Coronary Venous Retroperfusion Support During High Risk Angioplasty in Patients With Unstable Angina: Preliminary Experience

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Synchronized coronary venous retroperfusion was used during coronary balloon angioplasty to support the ischemic myocardium of 20 patients with unstable angina and anatomy at high risk of a coronary event. Hemodynamics and left ventricular function were the major end points of the study. Coronary venous catheterization and retroperfusion were successfully performed in 15 patients. The target vessel was an unprotected left main artery in 2, left anterior descending artery in 10, left circumflex coronary artery in 1 and right coronary artery in 2 patients. A nonsupported balloon inflation (mean 44 ± 13 s) was compared with a later retroperfusion-supported inflation (mean 145 ± 21 s). Right anterior oblique left ventriculograms, aortic blood pressure, pulmonary artery pressure and thermodilution cardiac output were obtained before and during peak untreated and treated balloon inflations and on completion of angioplasty.

All patients had either a baseline left ventricular ejection fraction <0.40 or >40% of contracting myocardium estimated to be at risk for severe ischemia during angioplasty. The cardiac (liters/min per m²) and stroke work (g·mlm²) indexes decreased from mean baseline values of 2.5 ± 0.52 and 52 ± 15 to 1.7 ± 0.47 and 27 ± 12 (mean ± SD), respectively, during nonsupported balloon inflations but decreased only to 2.1 ± 0.52 (p < 0.01 vs. nonsupported) and to 36 ± 14 (p = 0.01 vs. nonsupported), respectively, during retroperfusion-supported inflations. Ejection fraction (n = 8) decreased from a baseline value of 55 ± 13% to 27 ± 7.3% during nonsupported inflations but only to 39 ± 10% during retroperfusion-supported inflations (p = 0.01 vs. nonsupported). Regional wall motion (area change) in the ischemic (target) region was reduced from a baseline value of 49 ± 17% to 11 ± 16% during nonsupported inflations but only to 27 ± 15% during retroperfusion-supported inflations (p < 0.01 vs. nonsupported).

All but two patients had a favorable hemodynamic response to retroperfusion. There were no serious adverse effects related to the procedures and no hospital deaths. It is concluded from this preliminary study that coronary venous retroperfusion appears to be safe, to provide hemodynamic support and to improve left ventricular function during angioplasty in patients with unstable angina and anatomy at high risk of a coronary event.

In recent years, the use of coronary angioplasty has had a major impact in the early management of unstable angina. Initially proposed as an alternative revascularization technique for patients with stable angina and single-vessel coronary artery disease (1), its use and indications rapidly expanded to patients with multivessel coronary disease (2,3) and acute coronary syndromes (4,5), including acute myocardial infarction (6,7).

Within a wide spectrum of lesions for which coronary angioplasty is indicated, specific coronary lesions are known to be associated with a higher incidence of abrupt coronary closure during angioplasty, including presence of a large thrombus, extreme lesion eccentricity and lengthy lesions (8). Patients are also considered to be high risk candidates for angioplasty on the basis of poor left ventricular function or large amounts of contracting myocardium supplied by the target vessel, or both (9).

It has been well documented both in experimental (10) and in clinical studies (11) that severe regional myocardial dysfunction develops very rapidly after complete coronary occlusion, usually within 10 to 20 beats in the absence of significant collateral blood supply. Because many patients may not tolerate coronary occlusion and its consequences during balloon angioplasty, it may be necessary to support the ischemic myocardium and provide sufficient perfusion to vital organs during such an intervention.

To improve the outcome of angioplasty for patients at high risk, a variety of techniques have been recently proposed for supporting the circulation during the procedure (that is, "supported angioplasty" [12,13]). Such support can be accomplished by techniques that primarily provide direct

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myocardial blood supply to the jeopardized region during transient coronary artery occlusion, or primarily provide hemodynamic support, or do both.

Diastolic synchronized retroperfusion is in essence a myocardial circulatory assist technique. It is designed to provide autologous arterial blood to the ischemic myocardium by way of the coronary veins. Retroperfusion has been extensively studied in animal models (14–19) and it has proved to be safe and effective in restoring myocardial function and reducing infarct size. It is now being tested in humans (20–24). In this report we present our initial experience with retroperfusion for support of angioplasty in high risk patients with unstable angina.

