Preservation of distal coronary perfusion during prolonged balloon inflation with an autoperfusion angioplasty catheter

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ABSTRACT  A newly designed balloon coronary angioplasty catheter that allows passive antegrade blood flow during balloon inflation (autoperfusion catheter) was compared with a standard balloon coronary angioplasty catheter. In a randomized sequence, inflations were performed for 3 min in the left circumflex coronary artery of 12 dogs with the standard catheter followed by the autoperfusion catheter or vice versa. During inflation with the standard catheter, the ST segment of standard limb lead II increased from $-0.02 \pm 0.03$ mV to $0.39 \pm 0.08$ mV ($p < .001$), whereas during inflation with the autoperfusion catheter the ST segment did not change ($-0.03 \pm 0.03$ vs $-0.01 \pm 0.04$ mV; $p =$ NS). Regional myocardial blood flow measured by the radioactive microsphere technique in the posterior subepicardium and subendocardium was $0.12 \pm 0.03$ and $0.08 \pm 0.03$ ml/min/g, respectively, with the standard catheter as compared with $0.57 \pm 0.08$ and $0.61 \pm 0.14$ ml/min/g with the autoperfusion catheter (both $p < .01$ compared with the standard catheter). Thus, unlike the standard catheter, the autoperfusion catheter allows for inflations up to 3 min in duration without producing deleterious changes in the ST segment or severe reductions in regional myocardial blood flow. Circulation 75, No. 6, 1273–1280, 1987.

PERCUTANEOUS transluminal coronary angioplasty is widely used to dilate coronary arteries successfully in patients with single and multivessel atherosclerotic disease.1–2 Among the major problems associated with angioplasty are ischemia distal to the site of inflation, which limits its applicability in some very proximal (including left main) lesions, and the occurrence of restenosis arising within 6 months of angioplasty in 17% to 44% of patients.5,6 It has been suggested that prolonged balloon inflation at the time of coronary angioplasty would decrease the rate of restenosis.7 However, prolonged balloon inflation could induce severe ischemia when the distal coronary artery bed is not adequately supplied by collaterals. Several extracorporeal systems, using perfusion of blood or fluorocarbons, have been used in an attempt to achieve balloon dilatation without accompanying ischemia.8–11

We report here on the use of a balloon angioplasty catheter that allows blood to flow through sideholes in the catheter proximal to the inflated balloon, through a central lumen in the catheter, and to the myocardium distal to the inflated balloon via distal sideholes and an endhole. Such a system theoretically could allow more prolonged balloon inflations without the need for complex perfusion systems. The purpose of our study was to test whether this autoperfusion angioplasty catheter could deliver coronary blood flow distal to the inflated balloon and prevent severe ischemia, and to compare it with balloon inflation with a standard angioplasty catheter.

Methods

Angioplasty catheters. The autoperfusion balloon angioplasty catheter (USCI, Billerica, MA) used in this study (figure 1) is a three-lumen No. 4.3F catheter with a $2.5 \times 20$ mm balloon. It has eight sideholes proximal and three sideholes distal to the balloon and an endhole distal to the balloon. All sideholes are $0.3$ mm in diameter and are fenestrated so as to communicate with the central lumen. For comparison, a No. 4.3F standard $2.5 \times 20$ mm balloon dilatation catheter (USCI) was used.
Surgical procedures. Mongrel dogs* of either sex, weighing 16.4 to 34.6 kg, were anesthetized with sodiumpentobarbital (30 mg/kg iv), intubated, and artificially respirated with room air by means of a Harvard respirator. Cannulas were inserted into the leftjugular vein for administration of fluids and into the left carotid artery for the withdrawal ofreference blood samples to be used in the determination of regional myocardial blood flow (RMBF). A leftthoracotomy was performed at the fifth intercostal space and a pericardial cradle was temporarilyconstructed. A micromanometer-tipped catheter (Millar Instruments, Houston) was positioned in the leftventricle via the left atrial appendage for measurement of leftventricular pressure and leftventricular dP/dt. A saline-filled cannula was positioned in the left atrium for the injection of radioactive microspheres for the determination of RMBF. Electrodes were positioned on all limbs for the recording of electrocardiographic lead II. A prophylactic intra-atrial injection of 20 µg Tween, a concentration similar to that in the suspension of the radioactive microspheres, was administered approximately 30 min before beginning the protocol to nullify any Tween reaction during determination of RMBF. All electrocardiographic and hemodynamic variables were recorded continuously on a Gould multi-channel recorder.

