Arterial and Venous Coronary Pressure-Flow Relations in Anesthetized Dogs

Evidence for a Vascular Waterfall in Epicardial Coronary Veins

Paul N. Uhlig, Robert W. Baer, Gus J. Vlahakes, Frank L. Hanley, Louis M. Messina, and Julien I.E. Hoffman

From the Cardiovascular Research Institute, and the Departments of Pediatrics and Physiology, University of California, San Francisco, California

SUMMARY. The coronary circulation of anesthetized dogs was tested for the presence of vascular waterfalls by manipulating coronary arterial and coronary venous pressures. The left main coronary artery and the coronary sinus were cannulated, and relationships between coronary artery pressure, coronary sinus pressure, and coronary flow were studied. Experiments were conducted during diastolic arrests, under steady state conditions, in the absence of autoregulation. Relations of coronary flow to coronary sinus pressure at constant coronary artery pressure were consistent with the presence of a vascular waterfall in the coronary sinus. When the great cardiac vein was cannulated, relations of great vein flow to great vein pressure at constant coronary artery pressure were consistent with the presence of a vascular waterfall in the great vein, indicating that waterfall behavior can occur in epicardial veins other than the coronary sinus. In dogs on right heart bypass, with the coronary sinus and great vein uncannulated, the relationship between right atrial pressure and coronary sinus pressure showed a waterfall pattern, indicating that the waterfall is not an artifact of venous cannulation. In the right heart bypass experiments, venous waterfall behavior was seen in beating hearts as well as during diastolic arrests. We conclude that a vascular waterfall is present in epicardial coronary veins which can significantly influence coronary blood flow. (Circ Res 55: 238–248, 1984)

The term vascular waterfall was used by Permutt et al. (1962) to describe the pressure-flow characteristics of collapsible vessels subjected to external compressive forces. It is now generally accepted that vascular waterfalls influence flow in the systemic venous system (Holt, 1941) and in the pulmonary circulation (Permutt et al., 1962; Lopez-Muniz et al., 1968). Recently, several investigators have suggested that vascular waterfalls also influence coronary flow. Despite increasing interest in the possible existence of coronary vascular waterfalls, no uniform hypothesis has emerged: the waterfall proposed by Scharf et al. (1971) is located in the coronary venous system and influences the partition of venous flow between coronary sinus and noncoronary sinus pathways; the waterfall as conceived by Archie (1973) and Downey and Kirk (1974, 1975) results from systolic compression of intramyocardial veins and influences the transmural distribution of arterial flow; whereas the waterfall of Bellamy (1978) results from diastolic tissue pressure acting in concert with arterial smooth muscle tone, regulates arterial flow, and may be influenced by venous pressure (Bellamy et al., 1980).

If vascular waterfalls are present in a circulation, characteristic relationships between inflow pressure, outflow pressure, and flow should be present. These relationships are well understood for collapsible vessels in general (Conrad, 1969; Fry et al., 1980), and provide the means by which waterfalls have been shown to exist. The purpose of our study was to test for vascular waterfalls in the coronary circulation by examining relationships between coronary arterial pressure, coronary venous pressure, and coronary flow. To eliminate the effects of capacitance (Eng et al., 1982), changing smooth muscle tone (Spaan, 1979), and systolic-diastolic interactions (Spaan et al., 1981), data were recorded during equilibrated long diastolic arrests at constant inflow and outflow pressure, after autoregulation was abolished with chromonan. The conditions of our study thus prevented recognition of waterfalls produced by systole, or dependent entirely upon active smooth muscle tone.

The principal experiments were performed on dogs in which the left main coronary artery and the coronary sinus or great cardiac vein were cannulated. Additional experiments were performed with dogs on right heart bypass in which the coronary sinus and great cardiac vein were uncannulated. To aid in interpreting our results, an additional experiment was performed, using a mechanical Starling resistor.
Theoretical Model

We considered the coronary circulation to be a series-parallel circuit, with an upstream segment representing the arterial and capillary beds, and a downstream segment of parallel pathways representing the venous bed. This model is supported by anatomic studies showing no arteriovenous communications except by way of the capillary bed, and extensive communications between venous pathways (Baroldi and Scomazzoni, 1967). In addition, physiological studies have shown that venous flow can be shunted to alternate venous pathways if conditions of a primary pathway are changed (Baroldi et al., 1966; Scharf et al., 1971; Nakazawa et al., 1978). We considered a vascular waterfall to be a classical Starling resistor interposed at a chosen location within the circulation. Flow was predicted by pressure gradients and resistance, and reversed flow in any segment was allowed, if not blocked by a closed waterfall (i.e., waterfall pressure greater than pressure in either direction at the waterfall locus).

Figure 1 illustrates pressure-flow relations predicted from the model for experiments in which coronary sinus pressure is varied while coronary artery pressure is held constant. The venous circulation is represented as parallel coronary sinus and combined noncoronary sinus pathways. The subpanels of the figure illustrate the theoretical effects of the presence and location of vascular waterfalls.

