Interventricular Coronary Steal Induced by Stenosis of Left Anterior Descending Coronary Artery in Exercising Pigs

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Background. In pigs and humans, the left anterior descending coronary artery (LAD) supplies the left ventricular anterior wall (LVAW), anterior septum, and paraseptal band of the right ventricular anterior wall (RVAW). The purposes of our study were 1) to study the LAD flow distribution in these walls during preexercise, exercise, and exercise with LAD stenosis and 2) to analyze regional wall motion under these conditions.

Methods and Results. Nine pigs were instrumented with sonomicrometers for measuring percent wall thickening (%WTh) in LVAW, RVAW, and lateral (control) walls of both ventricles, a hydraulic occluder at the LAD origin, an LV pressure transducer, and catheters for radiofrequency microsphere injection (left atrium) and blood withdrawal (aorta). One month later, regional %WTh and flows were measured during preexercise, exercise, and continuing exercise with LAD stenosis resulting in more than 50% reduction in systolic LVAW %WTh with regard to exercise. LAD stenosis caused a dramatic decrease in total mean±SD LVAW subendocardial flow with regard to exercise (28.7±8 to 9.1±3.2 ml·min⁻¹, p<0.0001) but no significant changes in either LVAW subepicardial flow or RVAW flow. The transmural distribution of flows within the LAD bed (as percentages of the total LAD flow in each experimental condition) showed that LAD stenosis redistributed flows with regard to exercise such that the LV subendocardial flow decreased from 26.4±4.2% of the total LAD flow to 11.8±4.3% (p<0.0001), whereas LVAW subepicardial flow increased from 32.9±2.3% of the total LAD flow to 45.5±7.9% (p<0.0001) and RVAW increased from 12±4.9% of the total LAD flow to 18.7±7.2% (p<0.0005). With exercise plus LAD stenosis, LVAW %WTh decreased from 43.2±8.4% to 17.2±9.7% (p<0.0001), but RVAW %WTh did not change.

Conclusions. In the LAD bed of exercising pigs, LAD stenosis induces, in addition to transmural steal, an interventricular steal favoring the RVAW at the expense of the LVAW subendocardium. This steal results in preserved RVAW thickening despite severe LVAW hypokinesia. (Circulation 1991;83:1361-1370)

A normally autoregulating vascular bed may vasodilate to such an extent that it reaches its limit of autoregulation; thereafter, blood flow through it becomes pressure dependent. Under these conditions, the blood flow through the bed may be reduced by vasodilation of a parallel vascular bed that results in a decreased perfusion pressure. This phenomenon is called "vascular steal" and was first described for the subclavian-vertebral artery system.1 A stenosis of the subclavian artery proximal to the origin of the vertebral artery provides a site for flow limitation, and decreased vertebral artery flow with concomitant neurological symptoms may result from arm exercise. In the heart, a similar phenomenon termed "coronary steal" has been demonstrated in humans2 and in dogs with one-vessel3 or multivessel occlusions.4-7 When subendocardial blood flow becomes pressure dependent, the subepicardium is still

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capable of further vasodilation in response to increased myocardial oxygen demand, provoking a "transmural steal" away from the subendocardium to the subepicardium.8-12

In a recent study in the anesthetized pig, Guth et al13 demonstrated that the part of the anterior wall (AW) of the right ventricle irrigated by the left anterior descending coronary artery (LAD) exhibits vasodilation reserve at LAD perfusion pressures sufficiently low to cause pressure-dependent flow in the subendocardium of the anterior left ventricle. Under these conditions, positive inotropic stimulation of the muscle supplied by the LAD caused an interventricular redistribution of blood flow, with the right ventricular (RV) blood flow increasing at the expense of a further reduction in left ventricular (LV) subendocardial flow ("RV steal"). This phenomenon was observed using constant-flow perfusion of the LAD, permitting the RV vasodilation to decrease the perfusion pressure of the pressure-dependent LV subendocardium.

The present study was undertaken to see if this effect could be obtained in a more physiological setting. We used the chronically instrumented pig, with exercise as the positive inotropic stimulus in the presence of acute LAD stenosis. In addition, we monitored LV and RV wall thicknesses to determine whether the postulated blood flow redistribution was associated with local changes in wall motion.