A No. 9F USCI sheath was inserted into the right femoral artery by the Seldinger technique, either percutaneously or by isolation of the femoral artery. The dogs were given 5000 U of heparin intravenously. The side arm of the sheath was used to measure arterial blood pressure.

Protocol I. After a No. 8F guiding catheter was positioned in the ostium of the left main coronary artery, either the autoperfusion catheter or a standard angioplasty catheter was chosen in a randomized manner and positioned in the proximal circumflex coronary artery under fluoroscopic guidance with a single-plane General Electric Fluoricon 300 system. Upon adequate positioning of the angioplasty catheter, the guiding catheter was pulled back from the left coronary ostium. After obtaining baseline recordings of ST segment amplitude (measured 0.06 sec after the J point), left ventricular pressure, peak positive and negative left ventricular dP/dt, and heart rate at a paper speed of 50 mm/sec, the balloon of the catheter in place was inflated for 3 min at a pressure of 6 bars. The variables were recorded at a paper speed of 50 mm/sec every minute for 4 min. After 1 min of balloon inflation the RMBF was determined by the radioactive microsphere technique as described previously.12 After deflation of the balloon, the catheter was removed and the second type of catheter was positioned in the same location in the circumflex coronary artery. At least 20 min was allowed to elapse and then the above procedure was repeated with inflation of the second balloon catheter. Dogs in which no evidence of ischemia (no ST elevation) was present with inflation of the standard catheter were not included in this study. After completion of the balloon inflations and deflations the dogs were euthanized by an overdose of sodiumpentobarbital (intravenous) and potassium chloride (intra-atrial). The heart was excised for determination of RMBF.

Protocol II. Protocol II was designed to investigate the influence on RMBF of the guiding catheter alone and of the deflated angioplasty catheter. Dogs were prepared as above. A baseline determination of RMBF was performed after surgical prepara-
determination of the dogs, before insertion of any catheters in the coronary ostium. RMBF was also determined after positioning of the guiding catheter in the ostium of the left main coronary artery. A third determination of RMBF was performed after the positioning of an angioplasty catheter in the proximal circumflex coronary artery with simultaneous withdrawal of the guiding catheter back to the aortic arch. After completion of the protocol the dogs were euthanized as above and the heart was excised for determination of RMBF.

RMBF. RMBF was determined by intra-atrial injection of 2.0 \( \times \) 10^6 radioactive (cerium-141, ruthenium-103, niobium-95) microspheres (11 \( \pm \) 1 \( \mu \)m diameter) while a reference arterial blood sample was withdrawn from the carotid artery at 15.3 ml/min with a Harvard withdrawal pump. Samples of myocardium weighing approximately 1 g were cut from the subepicardium and subendocardium from the posterior, anterior and septal regions. RMBF in the tissue samples was calculated (in ml/min/g) by the formula: 

\[
RMBF = \frac{C_b}{C_r} \times \frac{C_s}{C_r}
\]

where \( C_b \) = counts in myocardial tissue sample corrected per gram; \( C_b \) = rate of withdrawal of reference blood sample; \( C_r \) = total counts in reference blood sample.\(^{12}\)

Statistics. Comparisons between absolute values of the groups over time were performed with two-way analysis of variance and Tukey's test to identify significance.\(^{13}\) A paired Student t test was used for comparison of changes of peak positive and negative left ventricular dp/dt over the 3 min inflation periods.

