 4) from 50 ± 4 to 45 ± 4 mm Hg (\( p = .02 \), paired t test) and no significant change in left ventricular end-diastolic pressure (24 ± 10 to 21 ± 11 mm Hg; \( p = .09 \)).

### TABLE 1

<table>
<thead>
<tr>
<th>Patient</th>
<th>Coronary anatomy</th>
<th>Left ventricular wall motion</th>
<th>Resting ECG</th>
<th>Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>LAD, 99% proximal lesion LMD, 99% lesion RCA, 80% lesion</td>
<td>Normal</td>
<td>Normal</td>
<td>Nitrates (iv), propranolol</td>
</tr>
<tr>
<td>2</td>
<td>LAD, 100% proximal lesion( ^a ) CM, 40% lesion</td>
<td>Mildly hypokinetic anterior wall</td>
<td>T wave inversion ( V_1-V_6 )</td>
<td>Nitrates (iv), propranolol</td>
</tr>
<tr>
<td>3</td>
<td>LAD, 100% proximal lesion( ^a ) LMD, 70% lesion CFX, 50% mid lesion RCA, 90% distal lesion</td>
<td>Akinetic mid &amp; distal anterior wall &amp; distal inferior walls; hypokinetic septum</td>
<td>Q waves ( V_1-V_6 ); T wave inversion I, aVL, ( V_2-V_6 )</td>
<td>Nitrates (topical, oral), propranolol</td>
</tr>
<tr>
<td>4</td>
<td>LAD, 99% proximal lesion( ^a ) LAD, 100% mid lesion CM, 100% lesion</td>
<td>Akinetic mid &amp; distal anterior wall &amp; distal inferior wall</td>
<td>Q waves ( V_2-V_6 )</td>
<td>Nitrates (iv), nifedipine, propranolol</td>
</tr>
<tr>
<td>5</td>
<td>LAD, 90% proximal lesion CFX, 99% proximal lesion RCA, 100% proximal lesion</td>
<td>Mildly hypokinetic anterolateral wall</td>
<td>Q waves II, III, aVF</td>
<td>Nitrates (iv), propranolol</td>
</tr>
<tr>
<td>6</td>
<td>LAD, 100% proximal lesion( ^a ) CM, 100% proximal lesion RCA, 60% mid lesion</td>
<td>Markedly hypokinetic anterior wall</td>
<td>ST depression ( V_4-V_6 )</td>
<td>Nitrates (iv, oral)</td>
</tr>
<tr>
<td>7</td>
<td>LAD, 100% proximal lesion( ^a ) RCA (nondominant), 99% proximal lesion</td>
<td>Dyskinetic anteroapical wall</td>
<td>Q waves ( V_2-V_6 )</td>
<td>Nitrates (iv)</td>
</tr>
</tbody>
</table>

LMD = left main diagonal coronary artery; RCA = right coronary artery; CFX = circumflex coronary artery; CM = circumflex marginal artery.

\( ^a \)Angiographically visible collateral vessels to LAD.

### TABLE 2A

**Effect of varying balloon volume on great cardiac vein flow (ml/min)**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Off</th>
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<td>36</td>
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<td>5</td>
<td>79</td>
<td>100</td>
<td>86</td>
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<td>7</td>
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<tr>
<td>Mean</td>
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<td>60</td>
<td>67</td>
</tr>
<tr>
<td>SD</td>
<td>20</td>
<td>26</td>
<td>20</td>
<td>25</td>
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</table>

\( p = .002 \)

### TABLE 2B

**Effect of varying assist ratio on great cardiac vein flow (ml/min)**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Off</th>
<th>1:4</th>
<th>1:2</th>
<th>1:1</th>
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</thead>
<tbody>
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<td>1</td>
<td>45</td>
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<tr>
<td>Mean</td>
<td>52</td>
<td>57</td>
<td>57</td>
<td>67</td>
</tr>
<tr>
<td>SD</td>
<td>20</td>
<td>27</td>
<td>25</td>
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</tbody>
</table>

\( p = .001 \)
There was a significant linear relation between great cardiac vein flow and mean aortic diastolic pressure across all balloon volumes and assist ratios in three of the five patients for whom micromanometer pressure measurements were obtained (figure 2). The aggregate of the slopes of the regression lines for these five patients differed significantly from zero (p = .02), thereby substantiating a linear relationship between great cardiac vein flow and mean aortic diastolic pressure.