Methods

Animal Preparation

The present study conforms to the guiding principles of the American Physiological Society concerning the use of experimental animals.

Nine pigs (Landrace) aged 3-4 months, of either sex, and weighing 22.7±2.5 kg (range, 19-28 kg) were surgically prepared. The animals had been familiarized with the personnel of our laboratory and accustomed to running on a treadmill during a 1-month period before surgery. Premedication was performed with phenothiazine maleate (1 mg/kg i.m.), and anesthesia was induced with thiopental sodium (20 mg/kg) administered through an ear vein. After orotracheal intubation, anesthesia was maintained using 0.8% enflurane carried in oxygen (4 l/min) through a Bain tube connected to a Bird Mark VIII respirator, thus delivering oxygen-enriched air. A sterile thoracotomy was performed at the left fourth intercostal space, and a silicone rubber catheter was inserted into the descending aorta for blood withdrawal during radioactive microsphere injection. The pericardium was opened, and four pairs of piezoelectric microcrystals (5 mHz) were positioned for continuous measurement of LVAW, RVAW, and LV and RV lateral wall (LW) thicknesses using a conventional technique.14 To minimize underestimation of RVAW and RVLW thicknesses, subendocardial crystals to be used for the right ventricle had no lens and were coated with only a thin layer of epoxy resin. In each ventricle, the AW pair was positioned within the LAD perfusion bed, and the LW pair was positioned in a zone remote from the territory to be rendered ischemic. Positioning of the crystal pairs was achieved using the superficial vascular distribution as a guide, and all crystal locations were verified postmortem (see below). The trunk of the left coronary artery was exposed, and its bifurcation into the left circumflex artery and the LAD was dissected free. A polyethylene balloon occluder was positioned around the origin of the LAD. Great care was taken to place the occluder proximal to all side branches perfusing the RV wall. To prevent spasm during manipulation, topical application of papaverine sulfate was used. An LV pressure microtransducer (Konigsberg P7, Pasadena, Calif.) and a fluid-filled catheter for calibration of the microtransducer were inserted through a stab wound in the apex. An RV fluid-filled catheter was also positioned. Instrumentation was completed with a left atrial silicone rubber catheter for radioactive microsphere injection. All catheters and wires were tunneled subcutaneously to emerge between the scapulae, and the thoracotomy was repaired without pericardial closure. Ampicillin (30 mg/kg/day) was given orally from the second postoperative day until the day of the experiment. All catheters were flushed daily with heparinized saline. Ten days after surgery, familiarization with the treadmill was resumed and continued until the day of the experiment.