Figure 1A illustrates the predicted relations of coronary artery flow and coronary sinus flow to coronary sinus pressure with no waterfall in the circulation. Flow into the arterial segment is determined by the difference between arterial pressure and a weighted mean outflow pressure for the combined venous pathways, and by the total coronary resistance. The partition of venous flow between coronary sinus and noncoronary sinus pathways depends upon the relative resistances and outflow pressures of the pathways. Any change of coronary sinus pressure influences arterial flow by altering the mean back pressure to flow, and influences coronary sinus flow by altering total flow and the fractional distribution of venous flow between coronary sinus and noncoronary sinus venous pathways.

Figure 1B illustrates the relations with a waterfall in the segment upstream from the common origin of the venous pathways. At a critical coronary sinus pressure, waterfall pressure becomes the back pressure to flow in the segment upstream from the waterfall. At coronary sinus pressures less than this critical pressure, changes of coronary sinus pressure do not influence arterial flow, but continue to influence coronary sinus flow by altering the fractional distribution of venous flow.

Figure 1C illustrates relations with a waterfall in the coronary sinus pathway. At a critical coronary sinus pressure, waterfall pressure becomes the back pressure to flow in the coronary sinus pathway. At coronary sinus pressures less than this critical pressure, changes of coronary sinus pressure influence neither arterial flow, nor the fractional distribution of venous flow.

Figure 1D illustrates the relations with two waterfalls, one in the segment upstream from the common origin of the venous pathways, and the second, with a lower waterfall pressure, in the coronary sinus pathway. Two critical coronary sinus pressures would be present. At coronary sinus pressures less than the lower critical pressure, changes of coronary sinus pressure influence neither arterial flow nor the fraction of flow which drains through the coronary sinus pathway. At coronary sinus pressures between the two critical pressures, changes of coronary sinus pressure influence coronary sinus flow by altering the fractional distribution of venous flow, but do not influence arterial flow.

The model does not account for regional variations in waterfall pressure which may exist across the heart wall during diastole (Baird and Adiseshiah, 1976). If such variations exist at the waterfall locus, a gradual transition rather than a sharp inflection at a critical pressure would be expected in the pressure-flow relations. The range of pressures in the transition area would reflect the range of waterfall pressures.

Methods

Venous Cannulation Experiments

Experiments were performed on nine mongrel dogs weighing 25–40 kg. Anesthesia was induced with sodium thiopental (25 mg/kg, i.v.) and was maintained by ventilation with halothane (1.0–1.5%) and oxygen (99.0 to 98.5%) from an anesthesia machine (Dupaco model 78 anesthesia apparatus; Fluotec 3 vaporizer). After adequate
anesthesia was assured, pancuronium bromide (0.05 mg/kg, i.v.) was given to produce muscle relaxation. Arterial $P_{O_2}$, $P_{C0_2}$, and pH were measured periodically, and the respirator was adjusted and sodium bicarbonate administered as necessary to maintain normal acid-base balance. A thermostatically controlled heating blanket and an infrared lamp were used to keep core temperature in the normal range.

The heart was exposed through a left thoracotomy with resection of the fifth rib. The pericardium was opened widely, parallel to the phrenic nerve, and suspended to provide support for the heart. Electrodes connected to a pacemaker (Medtronic 5880A) were sutured to the free wall of the right ventricle. Complete heart block was produced by injecting 40% formalin into the atrioventricular node (Steiner and Kovalik, 1968), and the ventricle was paced.

A specially formed stainless steel perfusion cannula (inside diameter, 0.45 cm; length, 27.5 cm) was placed into the left main coronary artery via the left subclavian artery and secured with a suture tied around the proximal portion of the coronary artery. Oxygenated blood flowed into the cannula from a pressurized reservoir heated by a water bath. Blood was supplied to the reservoir by roller pump from the femoral artery. The reservoir was connected to a compressed air source which could be rapidly regulated.

In eight of the nine dogs, the coronary sinus was cannulated with a special cannula constructed by attaching a 2-cm length of thin-walled aluminum tubing (o.d., 0.6 cm; i.d., 0.46 cm), with a small flange at the tip (tip diameter, 0.8 cm), to a 15-cm segment of flexible Tygon plastic tubing (o.d., $\frac{3}{16}$ inch; i.d., $\frac{5}{32}$ inch). The cannula was passed through a purse-string suture in the right atrial appendage. Coronary artery and coronary venous pressures were measured as depicted in the inset of Figure 3, by advancing one or more catheters upstream through the venous cannula. In other dogs, coronary venous pressure was measured with a Silastic pressure catheter placed directly into the coronary sinus through its wall by a modified Herd-Berger technique (Verrier et al., 1980), with the catheter end facing downstream. Orientation of the pressure catheter did not influence the results. The location of outflow pressure measurement, however, significantly influenced the results, as will be described in Results. Coronary artery pressure was measured at the tip of the perfusion cannula with a fluid-filled catheter. Left ventricular pressure was measured with a solid state pressure transducer (Millar Instruments, 7 Fr.) introduced through a purse-string suture in the left atrial appendage. Aortic pressure was measured in the ascending aorta with a solid state pressure transducer (Millar Instruments, 7 Fr.) inserted via the femoral artery. All fluid-filled catheters were connected to Statham P23Db pressure transducers. Zero pressure levels were assumed to be at mid-chest for all pressure catheters; the coronary sinus catheters were approximately 2 cm below mid-right atrial level, and the great vein catheter was approximately 2 cm above mid-right atrial level. Coronary artery and coronary venous flows were measured with cannulating flow transducers (Howell Instruments) in the perfusion circuits, coupled to electromagnetic flowmeters (Narcomatic RT-500). Pressure and flow signals were recorded on an eight-channel polygraph (Beckman R612), and on FM magnetic tape. Tape recorded signals were simultaneously digitized at 5-msec intervals (Horowitz and Glantz, 1979; Horowitz, 1980), and analyzed by digital computer (PDP 11/70, Digital Equipment Corporation).