**Discussion**

The present study demonstrates that progressive augmentation of aortic diastolic pressure by IABC leads to progressive increases in great cardiac vein flow in patients with severe proximal stenoses in the LAD who had unstable angina at rest that was unresponsive to maximal drug therapy. We and others have shown that the measurement of great cardiac vein flow by the thermodilution technique is reproducible and is most likely a reliable measure of the great majority of blood that effluxes from the territory supplied by the LAD when the distal thermistor is placed near the entrance of the great cardiac vein and the catheter position remains fixed. However, this measurement does not provide information on regional blood flow distribution across the wall (i.e., subendocardial vs subepicardial flow) nor does it distinguish between flow through native or collateral vessels. Therefore we cannot be certain which region(s) in the LAD territory

**TABLE 3A**

<table>
<thead>
<tr>
<th>Effect of varying balloon volume on mean aortic pressures (systolic/diastolic, mm Hg)</th>
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<tbody>
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<tr>
<td>Mean</td>
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**TABLE 3B**

<table>
<thead>
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<th>Effect of varying assist ratio on mean aortic pressure (systolic/diastolic, mm Hg)</th>
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<tbody>
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<td>Patient</td>
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<tr>
<td>7</td>
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<tr>
<td>Mean</td>
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</tbody>
</table>

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received the increased blood flow produced by IABC.

In addition, we cannot be certain that portions of the LAD territory were actually ischemic at the time we made our measurements. First, all our patients had multivessel coronary artery disease and thus their unstable angina may have resulted from ischemia occurring outside the LAD territory. Second, no patient developed pain during the periods when IABC support was temporarily suspended during the study. Moreover, the possibility always exists that unstable angina in these patients was caused by coronary artery vasospasm\textsuperscript{22} unrelated to their fixed stenoses. Nonetheless, all our patients did have high-grade stenoses in the LAD, and our finding of IABC-induced augmentation of coronary flow to the LAD bed suggests that a significant portion of the LAD bed had lost its autoregulatory vasodilatation reserve.\textsuperscript{11}

In our highly selected patient population, IABC augmented regional coronary flow proportionally to the induced increase in mean diastolic pressure. This was demonstrated in a bed supplied by a severely stenosed coronary artery and occurred in a graded fashion across changes in balloon displacement volumes. This finding is consistent with many previous findings in both man and experimental animals in which regional or global coronary flow was found to be increased during IABC in the setting of acute ischemia.\textsuperscript{3, 8, 12-17}

Two studies, however, reported findings that dif-

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|}
\hline
\textbf{Patient} & \textbf{Off} & \textbf{20 cc} & \textbf{30 cc} & \textbf{40 cc} \\
\hline
3 & 50.4 & 47.9 & 46.8 & 50.1 \\
4 & 48.5 & 43.7 & 42.3 & 42.8 \\
5 & 43.9 & 47.6 & 40.2 & 39.9 \\
6 & 55.0 & 50.2 & 52.1 & 47.0 \\
7 & 50.9 & 54.1 & 48.3 & 45.7 \\
\hline
\textbf{Mean} & 49.7 & 48.7 & 45.9 & 45.1 \\
\textbf{SD} & 4.0 & 3.8 & 4.8 & 3.9 \\
\hline
\end{tabular}
\caption{Effect of varying balloon volume on mean left ventricular pressures (mm Hg)}
\end{table}