Experimental Protocol

Experiments were performed at least 20 days after surgery. LV pressure, its first derivative (dP/dt), and LVAW, LVLW, RVAW, and RVLW thicknesses were recorded on paper (Gould Brush 2600, Cleveland, Ohio) and on FM tape (Hewlett-Packard 3968A, Palo Alto, Calif.). The pressure microtransducer was calibrated against a Statham P23Db transducer (Hato Rey, P.R.) connected to the LV fluid-filled catheter using the midthoracic level as the zero reference point and adjusting the microtransducer-generated signal to match the signal generated by the Statham transducer. The RV fluid-filled catheter was then connected to the Statham transducer until the end of the experiment. The four dimension signals were calibrated using the 1-mm step calibration facility of the sonomicrometer (Triton Technology, San Diego, Calif.). With the animal standing and eating on the treadmill (preexercise condition), all signals were recorded, and the first injection of radioactive microspheres was made. Subsequently, the pig was run on the treadmill at a rate of 4.5-5.2 km/hr and a grade of 25%. After at least 3 minutes running and observation of a hemodynamic steady state, a second recording was obtained, and a second injection of radioactive microspheres was made. Without stopping the running, the hydraulic cuff occluder was progressively inflated to produce a more-than-50% reduction in LVAW systolic wall thickening with regard to that observed during exercise without stenosis (Figure 1). The cuff pressure was monitored.
using a Statham P23Db transducer connected to a side port of the occluder and set to the pressure necessary to produce the desired effect, which had been noted in a test experiment performed the previous day. The ischemic wall thickness signal was held constant for at least 2 minutes before signals were again recorded and a third microsphere injection was performed. Finally, the running was stopped, the LAD stenosis was released, and the pig was anticoagulated with 20,000 units heparin before being killed by an overdose of thiopental sodium followed by a bolus injection of potassium chloride. The heart and both kidneys were excised, and the LAD, circumflex artery, and right coronary artery were individually cannulated. The LAD vascular bed was selectively stained by perfusion of methylene blue through the LAD at a constant pressure of approximately 100 mm Hg while saline was perfused at the same pressure through the other two vessels. After 48–72 hours of fixation in 10% formaldehyde, the atria, pericardium, and any scar tissue adhering to the epicardial surface of the crystal sites were removed. The heart was cut perpendicular to the apex-base axis into five to seven slices of approximately equal thicknesses. In each slice, the LAD territory (stained blue) was carefully isolated and then divided into LV myocardium (which included the AW and a portion of the interventricular septum) and RV free wall. All pieces of LV myocardium (including that containing the AW crystal pair) were further subdivided into subepicardial, midwall, and subendocardial thirds. The RV free wall pieces were not subdivided transmurally. Control myocardium from both LVLW and RVLW containing the respective crystal pairs was sampled, and the LV piece was subdivided into endocardium, midmyocardium,
and epicardium thirds. In all data reported, AW crystal pairs were well within the blue area, and LW crystal pairs were well within the unstained area. All subependocardial crystals lay within the subependocardial third of the wall, and crystal orientation was found to be acceptable. Three crystal placements were unsatisfactory and therefore excluded: the RVAW pair in one pig, the RVLW pair in a second pig, and the LVLW pair in a third pig. All tissue samples were weighed and placed into individual vials for later radioactivity measurement. Samples from both kidneys were also obtained to check for uniform microsphere distribution as an indication of satisfactory microsphere mixing: this was found to be so in all pigs.

**Blood Flow Measurements**

Regional myocardial flow was measured using 15-μm-diameter radionuclide-labeled microspheres (du Pont, Boston) according to the methodology described by Heymann et al. The radionuclides used were niobium-95, indium-114, and ruthenium-103, and the sequence of injection was randomized. The microspheres were suspended in 10% dextran with Tween-80. On the day before the experiment, 10% dextran (5 ml) was injected as a bolus through the left atrial catheter. This was done because we observed in experiments performed on pilot animals that dextran induced in most pigs a short-lasting anaphylactic reaction consisting of severe hypotension, peripheral vasodilation, and extreme bradycardia that was followed by full recovery and did not reappear after subsequent injections. We therefore prevented this phenomenon from occurring during the experiment. Immediately before injection, each batch of microspheres was agitated for at least 15 minutes to break up aggregations of spheres and achieve homogeneous dispersion. A total of 6–10 million microspheres was administered for each measurement to obtain at least 400 microspheres in each tissue sample of 0.5–1 g wet wt. The microspheres were injected as a bolus through the left atrial catheter. At the same time, a reference sample was withdrawn from the aortic catheter using a constant-rate (8 ml/min) withdrawal pump for 2 minutes. The radioactivity of the tissue and reference blood samples was measured in a spectrometer (Alfanuclear, Buenos Aires) at the windows corresponding to the primary emission peaks of each radionuclide. After correcting for background activity, the unknown number of counts in each window belonging to a specific radionuclide was determined by solving simultaneous equations using an overlap matrix obtained with standard samples of each nuclide. Myocardial blood flow was calculated by the reference sample method as reference blood flow multiplied by tissue sample activity divided by reference blood activity.

**Additional Experiments**

To test for the presence of collateral circulation in the LAD bed of the right ventricle, we studied three additional pigs under enflurane anesthesia. A microsphere injection was made during complete LAD occlusion lasting 3–4 minutes. After releasing the occlusion, the LAD was rapidly cannulated, and Lux Green dye was injected while the heart was beating. To avoid the passage of any dye to the circumflex bed, the circumflex artery was ligated immediately before infusing the dye. The pig was killed with a toxic level of enflurane followed by a bolus injection of potassium chloride, and the heart and kidneys were removed. After 48 hours of fixation in 10% formaldehyde, the heart was sliced as described above, and radioactivity was measured in all RV tissue stained green (LAD bed) and in normoperfused RV tissue. Flow results are expressed in milliliters per minute per gram.