After completing the surgical procedure, chromonar (10 mg/kg, i.v.) was given to abolish autoregulation; adequacy of the dose was confirmed by absence of reactive hyperemia after a 15-second occlusion of coronary flow. Additional chromonar (2 mg/kg, i.v.) was given if test occlusions later in the experiment revealed that reactive hyperemia had returned. Data were collected during long diastolic arrests induced by temporarily switching off the ventricular pacemaker. The interval between the onset of the arrest and the first escape beat could be prolonged by a bolus injection of lidocaine (1.5 mg/kg, i.v.), and this was done as necessary to provide arrests of adequate duration. Between arrests, the heart was paced at a rate of approximately 100 beats/min. At the onset of each arrest, coronary artery and coronary venous pressures were set to constant values. Data for each pressure-flow point were taken after complete equilibration of pressures and flows, usually about 6 seconds after the onset of arrest. Figure 2 shows data recorded during a typical arrest.

Two types of studies were conducted. In the first type, during a series of arrests, coronary artery pressure was repeatedly set to the same value, whereas coronary sinus pressure or great vein pressure was set to a range of values. In most dogs, several series of arrests were performed, using a different constant coronary artery pressure for each series. Plots of coronary artery inflow as a function of coronary sinus or great vein pressure were

**FIGURE 2.** Recording of a representative diastolic arrest. Each pressure-flow relation was constructed from a series of such arrests.
constructed. Additionally, plots of coronary sinus outflow as a function of coronary sinus pressure were constructed for dogs in which the coronary sinus was cannulated and the junction between the coronary sinus and the cannula was found to be secure. Plots of great vein outflow as a function of great vein pressure were constructed in the dog in which the great vein was cannulated.

In the second type of study, performed only in dogs in which the coronary sinus was cannulated, coronary sinus pressure was repeatedly set to the same value during a series of arrests, whereas coronary artery pressure was set to a range of values. In each dog, several series of arrests were performed, using a different, constant coronary sinus pressure for each series. Plots of coronary artery flow as a function of coronary artery pressure at the different coronary sinus pressures were constructed. Linear and quadratic regressions of coronary artery flow on coronary artery pressure for each series were advanced through the needles into the outflow cannula, the second catheter so that its tip rested just within the orifice of the outflow cannula, the second catheter so that its tip was upstream from the Penrose segment. The three catheters were connected to Statham P23Db pressure transducers which were calibrated simultaneously from a common pressure source.

In two of the three dogs, the left main coronary artery was ligated, the superior and inferior venae cavae were cannulated with size 32 Fr. right-angle cannulas, and the pulmonary artery was cannulated through the right ventricular outflow tract with a flexible perfusion cannula. A large cannula with multiple side holes was placed through the right atrial appendage across the tricuspid valve into the right ventricle. This cannula was drained to a collecting bottle; pressure in the right atrium and right ventricle could be set to any desired level by adjusting the height of this bottle. From the collecting bottle, blood was pumped into the femoral artery. The femoral artery and the aortic arch were ligated, and the ascending aorta was allowed to be free. A segment of Penrose tubing (Argyle, i.d. ¼ inch) was mounted on two tubular plastic cannulas (¼ inch o.d., ½ inch i.d.) and heated by a water bath. The combined volume of the bypass reservoir, the collecting bottle, and the associated perfusion tubing was approximately 700 ml; the system was primed with heparinized Ringer's solution.

In two of the three dogs, the left main coronary artery was cannulated and perfused as in the venous cannulation experiments; in these dogs, chromonar (10 mg/kg, i.v.) was given to abolish reactive hyperemia. In the third dog the coronary artery was not cannulated.

Right atrial pressure was measured with a polyvinyl catheter (0.030 inch i.d.) inserted through a purse-string suture in the right atrial wall several centimeters from the orifice of the coronary sinus. Coronary sinus pressure was measured with the modified Herd-Barger technique previously described. The tip of the catheter rested approximately 2 cm from the coronary sinus orifice and faced downstream. Both fluid-filled pressure catheters were connected to Statham P23Db pressure transducers calibrated from a common pressure source. Aortic pressure was measured with a solid state pressure transducer (Millar Instruments, 7 Fr.). In the two dogs in which the coronary artery was cannulated, left ventricular pressure was measured with a similar solid-state pressure transducer. In the third dog, left ventricular pressure was not measured.

In all three dogs, with the heart beating, right atrial pressure was varied by slowly raising then lowering the reservoir draining the right atrium and right ventricle. The relationship between right atrial and coronary sinus pressures was observed.

