Synchronized Coronary Venous Retroperfusion for Support And Salvage of Ischemic Myocardium During Elective and Failed Angioplasty

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To determine the safety and efficacy of synchronized coronary venous retroperfusion during brief periods of ischemia, 30 patients undergoing angioplasty of the left anterior descending coronary artery were studied. Each patient underwent a minimum of two angioplasty balloon inflations. Alternate dilations were supported with retroperfusion; the unsupported inflations served as the control inflations. Synchronized retroperfusion was performed by pumping autologous femoral artery blood by means of an electrocardiogram-triggered retroperfusion pump into the great cardiac vein through a triple lumen 8.5F balloon-tipped retroperfusion catheter inserted percutaneously from the right internal jugular vein. Clinical symptoms, hemodynamics and two-dimensional echocardiographic wall motion abnormalities were analyzed.

Retroperfusion was associated with a lower angina severity score (0.8 ± 1 vs. 1.2 ± 1) and delay in onset of angina (53 ± 31 vs. 37 ± 14; p < 0.05) compared with the control inflations. The magnitude of ST segment change was 0.11 ± 0.14 mV with retroperfusion and 0.16 ± 0.17 mV without treatment (p < 0.05). The severity of left ventricular wall motion abnormality was also significantly (p < 0.01) reduced with retroperfusion compared with control (0.7 ± 1.4 [hypokinesia] vs. −0.3 ± 1.6 [dyskinesia]). There were no significant changes in hemodynamics, except in mean coronary venous pressure, which increased from 8 ± 3 mm Hg at baseline to 13 ± 6 mm Hg with retroperfusion. Four patients required prolonged retroperfusion for treatment of angioplasty-induced complications. The mean retroperfusion duration in these patients was 4 ± 2 h (range 2 to 7). In the three patients who underwent emergency bypass surgery, the coronary sinus was directly visualized during surgery and found to be without significant injury.

There were no major complications. Minor adverse effects were transient atrial fibrillation (n = 2), jugular venous catheter insertion site hematomas (n = 4) and atrial wall staining (n = 1), all of which subsided spontaneously. Thus, retroperfusion significantly reduced and delayed the onset of coronary angioplasty-induced myocardial ischemia and provided effective supportive therapy for failed and complicated angioplasty.

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Percutaneous transluminal coronary angioplasty is an effective treatment for coronary artery stenosis, but results in transient interruption of regional blood supply, which can cause myocardial ischemia with consequent hemodynamic, electrophysiologic, metabolic and functional derangements (1–3). These ischemic changes are of particular concern in patients with a large area of jeopardized myocardium or significant preexisting left ventricular dysfunction. Furthermore, acute closure of the dilated coronary artery occurs in approximately 5% of all angioplasty procedures (4). This complication is usually managed by coronary bypass surgery but may sustain a mortality rate as high as 7% (5,6).

Among techniques employed in an attempt to mitigate these ischemic derangements are the administration of pharmacologic agents and infusion of oxygenated fluorocarbon solutions or arterial blood through the angioplasty catheter (7–11). These techniques allow extension of the angioplasty balloon inflation time, but have certain limitations. The requirement of some of the latter techniques for a larger catheter system limits their ability to cross a severely stenotic lesion or pass distally within a tortuous vessel. Perfusion may also be ineffective when there are additional sequential stenoses or when the perfusion catheter obstructs a significant side branch. Percutaneous femorofemoral cardiopulmonary bypass, hemopump left ventricular assist and intraaortic balloon pumping devices may provide systemic support.
circulatory support and reduce myocardial oxygen demand; however, blood supply to the jeopardized myocardium is not enhanced by these techniques and therefore myocardial ischemia may persist (12-14).

Synchronized coronary venous retroperfusion is a technique that provides perfusion of the patient's arterial blood to the jeopardized myocardium retrogradely through the coronary veins. Because perfusion is retrograde rather than anterograde, its efficacy is not influenced by the number, location or degree of stenoses, tortuosity or branching of the coronary artery. This method has been extensively investigated in animals (15-22) and has been shown to provide significant myocardial support in preliminary clinical studies (23-30).