**Data Analysis**

LV pressure, RV pressure, and the four dimension signals were digitized every 5 milliseconds using an analog-to-digital converter (Data Translation 2801-A, Marlborough, Mass.) and an IBM XT computer system. End diastole was defined to occur at the onset of the rapid upstroke of the digitally calculated LV dP/dt and end systole at the time of maximal wall thickness occurring within a period of 20 milliseconds preceding the peak negative value for the digitally calculated dP/dt. For each experimental condition, 15±3 consecutive beats were analyzed for the calculation of end-diastolic wall thickness, end-systolic wall thickness, heart rate (HR), RV end-systolic pressure (RVESP), LV end-diastolic pressure (LVEDP), LV peak systolic pressure (LVSP), and maximal LV dP/dt (dP/dtmax). Dimension data were expressed as end-systolic and end-diastolic wall thicknesses (mm) and percent systolic wall thickening (%WTh) calculated as the systolic–diastolic thickness difference divided by end-diastolic thickness and multiplied by 100.

Regional myocardial blood flows were expressed in milliliters per minute, milliliters per minute per gram, and percentage of the total LAD blood flow present in any given experimental condition. The endocardial-to-epicardial blood flow (endo/epi) ratio was calculated in the tissue samples containing the LV crystal pairs using the blood flow values expressed in milliliters per minute per gram.

**Statistical Analysis**

Statistical comparisons were made using analysis of variance. When the F ratio indicated significant differences (p<0.05), exercise versus preexercise conditions and exercise with LAD stenosis versus exercise conditions were compared using the Bonferroni correction. Comparison between the third experimental condition (exercise with LAD stenosis) and the first experimental condition (preexercise) was irrelevant for the purpose of the present study and therefore ignored. All statistical processing was performed using the Crunch Interactive Statistical Package (San Francisco). Values are given as...
TABLE 1. Hemodynamic Data

<table>
<thead>
<tr>
<th></th>
<th>Preexercise</th>
<th>Exercise</th>
<th>Exercise + ischemia</th>
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</thead>
<tbody>
<tr>
<td>HR</td>
<td>150±15</td>
<td>221±15*</td>
<td>232±16†</td>
</tr>
<tr>
<td>LVEDP</td>
<td>7±6</td>
<td>13±11</td>
<td>22±18</td>
</tr>
<tr>
<td>LVPSM</td>
<td>131±17</td>
<td>152±25‡</td>
<td>140±21</td>
</tr>
<tr>
<td>RVESP (n=8)</td>
<td>20±3</td>
<td>36±14‡</td>
<td>39±13</td>
</tr>
<tr>
<td>(dP/dt_{max})</td>
<td>3,419±600</td>
<td>5,924±1,271*</td>
<td>4,822±761§</td>
</tr>
</tbody>
</table>

HR, heart rate (beats/min); LVEDP, left ventricular end-diastolic pressure (mm Hg); LVPSM, left ventricular peak-systolic pressure (mm Hg); RVESP, right ventricular end-systolic pressure (mm Hg); \(dP/dt_{max}\), maximal first derivative of left ventricular pressure (mm Hg/sec).

Values are given as mean±SD (n=9).

*\(p<0.0001\) and ‡\(p<0.002\) versus preexercise; †\(p<0.02\) and §\(p<0.002\) versus exercise.

mean±SD. Probability values of less than 0.05 were considered statistically significant.

Results

Hemodynamics

Hemodynamic data are given in Table 1. Exercise induced significant increases in HR (\(p<0.0001\)), LVPSM (\(p<0.002\)), RVESP (\(p<0.002\)), and \(dP/dt_{max}\) (\(p<0.0001\)). During exercise with LAD stenosis, HR displayed a significant additional increase (\(p<0.02\)) with regard to exercise, whereas \(dP/dt_{max}\) decreased (\(p<0.002\)). In one animal, the RV catheter clotted before the experimental session; therefore, values for RVESP from only eight pigs are reported.