Results

A total of 19 dogs were entered into protocol I, of which four were excluded because no change of the ST segment occurred during inflation of the standard catheter (suggesting absence of ischemia), one was excluded because of failure in placing the guiding catheter into the left main ostium, one was excluded because of technical difficulties with the radioactive microsphere method, and one was excluded because of difficulties in maintaining pressure in the balloon inflation system. The remaining 12 dogs successfully completed the entire protocol. Of the 12 dogs that were randomized, seven received the standard catheter first and five received the autoperfusion angioplasty catheter first. An additional five dogs were used for protocol II.

Protocol I

ST segment elevation. The ST segment changes after inflation of the standard and autoperfusion catheters are shown in figure 2. With the standard catheter the ST segment changed from \(-0.02 \pm 0.03\) mV before inflation to \(0.39 \pm 0.08\) mV (\(p < .01\)) after inflation and returned to \(0.01 \pm 0.04\) mV 1 min after deflation. In contrast, with the autoperfusion catheter the ST segment was \(-0.03 \pm 0.03\) mV before inflation, \(-0.01 \pm 0.04\) mV after inflation (\(p = \text{NS}\)), and \(0.00 \pm 0.02\) mV 1 min after deflation.

RMBF. Figure 3 and table 1 show the RMBF measured during balloon inflation with the standard and autoperfusion catheters. In the left ventricular posteri- or subepicardium and subendocardium, an area perfused by the circumflex coronary artery, the RMBF was \(0.12 \pm 0.03\) and \(0.08 \pm 0.03\) ml/min/g during balloon inflation with the standard catheter; however, when the autoperfusion catheter was inflated, the RMBF was significantly higher at \(0.57 \pm 0.08\) and \(0.61 \pm 0.14\) ml/min/g (both \(p < .01\) compared with the standard catheter). The RMBF in the nonischemic anterior and septal subepicardium and subendocardium was not significantly different between catheters but was somewhat depressed from normal nonischemic values obtained in this laboratory in previous studies.\(^{14}\)

Hemodynamics. Table 2 shows the effects on the absolute values of the hemodynamic variables measured before inflation and after 3 min of inflation. There were no significant differences between the catheters before inflation or after inflation. However, as shown in figure 4, there were significant differences between the catheters in the change over the 3 min inflation period in left ventricular peak positive and negative dp/dt. With the standard catheter, left ventricular peak positive and negative dp/dt fell by \(254 \pm 62\) and \(321 \pm 74\) mm Hg/sec compared with a fall of \(63 \pm 23\) and \(83 \pm 39\) mm Hg/sec, respectively, with the autoperfusion catheter (both \(p < .05\)).

Protocol II. Due to the unexpected finding that RMBF in nonischemic areas was mildly depressed during angioplasty balloon inflation, protocol II was performed. Table 3 shows the RMBF values of five dogs measured after the surgical procedures outlined, after positioning of the guiding catheter in the left main ostium and after positioning, but not inflating, the angioplasty catheter in the circumflex coronary artery with the guiding catheter pulled back to the aortic arch. There was a trend for RMBF in the posterior, anterior, and septal subepicardium and subendocardium to be reduced from baseline by the positioning of the guiding catheter and the angioplasty catheter.

Discussion

Percutaneous transluminal coronary angioplasty has rapidly emerged as a major invasive technique in the treatment of severely stenosed coronary arteries. As this technique evolves, patient selection criteria and possibly the incidence of restenosis might be favorably influenced if ischemia during angioplasty could be prevented, allowing longer balloon inflation times. This study presents results on the use of an autoperfusion angioplasty catheter that allows passive antegrade perfusion of blood, resulting in significantly improved
regional myocardial blood flow compared with the standard angioplasty catheter.

In protocol I of this study, each dog acted as its own control in that both the autoperfusion angioplasty catheter and a standard catheter were positioned and inflated in the same location in the same circumflex coronary artery. Each balloon inflation was limited to 3 min to lessen the degree of myocardial stunning\(^1\) and to minimize the incidence of ventricular fibrillation occurring upon balloon deflation.