Coronary angioplasty offers a unique opportunity to examine the physiologic response to recurrent transient ischemic episodes (3). Therefore, using angioplasty as a short and reproducible ischemic model, the efficacy of various support systems has been studied (7-13). The purpose of the present study was to determine the safety and efficacy of a new synchronized coronary venous retroperfusion system (Retroperfusion Systems, Inc.) in this ischemic model.

Methods

Study design. The study included 43 patients with ≥70% stenosis of the left anterior descending artery scheduled for angioplasty of the artery at Cedars-Sinai Medical Center. The patients were selected if the investigator believed that balloon inflation would result in significant ischemia by obstruction of blood flow to the first septal perforator or a large first diagonal branch of the left anterior descending coronary artery. Informed consent was obtained from all patients with use of an institutional and Food and Drug Administration-approved human investigation form. In all patients, a 9F sheath was introduced percutaneously into the right internal jugular vein for insertion of the retroperfusion catheter, followed by placement of 8F arterial sheaths in both femoral arteries.

Coronary angioplasty. Coronary angioplasty was performed in the standard manner. The effects of a minimum of two angioplasty balloon inflations were studied in each patient. Retroperfusion was applied during alternate balloon inflations, the order of which was randomized. In some patients, the first angioplasty balloon inflation was of brief duration (30 s) and performed to ensure proper positioning of the balloon within the stenosed segment of the coronary artery. This inflation was not included in the analysis.

All patients received heparin to maintain the activated clotting time between 360 and 480 s. Hemodynamic variables (heart rate, aortic blood pressure and coronary venous pressure) and a single precordial electrocardiographic (ECG) lead (V2 to V3) was monitored and continuously recorded at 25 mm/s on an Electronics for Medicine VR-12 physiologic recorder.

The time to onset of angina was determined during all unsupported and retroperfusion-supported-balloon inflations. The severity of the pain was assessed on a semiquantitative scale of 0 to 4 (0 = no pain, 1 = mild, 2 = moderate, 3 = severe, 4 = intolerable). ST segment change was measured 0.06 s after the J point and expressed as absolute change from the baseline measurement.

Quantitative two-dimensional echocardiography. Two-dimensional echocardiograms were recorded before and during each balloon inflation in apical two- or four-chamber views using an Advanced Technology Laboratories Ultra Mark VIII echocardiograph. The echocardiographic window, contrast settings and depth were optimized during baseline imaging and then kept constant throughout the study. The images were digitized from videotape into a cine loop format using a commercial computerized analysis system (Microsonics, Inc.). Because the duration of the treated and control balloon inflations was not identical, the untreated being of shorter duration, echocardiographic images during treated inflations were analyzed at similar durations as the matched untreated inflations. A modified centerline analysis method as described by Jaffe et al. (9) was used to quantify extent and severity of regional left ventricular wall motion abnormality. Extent was expressed as the total number of chords of the entire left ventricular perimeter that were affected. Severity was the degree of percent chordal shortening in the 10 most affected contiguous chords. Global left ventricular ejection fraction was calculated with the modified Simpson's rule.

The retroperfusion system. The retroperfusion device consists of an electronic pumping console, a specially designed retroperfusion catheter (Fig. 1) and an arterial catheter. Arterial blood is withdrawn from the femoral artery through a 25 cm long 8F catheter, featuring end and multiple side holes. This catheter is introduced through a sheath.
Synchronized retroperfusion during angioplasty facilitated catheter placement. Each case to place the catheter deep into the coronary sinus, coronary venous drainage.

The third retroperfusion catheter lumen is used to monitor tension flow is interrupted and the balloon deflated to facilitate coronary venous pressure. During systole, the retroperfusion pump cassette, which is housed within the system console. Arterial blood is pumped during diastole by means of a piston whose motion is triggered by the R wave of the monitored ECG. The outlet of the pumping cassette is connected to the infusion lumen of the coronary sinus catheter (Fig. 2), which is a radiopaque 8.5F triple lumen catheter, featuring an inflatable balloon located 1 cm from the distal end of the catheter. Carbon dioxide gas is delivered through the catheter’s second lumen to inflate the balloon during diastole (maximal diameter 10 mm at full inflation). The third retroperfusion catheter lumen is used to monitor coronary venous pressure. During systole, the retroperfusion flow is interrupted and the balloon deflated to facilitate coronary venous drainage.