Wall Thickness

Absolute values for end-diastolic and end-systolic wall thickness as well as \(\%\text{WTh}\) are shown in Table 2. \(\%\text{WTh}\) in the LVAW and RVAW are also depicted in Figure 2. Treadmill exercise resulted in significantly increased \(\%\text{WTh}\) of the LVAW (\(p<0.005\)) and LVLW (\(p<0.003\)). LAD stenosis during exercise produced a significant reduction of \(\%\text{WTh}\) in the LVAW (\(p<0.0001\)) with regard to exercise but did not affect \(\%\text{WTh}\) in the RVAW. Control walls did not exhibit significant changes after the LAD stenosis.

Regional Myocardial Blood Flow

The mean differences of the values for blood flow in the kidneys were \(-0.48±0.66\) ml/min\(^{-1}\cdot g^{-1}\) at preexercise (\(p=NS\) against zero), \(-0.58±0.88\) ml/min\(^{-1}\cdot g^{-1}\) during exercise (\(p=NS\)), and \(0.36±0.5\) ml/min\(^{-1}\cdot g^{-1}\) during exercise plus LAD stenosis (\(p=NS\)). This is evidence of uniform microsphere distribution, indicating adequate microsphere mixing in all three experimental conditions.

Total regional flows. Figure 3 shows the values for regional blood flow in the LAD perfusion bed. Whereas exercise alone induced significant increases in blood flow to all four zones, the addition of LAD stenosis induced significant decreases in blood flow to the endocardial and midmyocardial layers of the LVAW with no significant effects on LVAW subepicardial and RVAW flows.

TABLE 2. Regional Wall Thickness

<table>
<thead>
<tr>
<th></th>
<th>Preexercise</th>
<th>Exercise</th>
<th>Exercise + ischemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVAW ESTh</td>
<td>12.5±3.2</td>
<td>13.6±3.5</td>
<td>10.5±3.2</td>
</tr>
<tr>
<td>LVAW EDTh</td>
<td>9.2±2.5</td>
<td>9.3±2.5</td>
<td>8.9±2.5</td>
</tr>
<tr>
<td>RVLW %WTh</td>
<td>34.3±9.9</td>
<td>43.2±8.4</td>
<td>35.0±10.6</td>
</tr>
<tr>
<td>LVLW ESTh</td>
<td>13.9±2.0</td>
<td>14.8±1.9</td>
<td>14.4±2.4</td>
</tr>
<tr>
<td>LVLW EDTh</td>
<td>9.7±1.4</td>
<td>9.6±1.5</td>
<td>9.6±1.8</td>
</tr>
<tr>
<td>LVLW %WTh</td>
<td>44.1±11.7</td>
<td>52.4±11.0‡</td>
<td>53.3±10.1†</td>
</tr>
<tr>
<td>RVAW ESTh</td>
<td>4.4±1.9</td>
<td>4.5±1.9</td>
<td>4.4±2.0</td>
</tr>
<tr>
<td>RVAW EDTh</td>
<td>3.3±1.5</td>
<td>3.4±1.5</td>
<td>3.4±1.5</td>
</tr>
<tr>
<td>RVAW %WTh</td>
<td>35.0±12.6</td>
<td>38.1±12.2</td>
<td>34.0±7.4</td>
</tr>
<tr>
<td>RVLW ESTh</td>
<td>7.2±1.9</td>
<td>7.5±2.1</td>
<td>7.5±2.1</td>
</tr>
<tr>
<td>RVLW EDTh</td>
<td>4.6±1.1</td>
<td>4.5±1.2</td>
<td>4.5±1.3</td>
</tr>
<tr>
<td>RVLW %WTh</td>
<td>58.5±25.4</td>
<td>65.0±25.5</td>
<td>67.5±26.0</td>
</tr>
</tbody>
</table>

LVAW, left ventricular anterior wall (n=9); ESTh, end-systolic thickness (mm); EDTh, end-diastolic thickness (mm); %WTh, wall thickening (%); LVLW, left ventricular lateral wall (n=8); RVAW, right ventricular anterior wall (n=8); RVLW, right ventricular lateral wall (n=8).

Values are given as mean±SD.

‡\(p<0.005\) and †\(p<0.003\) versus preexercise; \\(p<0.0001\) versus exercise.