The results clearly show that with occlusive inflation of the standard catheter, the ST segment became markedly elevated and RMBF to the posterior wall was severely reduced. In contrast, inflation of the balloon of the autoperfusion angioplasty catheter produced little change in the ST segment and only moderate reduction in RMBF to the posterior wall. Both catheters produced some reduction in myocardial contractility and relaxation over the 3 min inflation period as evidenced by changes in peak positive and negative left ventricular dP/dt; however, the standard catheter caused significantly greater change of these indexes of myocardial function than did the autoperfusion catheter.

The finding in protocol I that RMBF was mildly reduced in nonischemic areas not perfused by the circumflex coronary artery was unexpected. The results of protocol II show that both the guiding and deflated angioplasty catheters can cause a modest reduction in RMBF in all areas. This is probably caused by a reduction of the size of the lumen of the left main coronary artery while the catheter is in place. Other factors that could affect RMBF in nonischemic areas include heart rate and the effect of the contrast medium used to

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**FIGURE 2.** Effect of balloon inflation for 3 min on the ST segment of lead II of the electrocardiogram with the standard catheter (A) and the autoperfusion catheter (B).
visualize the coronary anatomy and location of the catheters. The heart rate was slower in this series of experiments than in others performed in this laboratory with sodium pentobarbital anesthesia and similar surgical techniques. Since heart rate is a major determinant of myocardial oxygen consumption it is possible that the lower heart rate observed in dogs used in this study would result in lower values in RMBF. Studies have shown that intracoronary injection of contrast medium causes a transient reduction in coronary blood flow lasting up to 6 sec and that this is superceded by a transient increase in coronary blood flow. This latter effect is an unlikely cause of the decrease in RMBF to nonischemic areas since measurement of RMBF was performed when coronary blood flow should have been stable.

In retrospect, the results of protocol II could have been foreseen since blood flow is dependent on the radius of the blood vessel and insertion of catheters in coronary arteries would reduce the lumen radius even if autoregulatory compensatory mechanisms induced vasodilatation. This phenomenon has important impli-

### TABLE 1

<table>
<thead>
<tr>
<th>Location</th>
<th>Standard catheter</th>
<th>Autoperfusion catheter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posterior ep</td>
<td>0.12 ± 0.03&lt;sup&gt;A&lt;/sup&gt;</td>
<td>0.57 ± 0.08</td>
</tr>
<tr>
<td>Posterior en</td>
<td>0.08 ± 0.03&lt;sup&gt;B&lt;/sup&gt;</td>
<td>0.61 ± 0.14</td>
</tr>
<tr>
<td>Anterior ep</td>
<td>0.62 ± 0.07</td>
<td>0.61 ± 0.09</td>
</tr>
<tr>
<td>Anterior en</td>
<td>0.81 ± 0.09</td>
<td>0.79 ± 0.10</td>
</tr>
<tr>
<td>Septum ep</td>
<td>0.56 ± 0.06</td>
<td>0.50 ± 0.05</td>
</tr>
<tr>
<td>Septum en</td>
<td>0.72 ± 0.09</td>
<td>0.67 ± 0.08</td>
</tr>
</tbody>
</table>

Epi = subepicardium; endo = subendocardium.

<sup>A</sup>p < .01; <sup>B</sup>p < .001 vs the autoperfusion angioplasty catheter.

FIGURE 3. Effect of balloon inflation on the RMBF of the circumflex subepicardium (A) and subendocardium (B) with the standard and autoperfusion catheters.
TABLE 2
Hemodynamic variables measured before balloon inflation (baseline) and after 3 min of balloon inflation (mean ± SEM)

<table>
<thead>
<tr>
<th></th>
<th>Standard catheter</th>
<th>Autoperfusion catheter</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>3 min</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>125 ± 5</td>
<td>121 ± 5</td>
</tr>
<tr>
<td>LVP (mm Hg)</td>
<td>110 ± 4</td>
<td>92 ± 4</td>
</tr>
<tr>
<td>+LV dP/dt (mm Hg/sec)</td>
<td>1479 ± 63</td>
<td>1225 ± 91</td>
</tr>
<tr>
<td>−LV dP/dt (mm Hg/sec)</td>
<td>1429 ± 70</td>
<td>1108 ± 75</td>
</tr>
</tbody>
</table>

LVP = left ventricular pressure.

cations in angioplasty since the majority of patients undergoing this procedure have severely stenosed coronary arteries. Positioning of the catheters in a coronary ostium or stenosed coronary artery will further reduce the radius of these blood vessels, thereby augmenting the imbalance between coronary blood flow and myocardial oxygen demand.