In one of the two dogs in which the coronary artery was cannulated, two series of diastolic arrests were performed. During each series of arrests, coronary artery pressure was repeatedly set to a constant value, whereas right atrial pressure was set to a range of values. Plots of coronary sinus pressure as a function of right atrial pressure were constructed.

In both dogs in which the coronary artery was cannulated, the influence of left ventricular pressure or coronary sinus pressure at low right atrial pressure was examined. With the heart beating, right atrial pressure was set to a minimum value by lowering the reservoir draining the right atrium and right ventricle. Left ventricular function was then depressed by intracoronary injection of pentobarbital (0.025 mg/kg), resulting in an increase of diastolic and a decrease of systolic left ventricular pressure. After recovery, the descending thoracic aorta was partially constricted, resulting in an increase of both diastolic and systolic left ventricular pressures. The effects of these interventions on coronary sinus pressure were observed.

Penrose Tubing Experiment

Outflow pressures were measured simultaneously at three locations within a mechanical Starling resistor, and the influence of the location of outflow pressure measurement on relations between flow and outflow pressure at constant inflow pressure was studied. A segment of Penrose tubing (Argyle, i.d. ¼ inch) was mounted on two tubular plastic cannulas (¼ inch o.d., ½ inch i.d.) and adjusted so that, with the cannulas separated by 6 cm, the tubing was under no tension. The tubing was not enclosed; thus, atmospheric pressure acted as surrounding pressure. The Penrose segment was perfused from a pressurized fluid reservoir. The inflow tubing contained a cannulating flow transducer (Howell Instruments) coupled to an electromagnetic flowmeter (Narcomatic RT-500). Inflow pressure was measured with a needle introduced into the perfusion tubing several centimeters upstream from the Penrose segment, connected to a Statham P23Db pressure transducer. A screw clamp was placed on the perfusion line between the Penrose segment and the site of inflow pressure measurement, and adjusted so that a perfusion pressure of 60 mm Hg produced a flow of approximately 500 ml/min. The Penrose segment was drained to a collection bottle open to the air; the bottle could be raised or lowered to vary outflow pressure. Ringer's solution was used as the perfusate, and was returned to the perfusion reservoir from the collection bottle by roller pump.

Needles were placed into the perfusion tubing just downstream from the Penrose segment, and three polyvinyl pressure catheters (0.030 inch o.d., 0.015 inch i.d.) were advanced through the needles into the outflow cannula and the Penrose segment. The first catheter was positioned so that its tip rested just within the orifice of the outflow cannula, the second catheter so that its tip was upstream from the first catheter, 1.5 cm within the Penrose segment, and the third catheter so that its tip was upstream from the second catheter, 3.0 cm within the Penrose segment (Fig. 7, inset). The three catheters were connected to Statham P23Db pressure transducers which were calibrated simultaneously from a common pressure source.

While inflow pressure was held constant, outflow pressure was increased stepwise by raising the collection bottle.
from its initial position well below the level of the Penrose segment. Flow and pressures were recorded with each increase in height of the collection bottle. This procedure was repeated at five constant inflow pressures (14, 20, 40, 60, and 80 mm Hg). Plots of flow as a function of outflow pressure were constructed for each of the three sites of outflow pressure measurement within the Penrose segment and outflow cannula.

**Results**

**Venous Cannulation Experiments**

Of the eight dogs in which the coronary sinus was cannulated, venous pressure was measured only at the orifice of the venous cannula in one dog, only within the coronary sinus in six dogs, and simultaneously at both locations in one dog. In the dog in which the great vein was cannulated, pressure was measured simultaneously at the orifice of the cannula and within the great vein. Unexpectedly, the location of venous pressure measurement influenced the relationships observed between coronary flow and coronary venous pressure at constant coronary artery pressure. This is illustrated in Figure 3, from the dog in which the coronary sinus was cannulated, and pressures were measured simultaneously at the orifice of the cannula and within the coronary sinus. When pressure was measured at the orifice of the cannula (catheter A, inset, Fig. 3), the relations of coronary artery flow and coronary sinus flow to cannula pressure showed distinct plateaus. This is illustrated in panel A for two constant coronary artery pressures, 59.8 ± 1.1 (s.o.) mm Hg (upper left), and 37.6 ± 0.8 mm Hg (lower left). At both constant coronary artery pressures, below a critical pressure of approximately 12 mm Hg cannula pressure ceased to influence either coronary artery or coronary sinus flow. At higher cannula pressures, coronary artery flow and coronary sinus flow varied inversely with cannula pressure; for a given increase in cannula pressure, there was a relatively greater decrease in coronary sinus flow as compared to coronary artery flow, thereby indicating a redistribution of flow away from the coronary sinus.

When pressure was measured actually within the coronary sinus (catheter B, inset, Fig. 3), plateaus were much less distinct. This is illustrated in panel B, for the same two constant coronary artery pressures illustrated in panel A. At both constant coronary artery pressures, the range of coronary sinus flow and pressures were measured simultaneously at the orifice of the cannula and within the coronary sinus.
pressures was much less than the range of cannula pressures, even though the data presented in panels A and B for each constant coronary artery pressure were recorded simultaneously. At the higher constant coronary artery pressure (upper right), no clear plateau was present in either the coronary artery or the coronary sinus pressure-flow relations. At the lower constant coronary artery pressure (lower right), below a critical pressure of approximately 12 mm Hg, coronary sinus pressure ceased to influence either coronary artery flow or coronary sinus flow; however, the plateau was much shorter than that seen in the corresponding relation of panel A (lower left). At higher coronary sinus pressures, coronary artery and coronary sinus flows decreased, and there was redistribution of flow away from the coronary sinus pathway.