Normalized regional flows. Values for regional myocardial blood flow per gram of tissue in the myocardial samples containing the four crystal pairs are shown in Table 3. All exercise values are significantly

![Graph showing regional systolic wall thickening](image-url)
higher than their respective preexercise values. The addition of LAD stenosis, however, did not affect all LAD territories similarly. Whereas significant decreases occurred in the subendocardium and midmyocardium of the LVAW, the subepicardium of the LVAW and the RVAW did not show significant changes in flow. In control normoperfused walls, all flows showed a tendency to increase during LAD stenosis with regard to exercise, but in no case did the differences achieve statistical significance.

Percent distribution of left anterior descending coronary artery flow. Figure 4 shows the distribution of flows in the LAD perfusion bed expressed as percent of the total flow found in the entire LAD perfusion bed during each experimental condition. LAD stenosis promoted a transmural redistribution of blood flow favoring the subepicardium of the LVAW. However, in addition, LAD stenosis induced an interventricular redistribution, such that the RVAW increased its share of the total flow in detriment of the LVAW subendocardium.

Endo/epi ratios. Table 4 shows the endo/epi ratios for the ischemic and normoperfused walls of the left ventricle calculated from the tissue samples containing the crystal pairs. In both walls, the addition of LAD stenosis resulted in decreased endo/epi ratio, but as expected, the decrease was much more pronounced in the ischemic wall. Decreased endo/epi ratio in the nonischemic LVLW was associated with increased epicardial blood flow without changes in endocardial flow.

Collateral flow. Finally, in the three additional anesthetized pigs with LAD occlusion, blood flow was 1.17±0.17 ml·min⁻¹·g⁻¹ in normoperfused RVLW and 0.05±0.06 ml·min⁻¹·g⁻¹ in acutely ischemic RVAW, thereby indicating negligible collateral blood flow into the RV wall perfused by the LAD.

Discussion

Critique of Methodology

The study by Guth et al. was the first to show interventricular steal in the LAD perfusion bed. In that study, a constant-flow pump was used to underperfuse the LAD vascular bed; dobutamine was then injected into the perfusion stream to provoke a local positive inotropic effect. In the present study, we first increased myocardial oxygen demand with treadmill exercise and then induced flow limitation by partial inflation of the hydraulic cuff around the LAD. Therefore, both protocols established the three conditions necessary for the development of vascular steal: flow limitation, one vascular bed operating outside its limits of autoregulatory reserve, and a parallel vascular bed operating within its range of autoregulation. In the present study, the metabolic stimulus (exercise) was begun first, before any coro-
nary stenosis. Inflation of the cuff then imposed a flow-limiting stenosis producing ischemic dysfunction in the LVAW. Despite the temporal reversal of stenosis and metabolic stimulus with regard to the naturally occurring sequence in effort-induced angina, the end result should in no way be affected. This experimental approach has been used in studies in which transmural steal was first described in the exercising dog,\textsuperscript{11} and the results were similar to those obtained in exercising dogs with a preexisting fixed coronary stenosis.\textsuperscript{18,19} The advantage of the present protocol was that the normal blood flow distribution during exercise could first be determined without stenosis for later comparison to the blood flow distribution with the stenosis in place.

It should be noted that a true resting condition was not present during the preexercise period. The pigs were fed small amounts of food while they stood on the treadmill to keep them occupied while catheters and wires were connected and data corresponding to the preexercise period were collected. The excitement associated with eating is clearly evident in the hemodynamics (Table 1) and in the myocardial blood flows (Table 3), which are appropriately higher than those reported in pigs in a more basal condition.\textsuperscript{21} The lack of a true resting condition did not interfere with the principal aim of the study, which was to compare exercise and exercise with LAD stenosis.

Myocardial perfusion in the preexercise condition showed a normal distribution with an LVAW endo/epi ratio of 1.4, which did not differ from that of the LVLW perfused by the intact left circumflex coronary artery. During exercise, there was a uniform increase in blood flow to the LVAW such that the endo/epi ratio was maintained (1.3, \(p=\text{NS}\)) and regional myocardial contractile function increased significantly by 26\%, indicating absence of ischemia before inflation of the coronary cuff.

There was a significant increase in blood flow to the LVLW (midwall and subepicardium) as well as to the RVLW upon placing the stenosis (Table 3). This tendency for nonischemic myocardium adjacent to acutely ischemic myocardium to increase its blood flow has been reported and is probably related to increased regional mechanical function observed in areas remote from the acutely ischemic myocardium.\textsuperscript{21} In addition, HR increased with the stenosis and probably accounts for some of the increased metabolic demands of the nonischemic myocardium. These observations further support the functional integrity of the preparation.