**Methods**

**Study patients.** Twenty patients were studied. Patients included in the study had rest angina refractory to maximal pharmacologic therapy in the coronary care unit, or angina with increasing frequency or severity of pain, or both, for ≤2 months before hospital admission. Rest angina was defined as chest pain at bed rest lasting >5 min accompanied by >1 mm ST segment elevation or depression in ≥2 electrocardiographic (ECG) leads and initial creatine kinase MB isoenzyme values ≤2 times the upper limits of normal. Patients were excluded from the study if there were contraindications to administration of an anticoagulant agent, or if they had a terminal illness, severe arterial hypertension (systolic blood pressure >180 mm Hg or diastolic pressure >115 mm Hg, or both), overt heart failure, severe valvular heart disease, akinesia or dyskinesia in the target region, cardiomyopathy, significant hypotension (systolic blood pressure <85 mm Hg) or shock.

**Clinical protocol.** Patients were initially assessed in the coronary care unit for the presence of angina (Canadian Cardiovascular Society class), heart failure (Killip class), associated cardiac abnormalities, general clinical status and drugs. The patients were then transferred to the cardiac catheterization laboratory and diagnostic arteriography was performed using the femoral artery approach. A 5 to 10 mg dose of sublingual isosorbide dinitrate was then administered with increasing frequency or severity of pain, or both, for ≤2 times the upper limits of normal. The culprit lesion was identified and other lesions were then treated. For retroperfusion of the myocardium supplied by the left anterior descending coronary artery, the catheter was positioned in the coronary sinus and advanced as far as possible into the great cardiac vein, avoiding wedging of the catheter. For retroperfusion of the myocardium supplied by the left circumflex or right coronary artery, the catheter was positioned in the coronary sinus and advanced with the use of a 0.018 in. (0.46 cm) diameter guide wire as far as possible into the great cardiac vein, avoiding wedging of the catheter (position 3, described by Berland et al. [21]). For retroperfusion of the myocardium supplied by the left circumflex or right coronary artery, the catheter was positioned in the coronary sinus and advanced with the use of a 0.018 in. (0.46 cm) diameter guide wire as far as possible into the great cardiac vein, avoiding wedging of the catheter (position 3, described by Berland et al. [21]).

For retroperfusion of the myocardium supplied by the left circumflex or right coronary artery, the catheter was positioned in the coronary sinus and advanced with the use of a 0.018 in. (0.46 cm) diameter guide wire as far as possible into the great cardiac vein, avoiding wedging of the catheter (position 3, described by Berland et al. [21]).

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For retroperfusion of the myocardium supplied by the left circumflex or right coronary artery, the catheter was positioned in the coronary sinus and advanced with the use of a 0.018 in. (0.46 cm) diameter guide wire as far as possible into the great cardiac vein, avoiding wedging of the catheter (position 3, described by Berland et al. [21]).

Retroperfusion-supported angioplasty was scheduled for the next day on the basis of high risk coronary anatomy (>40% of myocardium at risk) or low left ventricular ejection fraction, or both. Patients or immediate family members were asked to give written informed consent before the procedure, which was previously approved by the Institutional Ethical Committee. Patients were then given meperidine and diphenhydramine hydrochloride (both 50 mg intramuscularly). Angioplasty was performed with use of the (right) brachial artery approach. The ECG was monitored throughout the procedures.

**Retroperfusion technique.** Detailed operation of the system has been previously described (14–18,21,23). Briefly, the retroperfusion pump consists of an electronic console with an aligned disposable pumping cassette (Retroperfusion Systems). Arterial blood is shunted from the left femoral artery with an 8F single lumen withdrawal catheter with end and side holes. The withdrawal catheter is connected to the inlet of the pumping cassette, and the outlet of the cassette is connected to the infusion lumen of the retroperfusion catheter, which is a radiopaque, 8.5F triple lumen balloon-tipped catheter, with the balloon located 10 mm from its distal end. At full inflation pressure, the balloon is oval shaped and 10 mm in diameter. The balloon is inflated in diastole (second lumen) with a fixed volume of carbon dioxide, in synchronization with each pump stroke. Arterial blood is pumped in diastole by means of a piston activated by ECG triggering. In systole, the balloon deflates to allow for coronary venous blood drainage. The third lumen of the retroperfusion catheter is used for monitoring coronary venous pressures.