The results in this study with the standard angio-

plasty catheter are in agreement with clinical data.\textsuperscript{18} In patients undergoing coronary angioplasty with balloon inflations averaging 62 ± 6 sec, severe dysfunction, detected by two-dimensional echocardiography, was found in 100% of patients; 86% of patients demonstrated electrocardiographic signs of ischemia within 60 sec of balloon occlusion of the coronary artery. Repeated balloon inflations did not have any cumulative

FIGURE 4. Change over 3 min of peak positive (A) and negative (B) left ventricular dP/dt with the standard and autoperfusion catheters.
TABLE 3

Effect of positioning guiding and angioplasty (deflated) catheters on RMBF (ml/min/g; mean ± SEM)

<table>
<thead>
<tr>
<th></th>
<th>Guiding catheter in ostium</th>
<th>Deflated catheter in coronary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posterior epi</td>
<td>1.06 ± 0.10</td>
<td>0.64 ± 0.18</td>
</tr>
<tr>
<td>Posterior endo</td>
<td>1.48 ± 0.21</td>
<td>0.90 ± 0.26</td>
</tr>
<tr>
<td>Anterior epi</td>
<td>1.03 ± 0.06</td>
<td>0.65 ± 0.13</td>
</tr>
<tr>
<td>Anterior endo</td>
<td>1.40 ± 0.13</td>
<td>0.90 ± 0.22</td>
</tr>
<tr>
<td>Septum epi</td>
<td>0.87 ± 0.07</td>
<td>0.49 ± 0.14</td>
</tr>
<tr>
<td>Septum endo</td>
<td>1.21 ± 0.11</td>
<td>0.67 ± 0.18</td>
</tr>
</tbody>
</table>

Epi = subepicardium; endo = subendocardium.

effects. In another study with mean balloon inflation in 19 patients of 51 ± 12 sec, similar transient hemodynamic changes were noted. However, one must be cautious in applying such results to patients with severe underlying left ventricular dysfunction.

With the desire to perform repeated balloon inflations of longer duration to remodel stenosed coronary arteries, the need to reduce the ischemia distal to the stenosis with blood or other oxygen-carrying mediums becomes important. Several such perfusion systems have been used experimentally and clinically and have proved to be effective in reducing acute myocardial ischemia. However, such perfusion systems are complex and cumbersome. Erbel et al. have reported results in five dogs and 11 patients with an autoperfusion-type catheter; prolongation of time from onset of dilatation to appearance of ischemia was noted in three of the dogs and eight of the patients. Their catheter had a larger profile and fewer sideholes, which may account for some of the difference in results. They did not report coronary blood flow or hemodynamics. The autoperfusion angioplasty catheter used in this study also achieves distal coronary hemoperfusion without any extracorporeal perfusion system, while maintaining balloon inflation for relatively prolonged periods.

Because of the ability of the autoperfusion angioplasty catheter to perfuse myocardium distal to the coronary lesion, it is possible to envisage other situations in which this catheter may be useful. For example, in the event of coronary artery dissection or rupture it may be possible to position this catheter at the site of occlusion and provide distal coronary blood flow while the flap is held against the vessel wall. The dilatation of very proximal large epicardial vessels may be more safely accomplished. Potentially, a similar system may overcome at least some of the several potential hazards in dilating left main stenoses.

In conclusion, this study demonstrates that distal coronary hemoperfusion can be achieved with the autoperfusion angioplasty catheter, resulting in reduction of signs of acute myocardial ischemia. Placement of guiding and balloon catheters even without balloon inflation can interfere with coronary blood flow, a phenomenon not readily detected by usual hemodynamic and electrocardiographic monitoring.

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