Coronary sinus catheterization. An attempt was made in each case to place the catheter deep into the coronary sinus, preferably into the great cardiac vein with the tip of the catheter distal to the posterior vein of the left ventricle. Contrast material was hand-injected through the infusion lumen of the catheter into the coronary veins with the catheter balloon inflated to confirm both adequate catheter positioning and proper occlusion of the coronary vein by the balloon (Fig. 3). In three patients, a guide wire was used to facilitate catheter placement.

Modifications of the retroperfusion system. Changes were made in the catheter configuration and pump system during the course of the study. The objective was to optimize the retroperfusion system to permit use of larger diameter balloons on the retroperfusion catheter and obtain higher flow levels, and consequently higher coronary venous pressures, and thus be able to perform retroperfusion from proximal positions in the coronary sinus when distal catheter placement was not possible. The first eight patients were studied with use of an autoinflatable balloon retroperfusion catheter with two lumens and a maximal flow rate of 96 ml/min. The next eight were studied with use of a triple lumen gas-activated balloon catheter with dual-valve pumping cassettes, providing maximal flow rates of 124 ml/min. The last 14 patients were studied with use of the same triple lumen gas-activated retroperfusion catheter, but with a bladder pump cassette delivering maximal flow rates of 250 ml/min.

Statistics. All data are presented as mean values ± 1 SD. The change from preangioplasty balloon inflation to peak angioplasty balloon inflation in hemodynamic variables, magnitude of ST segment change and echocardiographic data was analyzed by the two-tail paired t test. Comparisons between the untreated and retroperfusion balloon inflation groups were made by the unpaired t test with these exceptions: the time of onset of chest pain and severity score of angina were analyzed by the Mann-Whitney rank-sum test and the incidence of ST segment change and angina was compared with chi-square analysis.

Results

Feasibility. Catheterization of the coronary sinus was successful in 36 (84%) of 43 patients, with a mean insertion time of 2.6 min (range 0.5 to 10) after the catheter was placed in the right atrium. Of the seven unsuccessful cases, the jugular vein could not be catheterized in three, the catheter could not be placed in the coronary sinus in three, and fluoroscopy demonstrated staining of the right atrial wall after contrast injection through the catheter in one case. In this patient no further attempts at coronary sinus catheterization were made, the staining disappeared after 10 min and the patient’s echocardiogram was normal. Six of the 36 patients undergoing catheterization did not complete the study. In three of the six, coronary angioplasty could not be performed for technical reasons; in one patient, ventricular fibrillation developed during the first control angioplasty balloon inflation and the patient was sent directly for coronary bypass surgery and in two patients, a stable coronary venous catheter position could not be maintained with pumping.

The retroperfusion technique was thus feasible in 34 (79%) of 43 patients, but because of the reasons just enumerated, only 30 patients completed the protocol. These patients underwent 128 angioplasty balloon inflations: 61 inflations were treated with synchronized retroperfusion and 67 were untreated. The mean duration of the retroperfused and untreated inflations was 81 ± 21 and 73 ± 18 s,
respectively (p < 0.01). The clinical characteristics of the 30 patients are listed in Table 1.

Hemodynamics. Heart rate and diastolic blood pressure did not change significantly during retroperfusion, but systolic pressure decreased significantly during untreated balloon inflations (from 125 ± 22 to 108 ± 24 mm Hg) and during retroperfusion (from 120 ± 22 to 111 ± 21 mm Hg). The mean coronary venous pressure was 13 ± 6 mm Hg (range 4 to 26) with retroperfusion compared with 8 ± 3 mm Hg (range 1 to 14) without retroperfusion (p < 0.01). The peak coronary venous pressure was 29 ± 12 mm Hg (range 6 to 59) with retroperfusion and 12 ± 5 mm Hg (range 4 to 26) without retroperfusion (p < 0.01) (Fig. 4). Coronary venous pressure did not change during angioplasty balloon inflations.

Angina. Angina occurred in 40% of the angioplasty balloon inflations supported by retroperfusion and in 53% of the unsupported inflations. The time to onset of angina was 53 ± 31 s in the retroperfusion-supported inflations compared with 37 ± 14 s without retroperfusion (p < 0.05). The angina severity score was 0.8 ± 1 with retroperfusion compared with 1.2 ± 1 without retroperfusion (p < 0.05).