**Catheterization procedures.** The retroperfusion catheter was inserted by way of the right brachial vein or the right internal jugular vein. For retroperfusion of the myocardium supplied by the left anterior descending coronary artery, the catheter was positioned in the coronary sinus and advanced with the use of a 0.018 in. (0.46 cm) diameter guide wire as far as possible into the great cardiac vein, avoiding wedging of the catheter (position 3, described by Berland et al. [21]). For retroperfusion of the myocardium supplied by the left circumflex or right coronary artery, the catheter was placed more proximal to the coronary sinus to retroperfuse its terminal tributaries. Coronary venography with use of meglumine diatrizoate (Renografin-76) was performed in all patients to rule out large venous shunts and to verify appropriate compartmentalization of the coronary veins and drainage of the contrast material. At this stage, heparin, 10,000 U, was given intravenously.

A 7F pulmonary artery flotation catheter was inserted by way of the right internal jugular vein or right brachial vein for measurements of pulmonary artery pressures and thermodilution cardiac output. Arterial blood pressure was monitored during the procedure through the side arm of the femoral artery introducer. The left ventricular stroke work index was determined with the following formula: Stroke work index (g·m/m²) = Thermodilution stroke volume index [Mean arterial pressure – Mean pulmonary capillary wedge pressure] × 0.0136.

**Right anterior oblique ventriculograms with use of meglumine diatrizoate, 0.5 ml/kg, were obtained with an 8F pigtail catheter before angioplasty, at peak retroperfusion-**
supported and nonsupported balloon inflations and on completion of angioplasty. End-diastolic and end-systolic volumes were derived from ventriculograms with use of the area-length method described by Sandler and Dodge (25), and global left ventricular ejection fraction was calculated. Regional wall motion (area change) was derived from contrast ventriculograms using a fixed axis (26) and dividing the ventricle into four regions: anterior, apical, inferior and basal walls. Wall motion in the ischemic (target) zone was then contrasted with wall motion in the opposite wall (nonschismic zone).

To compare retroperfusion-supported and nonsupported inflations during angioplasty, the first balloon inflation served as a control (nonsupported) inflation and the second inflation was treated by retroperfusion. Retroperfusion was always initiated simultaneously with balloon inflation. The second angioplasty attempt was made after normalization of the ECG and cardiac output and never <5 min after the first angioplasty occlusion. No drugs were given during the procedures, with the exception of heparin, which was administered to maintain an activated clotting time >400 s.

Successful angioplasty was defined as a residual diameter stenosis <50% by visual analysis of the angiogram, performed by an observer who had no knowledge of patient data, in the absence of complications such as myocardial infarction or bypass surgery.

After the patient was transferred to the coronary care unit, heparin was given intravenously at approximately 1,000 U/h to maintain a partial thromboplastin time of 1.5 to 2.5 times control values. Surgical backup was available for all patients.

Statistical analysis. A statistical analysis of the following variables was performed: heart rate, systolic and diastolic blood pressure, cardiac index, stroke work index, ejection fraction and regional wall motion in the ischemic (target) and nonischemic zones. These variables were first analyzed with use of repeated measures of one-way analysis of variance for differences across the four time periods, that is, before angioplasty, during nonsupported and retroperfusion-supported inflations and after angioplasty. If a significant difference (p < 0.05) was found across the four time periods, a paired t test was performed on the variables between the two time periods of interest, that is, nonsupported versus retroperfusion-supported balloon inflations, and a contrast between the average response at the pre- and postangioplasty periods to the average response during the nonsupported and retroperfusion-supported periods was tested against the one-way analysis of variance mean squared error. Results are expressed as mean values ± SD.