The relations in figure 3, panel A, are representative of the nine relations of coronary flow to cannula pressure obtained in these experiments. Distinct plateaus were present in the relations of both coronary artery flow and coronary venous flow to cannula pressure at all constant coronary artery pressures studied. Within each relation, cannula pressure ceased to influence both coronary artery and coronary venous flows at a common critical pressure. The approximate range of critical pressures was 5–15 mm Hg.

The relations in Figure 3, panel B, are representative of the 23 relations of coronary flow to actual venous pressure obtained in these experiments. Distinct plateaus were not present in these relations obtained at relatively high constant coronary artery pressures (50–60 mm Hg). Plateaus were present in some relations obtained at lower constant coronary artery pressures (30–40 mm Hg), but were relatively short. Within each relation containing a plateau, coronary venous pressure ceased to influence both coronary artery and coronary venous flows at a common critical pressure. The approximate range of critical pressures was 5–15 mm Hg.

The relationship between pressures at the two sites of venous pressure measurement used in these experiments is illustrated in Figure 4, panels A and B. The data illustrated in figure 4, panel A, are from the experiment presented in the upper half of Figure 3, in which the coronary sinus was cannulated. The data illustrated in Figure 4, panel B, are from the experiment in which the great vein was cannulated. In both sets of data, a critical cannula pressure is present, below which upstream venous pressure is independent of cannula pressure; at higher cannula pressures, upstream pressure varies directly with cannula pressure.

Table I summarizes the results of experiments in which relations between coronary artery flow and coronary artery pressure were determined at constant coronary sinus pressures. Analysis of variance was used to determine the significance of the improvement in fit offered by the quadratic regression.

Although the quadratic regression always reduced the residual sum of squares, this was significant for only five of the 11 relations. Slopes of the pressure-flow relations at different coronary sinus pressures in each dog were tested for change by analysis of covariance. In only one dog was there a significant difference in slope at different coronary sinus pressures. Pressure-axis intercepts calculated using either linear or quadratic regressions were greater than coronary sinus pressure by several mm Hg, at low constant coronary sinus pressures. The intercepts were less than coronary sinus pressure when constant coronary sinus pressures were high.

Figure 5 is representative of this group of experiments, and illustrates pressure-flow relations from dog number three (Table 1), obtained at three different constant coronary sinus pressures. Each pressure-flow relation shows mild curvilinearity extending over the entire range of coronary artery pressures studied. At low, constant coronary sinus pressure, the pressure axis intercept of the pressure-flow relation is greater than coronary sinus pressure by several mm Hg. At higher coronary sinus pressures, there is a rightward shift of the pressure-flow relation along the pressure axis; however, the magnitude of the shift is less than the magnitude of the change in coronary sinus pressure.

Right Heart Bypass Experiments

In all three dogs, with the heart beating, a characteristic relationship was seen between right atrial pressure and coronary sinus pressure as right atrial pressure was varied. When right atrial pressure was set equal to atmospheric pressure, coronary sinus pressure was greater than right atrial pressure. Coronary sinus pressure was more pulsatile than right atrial pressure, with a coronary sinus pulse pressure of approximately 4–8 mm Hg. Both right atrial and coronary sinus pressures varied with respiration. As right atrial pressure was gradually increased, there was no change in coronary sinus pressure until a certain, critical right atrial pressure was reached which was approximately 2–3 mm Hg below the minimum coronary sinus pressure. As right atrial pressure was elevated above the critical pressure, coronary sinus pressure increased with right atrial pressure. Both right atrial and coronary sinus pressures became more pulsatile at higher pressures because the right atrium and right ventricle were drained by a common cannula. As right atrial pressure was lowered from a maximum value, both right atrial and coronary sinus pressures decreased together until the critical right atrial pressure was reached. Below this pressure, further decreases in right atrial pressure resulted in decreased pulsatility of the right atrial pressure, but did not change coronary sinus pressure. The critical right atrial pressure was found to be approximately 5 mm Hg in one dog, approximately 18 mm Hg in another dog, and in the third dog approximately 5 mm Hg at the
beginning of the experiment and 15 mm Hg at the end of the experiment. The increase in critical pressure in the third dog coincided with volume loading which increased left ventricular pressure from approximately 60/10 mm Hg to approximately 60/20 mm Hg. The left ventricular pressure of the first dog was approximately 65/5 mm Hg, and the left ventricular pressure of the second dog was not recorded.

The relationship between coronary sinus pressure and right atrial pressure during diastolic arrests at constant coronary artery pressure is illustrated in Figure 4, panel C. Below a critical right atrial pressure of approximately 5 mm Hg, coronary sinus pressure is independent of right atrial pressure. Above this critical pressure, coronary sinus and right atrial pressures are directly related. The mean left ventricular pressure during this series of diastolic arrests was −2.1 ± 2.1 mm Hg; coronary artery pressure was 38.7 ± 1.6 mm Hg. The second series of arrests at a higher constant coronary artery pressure of approximately 60 mm Hg showed a similar pattern.