ST segment changes. ST segment change (≥0.1 mV) occurred in 46% of the balloon inflations with retroperfusion compared with 52% of the control inflations. The magnitude of the ST segment change was 0.11 ± 0.14 mV with retroperfusion and 0.16 ± 0.17 mV without retroperfusion (p < 0.05), despite longer duration of the inflations supported with retroperfusion.

Two-dimensional echocardiography (Table 2). Echocardiograms were recorded in 23 of the 30 patients. Quantitation of the echocardiograms was not possible in eight patients because of poor image quality. Moreover, two patients did not develop any ischemia during the angioplasty balloon inflations performed without retroperfusion and were not.
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*Prolonged retroperfusion; Ant = anterior; ASA = aspirin; Assoc = associated; BB = beta-blocker; CABG = coronary artery bypass grafting; CB = calcium channel blocker; CCS = Canadian Cardiovascular Society class; DM = diabetes mellitus; EF = left ventricular ejection fraction; F = female; HTN = hypertension; Inf = inferior; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; LMCA = left main coronary artery; M = male; MI = myocardial infarction; NTG = nitroglycerin; Occl = total occlusion; PTCA = coronary angioplasty; RCA = right coronary artery; SRP-Supp = retroperfusion-supported; patient numbers in italics indicate patients with analyzable echocardiograms; = missing data. Note: All coronary artery stenoses are marked positive only if >70% narrowing except of the left main lesion.

Global function (Table 2). Left ventricular ejection fraction decreased from 51 ± 13% to 43 ± 8% (p < 0.05) with angioplasty balloon inflations supported by retroperfusion compared with 52 ± 9% to 32 ± 10% (p < 0.01) in the untreated inflations. The difference in ejection fraction change was statistically significant (p < 0.01) between groups (Fig. 5A).

Regional function (Table 2). The ischemic zone percent chordal shortening decreased from 1.5 ± 1.7% at baseline to 0.7 ± 1.4% (mild hypokinesia) during the balloon inflations with retroperfusion, whereas in the control inflations, the ischemic zone percent chordal shortening decreased from 1.6 ± 1.6% to −0.3 ± 1.6% (p < 0.01), the negative value indicating dyskinesia of the regional wall (Fig. 5B). The difference in percent chordal shortening during angioplasty without and with retroperfusion reached statistical significance (p < 0.01). The extent of left ventricular wall motion abnormality during the angioplasty balloon inflation was significantly less with retroperfusion (21 ± 9%) compared with that during inflation without retroperfusion (36 ± 12%) (p < 0.01) (Fig. 5C).

Hematology. The mean red blood cell counts, hematocrit, hemoglobin and platelet counts were 4.5 million/mm³, 40.4%, 13.7 g/dl and 212,000/mm³, respectively, before retroperfusion and 4.4 million/mm³, 39.8%, 13.3 g/dl and 205,000/mm³ after completion of the protocol. The plasma-free hemoglobin increased from 5.6 mg/dl before retroperfusion to 21.7 mg/dl after retroperfusion (p = 0.25). These
Figure 4. Mean and maximal coronary venous pressure with and without synchronized retroperfusion (SRP) at three different flow rates in all the patients. Triangles = retroperfusion flow rate of 83 ± 12 ml/min; closed circles = flow rate of 115 ± 10 ml/min; open circles = retroperfusion flow rate of 203 ± 44 ml/min.

values include the four patients who underwent prolonged retroperfusion pumping.

Complications. There were no major complications due to retroperfusion. Minor adverse effects included transient atrial fibrillation (n = 2), hematoma at the internal jugular vein insertion site (n = 4) and atrial wall contrast agent staining (n = 1). All these complications resolved completely without specific therapy.

Retroperfusion During Complicated/Failed Angioplasty: Case Reports

Four patients required longer periods of synchronized retroperfusion because of postangioplasty abrupt occlusion in three patients and intolerable angina during the untreated angioplasty balloon inflations in the fourth patient.