Results

Excluded patients. Retroperfusion was successfully implemented in 15 of the 20 patients (Table 1). Of the other five patients, one had a large venous fistula connecting the anterior interventricular vein to the right atrium, and two patients with previous coronary bypass surgery (one with two previous operations) had a deformed coronary sinus so that appropriate placement of the retroperfusion catheter was not possible. In the fourth patient, the coronary sinus and great cardiac vein dimensions were very large; thus, the coronary venous system could not be compartmentalized after manual inflation of the balloon at the tip of the retroperfusion catheter with concomitant contrast venography. In the fifth patient there was a mechanical failure of the retroperfusion pump. The data from these five patients were excluded from further analysis.

Catheter placement. Among the 15 patients with successfully implemented retroperfusion, the retroperfusion catheter was introduced by way of the right brachial vein in 13 and by way of the right internal jugular vein in 2. Time for placement of the coronary sinus catheter ranged from 1 to 15 min (median 3.5).

Clinical and angiographic characteristics. Of the 15 patients, there were 3 with severe left main coronary artery stenosis who had previously undergone bypass surgery. Five additional patients had triple-vessel disease, four had double-vessel disease and the remaining three had single-vessel left anterior descending coronary artery disease. Seven patients had a previous Q wave myocardial infarction, and seven had a baseline left ventricular ejection fraction <40%. One patient with rest angina and signs of anterior wall ischemia on the ECG developed persistent ST segment elevation and prolonged chest pain while in the coronary care unit and was rushed to the catheterization laboratory for diagnostic catheterization and angioplasty. The left anterior descending coronary artery was not totally occluded. Blood sampling for creatine kinase collected before catheterization showed a fivefold increase in enzyme release, confirming some degree of myocardial necrosis in this patient.

An angiographic image suggestive of coronary artery thrombus in the culprit vessel was found in five patients at angioplasty. With use of the criteria of baseline left ventricular ejection fraction <40% or a target vessel supplying >40% of contracting myocardium, or both, all 15 patients were considered high risk candidates for angioplasty.

Coronary venous retroperfusion (Table 2, Fig. 1 to 4). Retroperfusion was applied at flow rates ranging from 125 to 250 ml/min (median 171). The duration of untreated balloon inflations ranged from 25 to 75 s (mean 44 ± 13), whereas retroperfusion-supported inflations during angioplasty ranged from 90 to 240 s, with a mean retroperfusion pumping time of 145 ± 27 s. Peak coronary venous pressures measured 13 ± 4 mm Hg before angioplasty and 15 ± 3 mm Hg (systolic) during nonsupported balloon inflations and increased to 42 ± 8 mm Hg (diastolic) during retroperfusion-supported angioplasty (range 22 to 60 mm Hg, p < 0.001 vs. baseline or nonsupported inflations). Heart rate and blood pressure measured during the control period, at the end of the nonsupported and retroperfusion-supported balloon in-
Table 1. Clinical and Angiographic Data in 15 Patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)/Gender</th>
<th>Clinical Status</th>
<th>Previous MI</th>
<th>Coronary Stenosis &gt; 50%</th>
<th>Site of Supported Angioplasty</th>
<th>Angiographic Collateral flow</th>
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<tr>
<td>1</td>
<td>45/M</td>
<td>Angina, class IV</td>
<td>No</td>
<td>LADp subtotal; Dia 1 subtotal; LCx 50%</td>
<td>LAD</td>
<td>No</td>
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<tr>
<td>2</td>
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<td>LAD</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
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<td>LADp subtotal; LCx 50%</td>
<td>LAD</td>
<td>No</td>
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<tr>
<td>4</td>
<td>41/F</td>
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<td>LAD/Dia 1*</td>
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<tr>
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<td>57/M</td>
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<td>No</td>
<td>LADp 90%; PDA 50%</td>
<td>LAD</td>
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<tr>
<td>6</td>
<td>70/M</td>
<td>Angina, class IV</td>
<td>Yes</td>
<td>RCA 90%; LADp 100%; Marg 1 70%</td>
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<td>RCA to LAD</td>
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<td>RCA to LAD</td>
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<tr>
<td>8</td>
<td>61/M</td>
<td>Angina, class IV</td>
<td>Yes</td>
<td>LADp 90%; Dia 1 90%</td>
<td>LAD/Dia 1*</td>
<td>No</td>
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<tr>
<td>9</td>
<td>63/M</td>
<td>Angina, class III</td>
<td>Yes</td>
<td>LADp subtotal</td>
<td>LAD/Dia 1*</td>
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<td>LAD/Dia 1*</td>
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<tr>
<td>11</td>
<td>70/M</td>
<td>Rest angina</td>
<td>Yes</td>
<td>LADp 90%; Dia 1 90%; RCA 100%</td>
<td>LAD/Dia 1*</td>
<td>No</td>
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<tr>
<td>12</td>
<td>62/M</td>
<td>Angina, class III</td>
<td>Yes</td>
<td>RCA 90%; LCxp 90%</td>
<td>LCx</td>
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<tr>
<td>13</td>
<td>66/M</td>
<td>Angina, class IV</td>
<td>No</td>
<td>LM 90%; LAD graft 100%; Marg 1 graft 100%; mid LCx 70%</td>
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<tr>
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<tr>
<td>15</td>
<td>59/M</td>
<td>Angina, class III</td>
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<td>LM 90%; RCA graft 90%; mid RCA 90%; LIMA-LAD 90%</td>
<td>LIMA-LAD</td>
<td>No</td>
</tr>
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</table>