In one dog on right heart bypass, a perfusion line was inadvertently clamped, causing left ventricular pressure to become unstable. During this period, right atrial pressure was held constant at a pressure just greater than atmospheric pressure by the reservoir draining the right atrium and right ventricle. Figure 6 illustrates that coronary sinus pressure varied with diastolic left ventricular pressure during this episode. This relationship was reproduced in two other dogs by depressing left ventricular func-

### Table 1

**Coronary Artery Pressure-Flow Relations at Constant Coronary Sinus (CS) Pressures**

<table>
<thead>
<tr>
<th>Dog</th>
<th>CS pressure (mm Hg) (mean ± 50)</th>
<th>No. of points</th>
<th>Pressure-axis intercept (mm Hg)</th>
<th>Slope (ml/min per mm Hg)</th>
<th>R²</th>
<th>Pressure-axis intercept (mm Hg)</th>
<th>R²</th>
<th>Significance*</th>
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<tr>
<td>1</td>
<td>11.5 ± 2.9</td>
<td>8</td>
<td>15.5</td>
<td>12.0</td>
<td>0.99</td>
<td>14.2</td>
<td>0.99</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>25.8 ± 3.3</td>
<td>11</td>
<td>20.6</td>
<td>11.4</td>
<td>0.99</td>
<td>17.8</td>
<td>0.99</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>2</td>
<td>4.2 ± 0.8</td>
<td>11</td>
<td>16.6</td>
<td>4.7†</td>
<td>0.99</td>
<td>13.7</td>
<td>0.99</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td></td>
<td>23.4 ± 0.4</td>
<td>11</td>
<td>25.9</td>
<td>5.5†</td>
<td>0.99</td>
<td>24.6</td>
<td>0.99</td>
<td>NS</td>
</tr>
<tr>
<td>3</td>
<td>7.5 ± 0.8</td>
<td>8</td>
<td>13.9</td>
<td>8.5</td>
<td>0.97</td>
<td>9.8</td>
<td>0.99</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td></td>
<td>13.8 ± 0.6</td>
<td>8</td>
<td>16.7</td>
<td>9.3</td>
<td>0.97</td>
<td>12.7</td>
<td>0.99</td>
<td>&lt; 0.001</td>
</tr>
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<td></td>
<td>30.0 ± 0.5</td>
<td>6</td>
<td>28.1</td>
<td>11.9</td>
<td>0.96</td>
<td>16.9</td>
<td>0.99</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>4</td>
<td>1.1 ± 4.2</td>
<td>8</td>
<td>14.3</td>
<td>6.5</td>
<td>0.95</td>
<td>6.6</td>
<td>0.96</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>26.9 ± 2.6</td>
<td>6</td>
<td>21.8</td>
<td>6.7</td>
<td>0.98</td>
<td>18.7</td>
<td>0.99</td>
<td>NS</td>
</tr>
<tr>
<td>5</td>
<td>4.0 ± 3.9</td>
<td>8</td>
<td>8.9</td>
<td>11.5</td>
<td>0.99</td>
<td>8.4</td>
<td>0.99</td>
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<td>26.1 ± 1.0</td>
<td>7</td>
<td>16.0</td>
<td>13.0</td>
<td>0.95</td>
<td>13.2</td>
<td>0.97</td>
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* Significance of the improvement in fit by quadratic regression.

† P < 0.01.
tion with an intracoronary injection of pentobarbital. When left ventricular systolic and diastolic pressures were increased by partial occlusion of the thoracic aorta, the same association of coronary sinus pressure and diastolic left ventricular pressure was seen.

Penrose Tubing Experiment

Relations between flow and outflow pressure are compared in Figure 7 for the three locations of outflow pressure measurement. In panel A, flow data are plotted against pressures in the outflow cannula. At all perfusion pressures, plateaus were present in the relations below a critical outflow pressure of approximately 0 mm Hg. In panel B, flow data are plotted against pressures within the collapsible tubing, just upstream from the outflow cannula. At low perfusion pressures, plateaus were clearly present below a critical pressure of approximately 0 mm Hg. At higher perfusion pressures, however, plateaus were less well defined. In panel C, flow data are plotted against pressures measured well within the collapsible tubing. No plateaus were present in the relations.

Discussion

The purpose of our study was to test the coronary circulation for the presence of vascular waterfalls by manipulating coronary arterial and coronary venous pressure. In the venous cannulation experiments, relations of coronary flow to coronary venous pressure at constant coronary arterial pressure were found to depend upon the location of venous pressure measurement. When venous pressure was measured at the orifice of the venous cannula (Fig. 3, panel A) distinct plateaus were present, similar to the theoretical pattern predicted for a vascular waterfall in the coronary venous system (Fig. 1, panel C). When venous pressure was measured actually within the coronary sinus or great cardiac vein, however, the pattern of relations was less easily interpreted. Relations performed at relatively low coronary artery pressures (Fig. 3, panel B, lower right) often had short plateaus suggesting the presence of a venous waterfall; yet relations performed at higher coronary artery pressures (Fig. 3, panel B, upper right) were without plateaus, similar to the theoretical pattern predicted for no waterfall in the circulation (Fig. 1, panel A).