Case 1 (Fig. 6). A 64 year old man presented with progressive exertional angina due to a 95% proximal left anterior descending coronary artery stenosis involving the first septal perforator (Fig. 6A). Five minutes after completion of the angioplasty-retroperfusion protocol, he suddenly developed severe chest pain, hypotension (blood pressure <60 mm Hg) and complete heart block; global hypokinesia was seen on the echocardiogram (Fig. 6C). Intracoronary nitroglycerin, right ventricular pacing and dopamine infusion did not reverse the cardiogenic shock, which was determined by angiography to be due to postangioplasty total occlusion of the proximal left anterior descending coronary artery (Fig. 6B). The retroperfusion catheter was repositioned and retrograde pumping begun in the hope of maintaining viability of the jeopardized myocardium. Within minutes the chest pain abated, blood pressure stabilized at 90 to 100 mm Hg and echocardiography showed marked improvement in global wall motion of the left ventricle (Fig. 6C). The patient was supported by retroperfusion for 2.5 h while several angioplasty balloon dilations were attempted but failed and the patient was sent for emergency coronary bypass surgery. The patient underwent successful double-vessel bypass grafting. The coronary sinus appeared normal on direct visualization during surgery. The patient had an uneventful hospital course and left the hospital with a left ventricular ejection fraction of 61% on radionuclide scans.

Case 2. A 73 year old man with diabetes, hypertension and a past history of myocardial infarction presented with severe chest pain. The ECG revealed complete right bundle branch block and the coronary angiogram showed 30% stenosis of the left main coronary artery, two severe serial stenoses in both the mid left anterior descending and proximal left circumflex coronary arteries and a severe proximal stenosis in the right coronary artery. During the angioplasty procedure for the left coronary arteries, both vessels kept intermittently occluding with development of significant ischemia as evidenced by severe angina. Echocardiograms were not recorded in this patient. Retroperfusion was performed throughout the 2 h angioplasty procedure with relief of the angina. Eventually both vessels were dilated with residual stenoses of 40%, but the patient died 7 days later.

Table 2. Echocardiographic Results in 13 Patients

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<th>Untreated Balloon Inflations</th>
<th>Retroperfusion During Inflations</th>
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<tr>
<td></td>
<td>Baseline</td>
<td>Balloon Inflation</td>
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<tr>
<td>Regional function</td>
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<td>Severity WMA (%CS)</td>
<td>1.6 ± 1.6</td>
<td>−0.3 ± 1.6∗</td>
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<td>Extent WMA (%LV)</td>
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<td>Global function</td>
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<tr>
<td>Ejection fraction (%)</td>
<td>52 ± 9</td>
<td>32 ± 10∗</td>
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∗p < 0.01 versus baseline, †p < 0.01 versus untreated; ‡p < 0.05. %CS = percent chordal shortening; %LV = percent of the left ventricle; WMA = wall motion abnormality.
At postmortem examination, the cause of death was found to be a fresh infarction in the left circumflex coronary artery territory. The coronary sinus and veins were normal.

Case 3 (Fig. 7). A 72 year old woman with diabetes, hypertension and congestive heart failure presented with unstable angina and anterolateral ischemic ECG changes. She had 90% complex stenoses of both the proximal left anterior descending (Fig. 7A) and left circumflex coronary arteries and severe sequential stenoses of the right coronary artery. The angioplasty procedure of the proximal left anterior descending coronary artery was complicated by rupture of the angioplasty balloon two times, followed by dissection of the left main coronary artery. The angioplasty procedure was therefore abandoned. The patient underwent prophylactic retroperfusion during the angioplasty procedure and while awaiting coronary bypass surgery; retroperfusion continued for a total of 7 h from the start of angioplasty to the institution of cardiopulmonary bypass in the operating room, during which time she was clinically stable. At operation, the coronary sinus was found to be normal and there was no evidence of acute myocardial infarction. At 1 year, the patient is asymptomatic and the ECG shows only a loss of the R wave in lead V₁ along with the preexisting anterolateral ischemic changes.

Case 4. A 62 year old man was admitted to the hospital with unstable angina. Angiography revealed two discrete 95% proximal stenoses of the left anterior descending coronary artery. During angioplasty, he began complaining of severe angina when the guidewire was inserted across the lesion even before the angioplasty balloon catheter was inserted. Synchronized retroperfusion was started and alleviated the angina. Echocardiograms were not recorded in this patient. Retroperfusion was continued during 13 successive angioplasty balloon inflations and thus the patient had to be excluded from the protocol because control inflations were not possible. Because angioplasty was not successful, the patient underwent coronary bypass surgery with saphenous vein grafts to the diagonal, circumflex and posterior descending arteries and an internal mammary graft to the left anterior descending coronary artery. The coronary sinus and veins were normal. The patient is asymptomatic at 2 years.