*Indicates occlusion of both arteries during balloon inflation. AMI = acute myocardial infarction; class III and class IV = Canadian Cardiovascular Society classes III and IV; Dia 1 = first diagonal branch of the left anterior descending artery; F = female; LAD = left anterior descending coronary artery; LADp = proximal left anterior descending coronary artery; LCx = left circumflex coronary artery; LCxp = proximal left circumflex coronary artery; LIMA-LAD = left internal mammary artery graft-left anterior descending artery anastomosis; LM = left main coronary artery; M = male; Marg 1 = first marginal branch of the proximal left circumflex coronary artery; PDA = posterior descending branch of the right coronary artery; RCA = right coronary artery.

Hemodynamics. With use of repeated measures of one-way analysis of variance, systolic blood pressure, cardiac index, stroke work index, left ventricular ejection fraction and ischemic zone wall motion showed a significant difference (p < 0.05) across the four time periods. In addition, a contrast between the average response at the pre- and postangioplasty periods to the average response during nonsupported and retroperfusion-supported inflations tested against the one-way analysis of variance mean squared error also showed a significant difference (p < 0.05) for these five variables. Coronary artery occlusion during nonsupported balloon inflations resulted in a significant reduction in systolic blood pressure, from a baseline of 116 ± 16 to 104 ± 22 mm Hg, p < 0.05. Systolic pressure tended to increase during retroperfusion-supported inflations and to return to preangioplasty levels after the procedure. Thermodilution cardiac output and left ventricular stroke work decreased significantly during nonsupported inflations but decreased significantly less during retroperfusion-supported inflations (Fig. 1 and 2).

Ventriculography. Patients with severe left main coronary stenoses or baseline pulmonary capillary wedge pres-

Table 2. Hemodynamic Variables Before and During Nonsupported and Retroperfusion-Supported Angioplasty and After the Procedure

<table>
<thead>
<tr>
<th></th>
<th>Before Angioplasty</th>
<th>During Angioplasty</th>
<th>After Angioplasty</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Without SRP</td>
<td>With SRP</td>
<td></td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>68 ± 20</td>
<td>72 ± 20</td>
<td>72 ± 20</td>
<td>0.30</td>
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<tr>
<td>SBP (mm Hg)</td>
<td>116 ± 18</td>
<td>104 ± 22</td>
<td>108 ± 21</td>
<td>0.0008</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>74 ± 10</td>
<td>70 ± 13</td>
<td>73 ± 12</td>
<td>0.23</td>
</tr>
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</table>

*One-way analysis of variance, difference across the four time periods. DBP = diastolic blood pressure; HR = heart rate; SBP = systolic blood pressure; SRP = supported retroperfusion.
Figure 1. The cardiac index (CI, L/min/m²) in 14 patients before (PRE) and during nonsupported (-SRP) and retroperfusion-supported (+SRP) balloon inflations during coronary angioplasty, and on completion of the procedure (POST). Mean values at each time are indicated by the barred circles (p < 0.001 for differences across the four time periods; p = 0.0002 during nonsupported vs. retroperfusion-supported; p < 0.05 before or after vs. nonsupported or retroperfusion-supported balloon inflations).