We believe that these results reflect the presence of a vascular waterfall in the downstream portion of the coronary venous system that varies in extent of collapse depending upon experimental conditions. Pressure-flow relations from the orifice of the venous cannula detected the waterfall under all conditions because the region of venous collapse was upstream from the location of pressure measurement. Pressure-flow relations from within the coronary sinus or great cardiac vein detected the waterfall at low constant coronary arterial pressures, when the region of venous collapse extended far enough upstream to incorporate the location of pressure measurement, but did not detect the waterfall at high constant coronary arterial pressures when the region of venous collapse was limited to a more downstream portion of the venous system.

This interpretation is supported by the results of the Penrose tubing experiment. At high perfusion pressures, the region of collapse was confined to the
most downstream portion of the Penrose segment, whereas at lower perfusion pressures the region of collapse included progressively more of the Penrose segment. This behavior of the collapsible segment of a Starling resistor is well known (Conrad, 1969; Fry et al., 1980). As illustrated in Figure 7, pressure-flow relations using pressure data from the orifice of the outflow cannula showed plateaus at all perfusion pressures (panel A); relations using pressure data from the middle of the collapsible segment showed plateaus at low perfusion pressure which disappeared at higher perfusion pressures (panel B); and relations using pressure data from the most upstream portion of the collapsible segment showed no plateaus at high or low perfusion pressures (panel C). Pressure-flow relations from the orifice of the outflow cannula are identical to those from the orifice of the venous cannula; relations from the middle of the Penrose segment are identical to those from the coronary sinus or great vein.

In these experiments, any change of venous pressure which produced a change of coronary venous flow also produced a change of coronary arterial flow. This finding argues against the presence of additional waterfalls upstream from the venous waterfall under the conditions of our study. It is possible, however, that because of variability in our data, the second break point which would indicate an upstream waterfall (Fig. 1, relation D) might not have been recognized. In addition, it is possible that a waterfall in which venous pressure influences arterial pressure such as that hypothesized by Bellamy et al. (1980) could be present and remain undetected by this type of experiment.

To test for the presence of an upstream waterfall, we performed experiments similar to those of Bellamy et al. in which coronary arterial pressure-flow relations were constructed at several constant coronary sinus pressures. Like Bellamy et al., we found that the pressure axis intercepts of arterial pressure-flow relations performed at low constant coronary sinus pressure were greater than coronary sinus pressure (Fig. 5; table 1). However, whereas Bellamy et al. found a large difference between intercept pressure and coronary sinus pressure, in our experiments the difference was small. At higher constant coronary sinus pressures, the pressure-flow relations were shifted to the right along the pressure axis. The magnitude of the shift was less than the magnitude of the change of coronary sinus pressure; in all dogs the pressure axis intercept at high coronary sinus pressures was less than coronary sinus pressure. This is in contrast to the results of the study of Bellamy et al., in which the pressure-axis intercept was found to exceed coronary sinus pressure at all coronary sinus pressures studied.

The observation that the pressure-axis intercept exceeded coronary sinus pressure when coronary sinus pressure was low implies that a back pressure to flow greater than the measured coronary sinus pressure was present at some point in the circulation under the conditions of these experiments. Because the magnitude of the difference between coronary sinus pressure and the pressure axis intercept was quite small in our studies, several alternative explanations can be considered. It is possible that pressure, as measured in the downstream portion of the coronary sinus, did not accurately reflect venous pressure.
waterfall pressure at low flows. This phenomenon was seen in the Penrose tubing experiment (Fig. 7), in which at lower perfusion pressures subatmospheric pressures were recorded within the downstream portion of the collapsible segment, even though waterfall pressure equaled to atmospheric pressure was the effective back pressure to flow. Intercept pressure might therefore correctly reflect venous waterfall pressure, yet appear to be several mm Hg higher than coronary sinus pressure. Because pressure was controlled only in the cannulated portion of the venous bed, pressure gradients must have existed within the venous system. This is evident from the observation that at very high coronary sinus pressures, backflow into the coronary sinus often occurred. In the absence of an upstream waterfall, intercept pressure should equal a weighted mean outflow pressure of the venous pathways; thus the non-coronary sinus pathways could cause intercept pressure to exceed coronary sinus pressure when coronary sinus pressure was low, and likewise could explain the observation that intercept pressure fell below coronary sinus pressure when coronary sinus pressure was elevated. Finally, it is possible that an upstream waterfall with a waterfall pressure several mm Hg higher than venous waterfall pressure was present.