For reasons discussed later, it would have been desirable to measure the poststenotic coronary perfusion pressure. We did not measure this pressure because of the difficulties associated with catheter placement and maintenance of patency in an already complex preparation. Poststenotic pressure was measured by Canty\textsuperscript{22} in conscious, sedated dogs and by Cohen\textsuperscript{7} in exercising dogs. In our experience, pig coronary arteries are more likely to enter into spasm in response to mechanical stimulation than are those of the dog. To prevent spasm when manipulating pig coronary arteries, we routinely use topical application of papaverine sulfate, which we have not found to be necessary in the dog. A poststenotic catheter

\begin{table}
\centering
\caption{Endocardial–to–Epicardial Blood Flow Ratios} 
\begin{tabular}{lccc}
\hline
 & Preexercise & Exercise & Exercise + ischemia \\
LVAW & 1.40±0.57 & 1.30±0.31 & 0.48±0.31* \\
LVLW & 1.32±0.24 & 1.24±0.24 & 1.00±0.24* \\
\hline
\end{tabular}
\end{table}

LVAW, left ventricular anterior wall; LVLW, left ventricular lateral wall.

Values are given as mean±SD (\(n=9\)).

*\(p<0.0002\) and \(t\)\(p<0.05\) versus exercise.
would be a very likely source of mechanical stimulation during exercise. If direct contact of the catheter with the main trunk of the LAD was to be prevented, it would have been necessary to cannulate and ligate a side branch of the artery, thus rendering necrotic a portion of the LAD bed and thereby interfering with the purpose of the present study.

Major Findings

The main finding of the present study concerns the role of the LAD-perfused RVAW in the coronary steal phenomenon.

The occluding cuff was inflated during exercise to produce a significant degree of LVAW hypokinesia. Under these conditions, the RVAW supplied by the same vessel as the LVAW showed no change in wall thickening. The absolute value for LAD flow (sum of individual regional flows) decreased to 67% of the prestenosis value. Examination of the individual regional flows revealed that the LVAW subepicardial and RVAW absolute flows were maintained at their prestenosis levels, thus confining the reduction in total LAD flow to LVAW subendocardium (31.7% of prestenosis flow) and LVAW midwall (53% of prestenosis flow). When regional flows were expressed as percent of the total LAD flow available during exercise and exercise with LAD stenosis (Figure 4), the LVAW subepicardium increased its share from 32% to 45.5% of the available flow and the RVAW increased its share from 12% to 18.7% with concomitant decreases from 24.6% to 11.8% in the LVAW subendocardium and from 30.5% to 24% in the LVAW midwall.

This behavior suggests that in addition to the well-described phenomenon of transmural steal, there also is an interventricular steal favoring the RVAW at the expense of the LVAW subendocardium and midwall. As a result of this behavior, the RVAW supplied by the LAD preserves its degree of wall thickening, whereas the LVAW exhibits severe hypokinesia.

Hypotheses

Collateral circulation. The pig is known to have a sparse native collateral circulation;23–27; acute LAD occlusion results in essentially zero transmural blood flow.24,26,28–32 However, the possibility existed that the RVAW, about which little information concerning collateral circulation is available,23 received blood flow through collaterals during LAD stenosis. The results from the three anesthetized open-chest pigs studied for this purpose indicated that flow to the LAD-supplied RVAW was essentially zero after 3–4 minutes of acute LAD occlusion. Thus, the preservation of RVAW flow and wall thickening was not due to the presence of collateral circulation.

Coronary steal. Our results strongly suggest that the RVAW acts with the LVAW subepicardium to decrease the pressure head available for LVAW subendocardial perfusion in the presence of a flow-limiting stenosis.