sure >22 mm Hg, or both, had only one ventriculogram before angioplasty. Thus, complete global and regional left ventricular function data derived from contrast ventriculograms were available in eight patients. These data are presented in Figures 3 and 4, respectively. Global left ventricular ejection fraction decreased from a baseline of 55 ± 13% to 27 ± 7.3% during nonsupported inflations, but decreased to only 39 ± 10% during retroperfusion-supported inflations (p = 0.0016 vs. nonsupported inflations). After angioplasty, the ejection fraction was 58 ± 7.6%. Regional wall motion in the ischemic zone (Fig. 4) decreased significantly less during retroperfusion-supported angioplasty, from a baseline of 49 ± 17% to 11 ± 15% during nonsupported inflations compared with 27 ± 15% during retroperfusion-supported inflations (p < 0.01 vs. nonsupported infla-

Figure 2. The stroke work index (SWI, g·m/m²) in 14 patients (p < 0.001 for differences across the four time periods; p = 0.001, -SRP vs. +SRP; p < 0.05, PRE or POST vs. -SRP or +SRP). Mean values at each time are indicated by the barred circles. Abbreviations as in Figure 1.

Figure 3. Global left ventricular (LV) ejection fraction in eight patients before and during unsupported and retroperfusion-supported balloon inflations during angioplasty, and after the procedure (p < 0.001 for differences across the four time periods; p < 0.05 PRE or POST vs. -SRP or +SRP). Abbreviations as in Figure 1.

Figure 4. Regional wall motion (RWM) in eight patients in the angioplasty target area (ischemic zone) and in the opposite wall (nonischemic zone) (p < 0.001 for differences across the four time periods in the ischemic zone; p = NS in the nonischemic zone; p < 0.01 PRE or POST vs. -SRP or +SRP). Abbreviations as in Figure 1.
There was no significant change in wall motion in the nonischemic zone. Figure 5 shows left coronary arteriograms from Patient 4, and contrast ventriculograms from the same patient are shown in Figure 6.

Complications. There were no serious complications during the procedures. Two patients (Patients 7 and 13) had a local hematoma at the puncture site in the groin, requiring transfusions of 1 and 2 U of blood, respectively. Transient atrial arrhythmias occurred in four patients during coronary sinus catheterization, but spontaneously subsided a few minutes after catheter placement. There were no deaths related to the procedures or during the hospitalization period.

Angioplasty. Coronary angioplasty was performed in 1.4 vessels/patient and was successful in 95% of vessels, including dilation of the left main coronary artery in three patients. Mean coronary stenosis diameter decreased from 91% to 30%. None of the patients sustained a myocardial infarction.

Figure 5. Left coronary arteriograms in Patient 4. A, Before angioplasty there is a discrete, severe obstruction with an apparent filling defect in the proximal left anterior descending artery (arrow) just before the first diagonal branch. B, The inflated balloon during retroperfusion-supported angioplasty (the arrow points to the tip of the retroperfusion catheter). C, The proximal left anterior descending artery (arrow) after angioplasty.

Figure 6 (opposite page). Patient 4. Sequential contrast left ventriculograms at end-diastole (left panels) and end-systole (right panels). A and B, Before angioplasty, there is hypokinesia of the anterior wall and apex, with a global ejection fraction of 37%. C and D, During nonsupported balloon inflations, there is akinesia of the anterior wall and apical dyskinesia (arrows) and hypercontraction in the inferior wall, with an ejection fraction of 26%. E and F, During retroperfusion-supported inflation, regional wall motion in the ischemic region improves and hypercontraction in the inferior wall decreases, with an ejection fraction of 32%. G and H, Immediately after angioplasty, there is only mild hypokinesia in the apical region and global ejection fraction increased to 55%.
or abrupt coronary closure after angioplasty and none required emergency bypass surgery.