Discussion

In this study in 36 patients coronary sinus retroperfusion during balloon angioplasty was safe, feasible and effective in ameliorating and delaying the onset of ischemia. Furthermore, retroperfusion provided myocardial support during complicated and failed angioplasty and reversed cardiogenic shock in one patient.

Safety of the retroperfusion technique. There are three safety issues: 1) safety of coronary sinus catheterization through the jugular vein; 2) the effects of retroperfusion on the coronary venous system; and 3) the effects of retroperfusion on the formed blood elements. Coronary sinus cath-
eterization is a safe technique for measuring coronary blood flow (31–33). In our study, the small hematomas at the jugular venous insertion site could probably have been avoided by a left brachial artery approach. Nevertheless, the hematomas resolved without specific treatment and no patient required blood transfusion. Atrial fibrillation occurred probably secondary to irritation of the atrial wall. It resolved spontaneously and was not associated with any chest pain or hemodynamic effects. In one patient, there was evidence of injury to the atrial wall as demonstrated by staining after contrast injection through the retroperfusion catheter. However, because of the injury, retroperfusion was not employed to avoid the potential for extensive damage.

The effects of synchronized retroperfusion on the coronary sinus and coronary veins have been studied extensively in the experimental model (15–22) and humans (23–30). On direct visualization of the coronary sinus in three patients undergoing coronary bypass surgery and in one patient at postmortem examination, Gore et al. (28) noted minor bruising of the coronary sinus and one instance of a microscopic nonocclusive thrombus. These findings were corroborated in our study, in which the coronary sinus was visualized in the three patients who were sent for coronary bypass surgery and one in whom a postmortem study was performed. The coronary sinus was normal in three and only superficially bruised in one.

Previous studies (16,17) indicate that severe damage to venules occurred when coronary venous pressures exceed 60 mm Hg peak or 40 mm Hg mean pressure. In our study, the average mean and peak coronary venous pressures were kept well below those levels at 13 ± 6 and 29 ± 12 mm Hg, respectively. The pump is equipped with a safety mechanism that terminates retroperfusion when coronary venous pressures exceed prescribed limits.

We also confirmed prior studies (16,28) that showed no significant changes in red cell, white cell and platelet counts or plasma-free hemoglobin levels. Thus, the safety of the retroperfusion technique was confirmed in the current study.

Figure 6. Case I. Left coronary artery angiogram taken before angioplasty, showing tight proximal stenosis in the left anterior descending coronary artery (arrow) but with some distal filling (A) and after angioplasty when the patient was in cardiogenic shock, showing total occlusion of the artery (arrow) and very poor distal filling (B). C. End-systolic two-dimensional echocardiographic images recorded during abrupt occlusion of the left anterior descending coronary artery as a result of dissection (left) and after 150 min of retroperfusion (right). Note the severe global hypokinesia of the left ventricle during shock, which was reversed to normal contraction after retroperfusion as represented by the significantly reduced end-systolic cavity.
by the absence of any hemodynamic, hematologic, morphologic or clinically evident adverse effects.

Optimization of the retroperfusion technique. It has been suggested by previous studies (20,27,34) that high flows and increased coronary venous pressures are required to overcome the rich alternating drainage that may shunt the retroperfusate away from the ischemic bed. Therefore, the system was modified to increase the maximal flow rate from 100 to 250 ml/min. An attempt was made to correlate flow rate, coronary venous pressure, catheter position and efficacy. There was significant correlation ($p < 0.01$) between retroperfusion flow rate and coronary venous pressure; however, differences in echocardiographic wall motion could not be appreciated because of the small number of patients ($n = 4$) in the groups with different flow rates. In the three patients in whom there was no efficacy, the catheter tip was very proximal in the coronary sinus and venography showed inadequate retrograde penetration of the contrast material. Thus, efficacy is related to multiple factors, including flow rate, coronary venous anatomy, catheter position relative to the site of coronary artery obstruction and pressure gradient between the coronary venous and distal arterial beds, as shown by Meesman et al. (35) in a canine model.