Gallagher et al5 summarized the evidence5,33–37 demonstrating that in the absence of stenosis, the vascular resistance of the subepicardium during diastole is greater than that of the subendocardium, thus favoring blood flow to the latter during diastole. This must also be the case for the LAD-supplied RVAW whose preexercise total flow was less than half that of the LVAW subendocardium, indicating a vascular resistance at least twice as high as that of the LVAW subendocardium. During exercise without stenosis, the three principal beds (LVAW subepicardium, LVAW subendocardium, and RVAW) vasodilate in similar proportions, as indicated in Figure 4, where it is seen that the distribution of total available flow remains unaltered between preexercise and exercise without stenosis.

At this stage, we must take into account that the LVAW subendocardium is perfused principally during diastole, whereas the other two beds receive perfusion throughout the cardiac cycle.38 The higher-resistance LVAW subepicardial and RVAW beds are therefore favored during systole, and the lower-resistance LVAW subendocardial bed is favored during diastole. The vasodilation that occurs with exercise coupled with freely available flow at a near-aortic pressure head allows the LVAW subendocardium to stay within its autoregulatory range despite its perfusion being limited effectively to the diastolic period.

This situation changes dramatically when a stenosis is superimposed during exercise. The generalized vasodilation produces a large pressure drop across the stenosis during diastole, when all three beds are competing for perfusion. This pressure drop results in an effective perfusion pressure for the LVAW subendocardium, which places it outside of its autoregulatory range and results in hypokinesia59 and a diminished share of the total available flow.

During systole, the LVAW subendocardial bed is largely excluded due to collapse of its irrigating vessels caused by the raised intramyocardial pressure accompanying systole. Exclusion of the LVAW subendocardium results in a smaller pressure drop across the stenosis, and therefore the pressure head available for perfusion of the LVAW subepicardium and the RVAW is higher than during diastole. This pressure head is further augmented by aortic systolic pressure being greater than aortic diastolic pressure and by a possible reduction of turbulent pressure drop across the stenosis40 as a result of a smaller absolute flow during systole than during diastole. All of these factors aid in producing adequate perfusion of the LVAW subepicardial and RVAW beds, whose mean perfusion pressures will therefore be greater than that for the LVAW subendocardium, thus permitting them to stay within their autoregulatory ranges.

The RV chamber systolic pressure did not change after stenosis, thus excluding a change in RV systolic intramyocardial pressure as a further possible mechanism of altering mean resistance of the RVAW.
This same argument applies to the LVAW, as there was no change in LV peak systolic pressure after stenosis.

The LVAW midwall showed a behavior midway between those of the subendocardium and subepicardium but was also forced out of its autoregulatory range despite the possibility of its receiving a greater degree of perfusion during systole than the subendocardium.34

A clear example of the diastolic-systolic variation of poststenotic pressure is given in Figure 2 of a study by Canty22 using sedated conscious dogs. In the left circumflex bed of these dogs, at a mean poststenotic pressure of 30 mm Hg, the LV wall thickening decreased to 40% of the control value, which is equal to the decrease exhibited by our exercising pigs; the systolic poststenotic pressure was approximately 60 mm Hg, whereas the diastolic poststenotic pressure was approximately 20 mm Hg. In addition, the difference between aortic systolic and poststenotic systolic pressures under this degree of stenosis (approximately 40 mm Hg) clearly indicates that in the left circumflex territory there existed systolic perfusion of some vascular bed, most likely the subepicardium.

The fact that we did not record poststenotic pressure in our pigs is unfortunate from the point of view of extracting the maximum amount of information from the experimental preparation, especially regarding the lower pressure limit of autoregulation that Canty22 has shown to be 40 mm Hg in the conscious animal compared with 70 mm Hg in the anesthetized animal; however, in no way does this alter our findings that the RVAW participates in the steal phenomenon and that the mechanism of this phenomenon is likely to be that discussed above.

Because the RV myocardium supplied by the LAD is only 14% of the LAD bed, it is reasonable to suppose that in the right coronary artery bed, where the percentage of total flow going to the right ventricle is considerably greater, the magnitude of the steal from the posterior LV subendocardium will be much more pronounced and probably of clinical relevance.

Conclusion

The results of the present study demonstrate that in the LAD perfusion bed of exercising pigs, there is, in addition to the well-described phenomenon of transmural steal, an interventricular steal such that the LAD-supplied RVAW preserves both blood flow and normal wall thickening under conditions in which LAD stenosis causes significant reduction of blood flow to the LVAW subendocardium, resulting in LVAW hypokinesia.

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