Discussion

The high risk patient for coronary angioplasty. An increasing number of patients with atherosclerotic coronary artery disease are considered to be high risk candidates for the procedure. In a relatively large proportion of such patients, temporary obstruction of the target vessel imposes an unacceptable risk for the procedure. Included in this category are patients with low baseline left ventricular ejection fraction, and patients with a target vessel supplying large portions of contracting myocardium, in whom hemodynamic collapse or pulmonary edema, or both, are more likely to occur during angioplasty. Patients with unstable angina may have these conditions as well as an increased risk for developing abrupt coronary closure during or immediately after angioplasty (4,5). During elective angioplasty, 4% to 7% of the patients develop abrupt coronary artery closure (27,28). A significant proportion of these patients currently undergo emergency bypass surgery with an approximate 50% incidence of perioperative myocardial infarction and a reported mortality rate of approximately 7% (27,29). Therefore, it is important to develop rational therapeutic strategies for temporary circulatory assistance during high risk intracoronary arterial interventions.

Supported angioplasty. The term assisted or supported angioplasty has been suggested to characterize the prophylactic use of circulatory assist devices during high risk angioplasty (12). Obviously, some of these techniques can also be used in a standby fashion to be implemented in case complications occur.

Several techniques have been proposed for support of high risk angioplasty, including techniques that provide systemic circulatory or hemodynamic support and techniques that primarily provide myocardial blood supply. Among the first group of techniques are the intraaortic balloon pump (30), hemopump (31), percutaneous femorofemoral cardiopulmonary bypass (12) and percutaneous left atrial-aortic bypass pumping (32). These techniques do not provide direct myocardial perfusion. Among the myocardial circulatory assist procedures there are three general categories: 1) techniques that provide active myocardial perfusion, such as coronary venous retroperfusion (21), anterograde diastolic phased coronary perfusion (33) or active anterograde catheter hemoperfusion (34); 2) techniques that provide passive myocardial perfusion, such as the Stack autoperfusion catheter (35); and 3) techniques that provide perfusion with blood substitutes, such as perfluorocarbons (36).

Clinical experience with the majority of these devices for support of high risk angioplasty is still relatively limited, and there are no controlled clinical studies comparing their relative efficacy under this condition. Clearly, there are advantages and disadvantages inherent to each of these techniques for specific clinical situations in patients at high risk for angioplasty.

Retroperfusion for support of high risk angioplasty. Preliminary studies (20,21) of retroperfusion for support of left anterior descending coronary artery angioplasty in patients with stable angina have demonstrated the feasibility of this technique, with minor complications in few patients. Berland et al. (21) recently reported significant reduction in chest pain and ECG ST segment elevations during retroperfusion-supported balloon inflations during angioplasty, along with a moderate improvement in global left ventricular ejection fraction. However, the efficacy of retroperfusion in patients at high risk during angioplasty has not been clearly demonstrated.

In this study we sought to investigate the effects of retroperfusion on hemodynamics as well as global and regional left ventricular function using contrast ventriculography in a subset of patients at high risk for angioplasty. Hemodynamic improvement was observed in 13 of the 15 patients studied. However, based on our limited observations we cannot be sure that retroperfusion alone will be sufficiently efficacious to prevent hemodynamic collapse in patients at high risk or to rescue patients who develop severe hypotension or cardiogenic shock after angioplasty. In our small series, only two patients developed severe hypotension during nonsupported angioplasty and in both patients blood pressure was well maintained during retroperfusion-supported occlusions.

Efficacy of retroperfusion. On the basis of previous experimental studies (14-17) and our own limited experience in the catheterization laboratory, several points appear to be critical for efficacy of retroperfusion. First, inflation of the balloon during diastolic retroperfusion must be fully occlusive to compartmentalize the coronary venous system. In some patients, positioning of the catheter proximally in the coronary sinus or even in the midportion of the great cardiac vein will not be completely occlusive during balloon inflation, allowing part of the retroperfusate to regurgitate into the right atrium and precluding diastolic coronary venous pressure augmentation during retroperfusion. Second, appropriate positioning of the catheter tip also seems to be critical. For example, for retroperfusion of the left anterior descending coronary artery supply region, the tip of the retroperfusion catheter should be positioned deep into the great cardiac vein, in the vicinity of the anterior interventricular vein (Fig. 5). Other factors may be important, such as more coaxial retroperfusion flows. A third crucial point is diastolic coronary venous pressure augmentation during retroperfusion. Previous experimental studies (37-41) have indicated that effective delivery of the retroperfusate is pressure-dependent. Diastolic pressure augmentation during synchronized retroperfusion depends on three major factors: 1) effective compartmentalization of the coronary venous bed, 2) retroperfusion flow rate, and 3) coronary venous shunting.