The most likely cause of the differences between our studies and those of Bellamy et al. is the way in which the pressure-flow relations were constructed. Data for each pressure-flow relation in the experiments of Bellamy et al. were recorded in the left circumflex coronary artery during a single long diastole during which coronary artery pressure was declining. Vasodilation was produced by temporarily occluding the coronary artery prior to the arrest. In our experiments, data for each pressure-flow relation were recorded in the left main coronary artery during a series of diastolic arrests after complete equilibration of pressures and flows. Vasodilation was produced by abolishing autoregulation with chromonar. Recently, we have shown that the zero-flow pressure-axis intercept in the left circumflex coronary artery is artifactually elevated by collateral inflow from other branches of the left coronary artery (Messina et al., 1983). Furthermore, it has been suggested that effects of capacitance (Eng et al., 1982) and autoregulation of the coronary bed during collection of pressure-flow data (Spaan, 1979) may influence the results of pressure-flow studies performed under non-equilibrated conditions. Although the significance of capacitance and autoregulation effects is controversial (Bellamy, 1979; Klocke et al., 1981), it is possible that the pressure-axis intercepts in the study of Bellamy et al. overestimate back pressure to flow.

At least two other studies have identified waterfall behavior in the coronary venous circulation. In an isolated, beating heart preparation with the coronary sinus cannulated, Scharf et al. (1971) found a critical coronary sinus pressure of approximately 12 mm Hg, below which coronary sinus pressure did not influence the partition of coronary venous flow between coronary sinus and non-coronary sinus venous pathways. In a similar preparation, Traystman (1971) found a critical coronary sinus pressure in the range of 0-15 mm Hg, below which coronary sinus pressure did not influence either intramycocardial blood volume or coronary artery pressure at constant coronary flow. Both Scharf et al. and Traystman measured coronary sinus pressure at the orifice of the cannula draining the coronary sinus.

Although both Scharf et al. and Traystman concluded that a waterfall is present in the coronary venous system, they did not more completely define its location. It seems probable that the waterfall recognized by Scharf et al. and Traystman is the same waterfall we have identified in the great vein and coronary sinus. This hypothesis is strengthened by the similarity of critical pressures in the three studies, and by the fact that in the Traystman study intramycocardial blood volume did not increase until the critical coronary sinus pressure was exceeded.

The mechanism producing the waterfall cannot be determined with certainty from our experiments. The right heart bypass experiments were undertaken to determine whether waterfall behavior observed in the coronary sinus and great cardiac vein was an artifact of cannulation. As illustrated in Figure 4, the relationship between pressures in the right atrium and the uncannulated coronary sinus during diastolic arrests (panel C) was identical to relationships between pressures in the venous cannula and the coronary sinus (panel A), and the venous cannula and the great vein (panel B) in the venous cannulation experiments. This implies that the waterfall is not an artifact of venous cannulation.

A serendipitous observation in the right heart bypass experiments was an apparent association of coronary sinus pressure with diastolic left ventricular pressure, in the absence of a change of right atrial pressure, during an episode of acute left ventricular failure (Fig. 6). This relationship was reproduced by intracoronary injection of pentobarbital, and by partial occlusion of the thoracic aorta. This association of venous waterfall pressure with the filling state of the left ventricle is consistent with a hypothesis that the venous waterfall is produced by compression of epicardial veins between the heart wall and surrounding tissues. Although the pericardium was open in the right heart bypass and venous cannulation experiments, the coronary sinus was dependent and thus compressed by the heart against the pericardial cradle. However, waterfall behavior was also seen in the cannulated great cardiac vein on the exposed surface of the heart. Additionally, the waterfall behavior noted by Scharf et al. and by Traystman occurred in isolated, suspended hearts. Although the epicardial veins are surface vessels, they lie beneath the epicardium (visceral pericar-
dium). It is possible that the epicardium acts as a restraining influence, allowing subepicardial pressures to be transmitted to epicardial coronary veins. Baird and Adisehiah (1976) studied the effect of volume loading on diastolic intramyocardial tissue pressure and found that pressures in the subepicardium increased from 11 mm Hg at left ventricular end-diastolic pressures of 0–4 mm Hg, to 24 mm Hg at left ventricular end-diastolic of greater than 20 mm Hg. These values for subepicardial tissue pressure are similar to values of venous waterfall pressure in our studies, and those of Scharf et al. and Traystman.

We conclude that under appropriate conditions a vascular waterfall exists in the epicardial venous system which is capable of influencing arterial as well as venous coronary flow. Diastolic left ventricular pressure appears to be a determinant of venous waterfall pressure. However, in our experiments, we could not determine whether venous waterfall pressure was changed by left ventricular systolic pressure, diastolic pressure, or diastolic dimensions. Because waterfall pressure, rather than right atrial pressure, can be the back pressure to flow in large portions of the coronary venous bed, the venous waterfall should be considered when interpreting studies of flow and pressure across the coronary circulation. If the venous waterfall operates in the intact circulation, its influence on coronary flow should be small under normal conditions. However, when left ventricular diastolic pressure increases without a comparable increase in right atrial pressure, a condition often seen in disease, the coronary venous waterfall may uncouple coronary venous pressure from right atrial pressure, and thus substantially reduce the driving pressure for coronary perfusion.

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Dr. Uhlig’s present address is: Department of Surgery, Massachusetts General Hospital, Boston, Massachusetts 02114.

Address for reprints: Julian I.E. Hoffman, M.D., 1403 HSE, University of California, San Francisco, California 94143.

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P N Uhlig, R W Baer, G J Vlahakes, F L Hanley, L M Messina and J I Hoffman

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