Feasibility of the technique. Feasibility of retroperfusion involves three issues: ease and rapidity of application, special training requirements and patient applicability. The retroperfusion catheter was successfully positioned in 84% of patients and the technique was feasible in 79%. Catheter placement took 2.5 min (range 0.5 to 10) after placement of the catheter in the right atrium; this timing included the time taken by both experienced and inexperienced physicians who attempted the technique. An additional 20 min was required to prime the pump and start synchronized retroperfusion. Neither a perfusionist nor a surgical team was required. Moreover, retroperfusion has been used success-
fully in hospitals lacking a catheterization laboratory, intraaortic balloon pump or cardiac surgery facilities (29,30).

In this study, patients between 18 and 85 years of age were included; therefore, patient age was not a contraindication to retroperfusion. We limited the use of retroperfusion to left anterior descending coronary artery support. The efficacy of retroperfusion in the reduction of left circumflex coronary artery ischemia in evolving myocardial infarction was reported by Barnett and Touchon (29).

**Efficacy of retroperfusion.** Experimental studies (15–22) of retroperfusion during acute ischemia have demonstrated a significant reduction in infarct size, enhanced myocardial perfusion, restoration of glucose metabolism and significant improvement in left ventricular function. Clinical studies (23–29) have suggested efficacy in the treatment of unstable angina, acute myocardial ischemia and as an adjunct during balloon angioplasty in the left anterior descending coronary artery distribution.

In this study the effects of retroperfusion on brief left anterior descending coronary artery occlusion during angioplasty were studied in patients who were predicted to develop severe ischemia. Moreover, in this study design, each patient was his or her own control. No patient had left bundle branch block or QS patterns on the ECG in the region of interest, which could also affect the results. The efficacy of retroperfusion was demonstrated by significant diminution and delay in the onset of ischemia, as evidenced by left ventricular wall motion, angina and ST segment change. This efficacy suggests that retroperfusion may be used prophylactically as a device for "supported angioplasty" in high risk patients, as described by Vogel et al. (14) when defining the role of cardiopulmonary bypass in high risk angioplasty. Also, in cases where prolonged angioplasty balloon inflation times are required, the support of retroperfusion may be beneficial. Retroperfusion was not effective in all patients, but in the majority of patients the ischemic response was delayed or decreased although not totally abolished. The role of this technique, therefore, is as a prophylactic support technique during high risk and complex angioplasty rather than for routine angioplasty.

**Prolonged retroperfusion for complicated angioplasty.** The complication rate of coronary angioplasty in this study was 13%. This high rate may be attributed to the fact that patients predicted to develop significant ischemic events were selected. Abrupt occlusion occurred in two patients (Cases 1 and 2), resulting in cardiogenic shock and severe angina, respectively. In both patients conventional therapy was unsuccessful, but retroperfusion promptly reversed the ischemia. Thus, retroperfusion can reverse cardiogenic shock due to abrupt coronary occlusion during angioplasty and is helpful in difficult and prolonged multivessel angioplasty complicated by symptomatic vessel closure.

Left main coronary artery dissection developed during angioplasty of the left anterior descending coronary artery in another patient (Case 3). This is a rare complication that has been reported by Lotan et al. (36). This patient also had a thrombus in the left anterior descending coronary artery and was thus at greater risk for abrupt occlusion (27). Even though she was asymptomatic and hemodynamically stable, retroperfusion was performed prophylactically because of her high risk for a sudden severe ischemic event. This case suggests that synchronized retroperfusion may be helpful if kept as standby during high risk angioplasty.

Case 4 illustrates the development of severe ischemia due to occlusion by a guide wire of a coronary artery supplying a large portion of viable myocardium. The patient's severe chest pain was refractory to intracoronary nitroglycerin. Retroperfusion decreased the chest pain and allowed the patient to undergo angioplasty, although the latter was unsuccessful and emergency coronary bypass surgery was required. This case suggests the efficacy of retroperfusion in difficult angioplasty, where the ischemia is so significant that occasionally the procedure has to be abandoned.

It has been reported (37,38) that the incidence of Q wave infarction is 55% to 77% and the mortality rate 5% to 12% in patients requiring emergency coronary bypass surgery after failed angioplasty. The risk is greater when the failed angioplasty is complicated by hemodynamic instability or the presence of ischemic symptoms (39). All three patients in our study who required emergency bypass surgery were in the greater risk group and yet did not develop Q waves or die after surgery.