An important observation in human studies (21) com-
pared with previous reports in animals is the lower diastolic pressure augmentation during retroperfusion in humans. As previously mentioned, several factors could be responsible for this difference, including the richer thebesian circulation in humans compared with animals. In our study, coronary venous pressures were higher than in a recent study (21), but were still much lower than the maximal safety limit of 60 mm Hg peak pressure. This could be explained in part by the fact that we positioned the retroperfusion catheter deeper in the great cardiac vein for perfusion of the left ventricular anterior wall. Also, retroperfusion flow rates in our study were higher than those reported in the study of Berland et al. (21). Because retroperfusion efficacy seems to be directly related to the coronary venoarterial and coronary venous-left ventricular diastolic pressure gradients, as previously suggested in animal studies (14,37-41), it may be possible to enhance efficacy of retroperfusion by optimal catheter positioning and catheter operation mechanisms that can provide higher coronary venous pressures.

Limitations of the study. One of the limitations of this study is that retroperfusion-supported inflations during angioplasty were not randomized. Because the retroperfusion-supported inflations were expected to be of longer duration, we decided not to randomize balloon inflations for the following reasons: First, a more prolonged initial retroperfusion-supported balloon inflation could have caused myocardial stunning (42) or ischemic preconditioning (43), precluding adequate assessment of ischemic changes during later inflations. Second, a more prolonged initial unsupported inflation compared later against a retroperfusion-supported inflation of the same duration would be associated with the same problems. To our knowledge, there is no evidence that a single coronary occlusion ≤60 s (only one patient had an initial unsupported occlusion >1 min) is associated with significant collateral flow recruitment, ischemic preconditioning or myocardial stunning.

Another potential problem is that repeated ventriculograms over a relatively short period of time could have affected our hemodynamic and ventricular function measurements adversely, although we waited for normalization of the ECGs and cardiac output and extended the time interval between supported and nonsupported balloon inflations as much as possible. Also, contrast ventriculograms could not be obtained in all patients.

State of the art retroperfusion equipment (with flow rate capability up to 250 ml/min) could be applied to only the last six patients in our study. It is possible that higher flow rates would have improved our results. Because the pumping time was restricted to a maximum of 4 min in this preliminary study, we cannot rule out the possibility of enhanced effectiveness (or even loss of efficacy) if retroperfusion had been extended for prolonged periods of time. Clearly, further clinical evaluation with optimized flows and particularly ideal coronary venous pressures is needed before issues such as retroperfusion safety and efficacy can be definitely assessed.

Although two of the three patients who had supported angioplasty of the right or left circumflex coronary artery had a positive response, more studies are needed to assess retroperfusion efficacy in these perfusion territories. Selective catheter positioning in the posterior ventricular or left marginal vein could be critical for perfusion of the left ventricular posterior and lateral walls, respectively, but additional factors such as better compartmentalization of the coronary venous bed and improved catheter stability may also be important.

Conclusions. This preliminary study of retroperfusion-supported angioplasty suggests that retroperfusion may be of value in supporting high risk intracoronary intervention procedures. Retroperfusion-supported angioplasty appears to be safe, and a moderate positive hemodynamic response, possibly secondary to improvements in myocardial perfusion, was observed. Although this effect was seen in most of our patients, it is not possible to conclude from our data whether retroperfusion alone will be sufficient for hemodynamic support during high risk angioplasty, particularly in patients with severe hypotension or shock. Other techniques for myocardial and hemodynamic support are currently being investigated; it is clear that many of them are not mutually exclusive, and further studies are needed to clarify not only which patients need support during intracoronary intervention, but also which techniques alone or in combination will be most appropriate for specific clinical situations.

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References