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|}
\hline
\textbf{Patient} & \textbf{Off} & \textbf{1:4} & \textbf{1:2} & \textbf{1:1} \\
\hline
3 & 50.4 & 47.0 & 44.4 & 50.1 \\
4 & 48.5 & 41.3 & 42.9 & 42.8 \\
5 & 43.9 & 47.9 & 49.5 & 39.9 \\
6 & 55.0 & 48.0 & 48.1 & 47.0 \\
7 & 50.9 & 46.5 & 47.9 & 45.7 \\
\hline
\textbf{Mean} & 49.7 & 46.1 & 46.6 & 45.1 \\
\textbf{SD} & 4.0 & 2.8 & 2.8 & 3.9 \\
\hline
\end{tabular}
\caption{Effect of varying assist ratio on mean left ventricular pressures (mm Hg)}
\end{table}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure2}
\caption{Relation between mean aortic diastolic pressure and great cardiac vein flow across all balloon volumes and assist ratios for the five patients in whom micromanometer pressures were available. Patient 3 ( ), y = 0.66x - 18.44 (r = .90, p = .01); patient 4 ( ), y = 0.53x + 0.65 (r = .78, p = .07); patient 5 ( ), y = 1.20x + 1.97 (r = .72, p = .11); patient 6 ( ), y = 0.25x + 60.42 (r = .84, p = .04); patient 7 ( ), y = 0.91x - 19.68 (r = .81, p = .05).}
\end{figure}
ferred from ours. Leinbach et al. found that IABC led to increased coronary flow in only four of 14 cases and actually decreased flow in seven cases. However, these authors investigated a very different population (patients with cardiovascular collapse after myocardial infarction) from ours (patients with unstable angina). Moreover, they studied global coronary flow, probably measuring an admixture of flows from pressure-dependent and pressure-independent beds.

Williams et al. reported that despite aortic diastolic pressure augmentation, IABC decreased great cardiac vein flow in six patients with unstable angina. Their patients differed from ours as well. First, the LAD stenoses were less severe than those in our patients, so it is likely that some of those LAD beds may have retained the ability to autoregulate. Second, the peak systolic pressure before IABC was 140 ± 20 mm Hg as compared with 111 ± 27 mm Hg in our study; it is therefore likely that those ventricles were facing a greater load, perhaps because they may have received less aggressive drug therapy before balloon insertion.

Although it would have been desirable to measure a physiologic parameter reflecting the presence or absence of ischemia, such as regional oxygen consumption or lactate production, the coronary sinus catheter did not permit reliable aspiration of blood. However, we did measure mean left ventricular pressure, which is one reliable reflection of load facing the ventricle and should be an indirect index of oxygen demand. In our patients, maximal IABC augmentation produced a significant decrease in this index of demand.

Since both great cardiac vein flow and mean left ventricular pressure were altered by IABC in our patients, we cannot definitively state which was of greater importance in relieving the ischemic pain. Most likely, each mechanism was significant clinically and each may have diminished the need for the other. In other patients, such as those studied by Williams et al., it is possible that IABC could decrease demand sufficiently to enable the preexisting or decreased levels of coronary blood flow to satisfy the greatly reduced oxygen demand; alternatively, augmentation of coronary blood flow could enable the heart to face greater levels of afterload without becoming ischemic.

Despite widespread use of the traditional means of weaning patients from balloon augmentation by progressively decreasing the assist ratio from 1:1 to 1:2 to 1:4, there is surprisingly little documentation of the hemodynamic effects of these intermediate levels of counterpulsation. In our patients, the lower assist ratios produced only small decreases in systolic pressure and small increases in diastolic pressure, and great cardiac vein flow did not differ significantly from that obtained without balloon support. In contrast, the values for great cardiac vein flow at the intermediate balloon volumes (20 and 30 cc) were significantly greater than those obtained with the balloon off, which is in accord with the results of studies emphasizing the dependence of augmentation on balloon volume. Our data suggest that graded reduction in balloon volume might be a useful alternative to graded reduction in assist ratio when patients are weaned from IABC, especially when small changes in hemodynamic status are critical; however, we have not examined this question in a clinical trial of weaning.

In summary, this study suggests that IABC can increase flow to a bed perfused through a critical stenosis or collaterals and that this increased flow correlates with increased aortic diastolic pressure.

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