These cases suggest that retroperfusion is an effective support system in the event of angioplasty-induced complications. However, immediate permanent revascularization should always be the goal of therapy, retroperfusion providing a bridge until reperfusion is established.

**Retroperfusion and other myocardial support techniques.** Systemic support systems (namely, the intraaortic balloon pump, percutaneous cardiopulmonary bypass and hemopump left ventricular assist devices) maintain peripheral perfusion and systemic hemodynamics but have no direct myocardial protective effects. In contrast, retroperfusion provides nutrient blood flow to the myocardium and enhances washout of toxic metabolites from underperfused areas but does not directly support the systemic circulation. Therefore, there may be some value in combining retroperfusion with one of the other techniques to provide both myocardial and systemic support in some very high risk patients.

**Arterial blood perfusion (passive) or infusion (active) through the angioplasty catheter** effectively prevents the onset of ischemia, allowing prolonged angioplasty balloon inflation times (7). The limitations of this technique are low flow rates, clot formation, inadequate driving pressure in severely hypotensive patients and a potential risk of perforation or dissection of the coronary artery with the catheter tip. Moreover, because it provides perfusion to the territory supplied by the vessel in which it is placed, global myocardial perfusion is not provided as required in diffuse multivessel disease. During abrupt vessel closure after removal of
the angioplasty balloon catheter and wire, recrossing the lesion may be unsuccessful in 30% to 50% of cases (39).

Intracoronary perfusion of oxygenated Fluosol-DA 20% (Alpha Therapeutic Corporation), a fluosol emulsion, does improve left ventricular function, but does not return it to normal in experimental and clinical studies (8,9). There are also several limitations. It takes 30 to 40 min to defrost and oxygenate, which may limit its use in emergency situations; also, it is not as effective as arterial blood (40). Moreover, because of limitations in the total volume that may be infused, fluosol may be restricted in its use as support or maintenance therapy in failed angioplasty.

Because all the myocardial support techniques require special catheters to be introduced through the target lesion of the coronary artery, when access is lost and cannot be regained rapidly, coronary venous retroperfusion may provide the only means of rapidly perfusing the myocardium until surgery. In addition, cardioprotective drugs and cardioplegia may be delivered effectively by this route in the presence of an arterial occlusion (27).

Limitations of the study. In this study, a single precordial lead ECG was monitored. A 12 lead ECG or perhaps an epicardial electrogram would have provided a more sensitive marker of ischemia (41). Wall motion abnormality measurement obtained by two-dimensional echocardiography was feasible in only 50% of patients. The supine position of the patient posed problems in attaining good echocardiographic windows. Cardiac hemodynamic variables such as cardiac index and stroke work index were not measured in this study. These variables were monitored in a study by Costonitini et al. (26), who reported that retroperfusion significantly improved cardiac index and stroke work index. Their results suggest that retroperfusion does preserve cardiac hemodynamics during ischemia. In this study, only short duration angioplasty balloon inflations were studied. The results in the complicated cases, however, indicate its potential during prolonged ischemia. It is also important to note that this study deals with retroperfusion of the left anterior descending coronary artery territory only. The role of retroperfusion in other vessel territories remains to be adequately defined.

Retroperfusion is invasive and requires two additional puncture sites. However, unlike intraaortic balloon pumping or cardiopulmonary bypass, the vascular complications have been negligible as a result of the smaller size sheaths. Significant vascular occlusive disease was not encountered in this study but may pose a problem. If retroperfusion is performed in conjunction with intraaortic balloon pumping or the cardiopulmonary pump system, a separate sheath and arterial catheter are not mandatory. Blood may be obtained from the side arm of the angioplasty sheath in extreme conditions. As mentioned earlier, to prevent jugular venous hemioma, left brachial insertion sites may be used. Lastly, it is important to note that this technique requires training in right heart and coronary sinus catheterization before it can be applied.

Conclusions. This new synchronized coronary venous retroperfusion system was safe and feasible during coronary angioplasty. It significantly reduced and delayed the onset of ischemia during angioplasty and preserved regional and global myocardial function. It also reversed severe ischemia and cardiogenic shock during angioplasty complicated by abrupt coronary artery occlusion and supported these patients until definitive revascularization therapy was carried out. Retroperfusion thus appears to be an effective standby technique for high risk and complex coronary angioplasty and a support device in complicated and failed cases.

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References