Coronary Interarterial Anastomoses in Young Pigs and Mongrel Dogs

By Richard W. Eckstein, M.D.

Interarterial anastomoses in young pigs have been compared with those in mongrel dogs by direct flow measurements during life and by injections after death. Results indicate that pigs have minimal functional collaterals in comparison with dogs and that injection studies roughly predict the degree of collateral function. The data indicate that the extent of collateral development in dogs is independent of dog or heart weight and hence offers more protection against the effects of coronary occlusion in small hearts than in large hearts. Other studies indicate that coronary flow, myocardial oxygen consumption and coronary vasomotor responses in pigs are similar to those in dogs.

The functional importance of coronary interarterial anastomoses in normal hearts is not clear. Studies based on a variety of methods have led some to the conclusion that collaterals in normal hearts play a considerable role in the prevention of myocardial infarction following coronary occlusion. However, Wiggers contends that their value is quite unimportant. In the human heart where measurements are limited, collateral function during life can only be deduced from anatomic findings after death. It is noteworthy that these postmortem studies usually employ injection technics often at pressures which exceed those existing during life. In addition, injections are often made simultaneously into all three major coronary arteries. There may be doubt as to whether the filling of an interarterial anastomosis by the simultaneous application of a high pressure to each end bears any relationship to the volume of unidirectional blood flow which exists during life following a coronary occlusion. Consequently, comparisons between results based on injection technics and those based on direct collateral flow measurements are needed.

Recently, Blumgart was unable to demonstrate coronary interarterial anastomoses in young pigs by injection technics which was in marked contrast to his findings in dogs. It is the purpose of this report, therefore, to present comparisons of direct flow measurements in pigs and dogs with the results of Blumgart in an effort to correlate postmortem findings with the situation existing during life. In addition, we aim to portray the wide range of collateral function in dogs, its independence of dog and heart weight, and its relationship to electrocardiographic changes induced by coronary occlusion.

METHODS

Pigs between 6 and 11 weeks in age and between 15.9 and 21.3 Kg. in weight were compared with dogs whose ages varied from 3 months to about 9 years and whose weights varied from 6.8 to 27 Kg. Anesthesia was produced by morphine and pentobarbital. The trachea was intubated in the dogs and cannulated in the pigs for intermittent positive pressure respiration. The hearts were exposed through the left chest. The circumflex artery was isolated and cannulated in the dogs and the ramus descendens anterior was cannulated in the pigs. Blood coagulation was prevented with heparin* in the dogs, but the pigs required heparin plus 500 mg. of chlorazol fast pink. The coronary arteries were perfused with blood under pulsatile aortic pressure via the cannulated left common carotid artery. Blood flow into the ramus descendens in the pigs was metered with a Shipley recording rotameter. During flow measurements simultaneous blood samples were drawn from the aorta and the

* Part of the heparin used in these experiments was generously supplied by the Upjohn Co., Kalamazoo, Mich.
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TABLE 1.—Results of Measurements on the Ramus Anterior Descendens in Pigs

<table>
<thead>
<tr>
<th>Exp.</th>
<th>Pig Wt. Kg</th>
<th>Heart Wt. Gm</th>
<th>Perfused Anterior Descendens Muscle Wt</th>
<th>Retrograde Flow cc/min</th>
<th>Retrograde Flow cc/min/100 Gm</th>
<th>Mean Peripheral Coronary Pressure mm. Hg</th>
<th>Coronary Flow cc/min</th>
<th>Coronary Flow cc/min/100 Gm</th>
<th>Oxygen Content Vol.%</th>
<th>O2 Consumption cc/min/100 Gm</th>
<th>Effects of Coronary Clamping</th>
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<tr>
<td>11</td>
<td>18.6</td>
<td>91</td>
<td>30.9</td>
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<td>13</td>
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<td>12</td>
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<tr>
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<td>18.1</td>
<td>97</td>
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<td>10</td>
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<tr>
<td>15</td>
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<td>81</td>
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<td>11.8</td>
<td>1.9</td>
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The hearts were removed at the end of the experiment. The cannulated coronary arteries were flushed with saline and injected with dilute India ink to stain the perfused muscle. This was followed by a barium sulfate gelatin mixture injected at a pressure of 100 mm. Hg for 30 seconds at 45 C. The hearts were chilled, opened by the Schlesinger method, and x-rayed. The amount of barium in extracircumflex vessels was estimated from the x-ray. The weight of the total heart as well as that of the India ink stained area was obtained.

RESULTS

Pigs

The results of seven successful pig experiments are shown in table 1 and figure 1. The retrograde flows in cubic centimeters per minute, or cubic centimeters per minute per 100 Gm. of India ink stained area, are not only lower but are also less variable than those in dogs previously reported, and in the larger group of dogs reported here (fig. 1). The mean peripheral coronary pressure in these pigs averages 10.4 mm. Hg, while that for the 41 dogs averages 14.7 mm. Hg. The average coronary flow of 81 cc. per 100 Gm. of muscle per minute, and the oxygen consumption of 8.9 cc. per 100 Gm. per minute are in the same range of the values in dogs under similar conditions. In addition to the data shown in table 1, the effect of coronary occlusion on the electrocardiogram was tested on nine pigs. In eight of the nine, marked T-wave and S-T segment changes occurred. Successful barium

Fig. 1. Retrograde flows plotted against heart weights. Dogs are represented by points and pigs by open circles. P shows dogs with minor electrocardiographic changes after clamping circumflex artery; 1, 2, 3, and 4 designate pups. Horizontal line drawn through median retrograde flow. Vertical line drawn through median heart weight.
CORONARY INTERARTERIAL ANASTOMOSES

injections were done in 12 pig hearts, and in no instance was there evidence of barium in extracircumflex arteries to indicate interarterial anastomoses.

To test whether the reactivity of the coronary arteries in the pig varies in any manner from that in the dog, intracoronary injections of adenosine triphosphate (ATP), epinephrine, and Pitressin were given. As is the case in dogs, increased flow occurred after injections of adenosine triphosphate and of epinephrine, and decreased flow resulted from pituitrin. Likewise, as is true in dogs, temporary coronary clamping (5 seconds) is followed by temporary increases in flow above normal upon release of the clamp.

Dogs

Figure 1 shows the retrograde circumflex flows in 41 dogs plotted against the heart weight. The horizontal and vertical lines are drawn through the median retrograde flows and heart weights, respectively. The points indicated 1, 2, 3 and 4 represent values found in four pups between 3 and 4 months in age and raised under optimum conditions. When compared with the pigs, even these young dogs show significantly elevated retrograde flows (P < 0.01), ranging widely from 1.3 to 5.6 cc. per minute.

Figure 1 displays the wide range of retrograde flows. The range is particularly great in the large dogs. Of more interest, however, is the relation between retrograde flow and heart weight. Statistically, the ratio of the number of small hearts above median to small hearts below median is not significantly different from the ratio of the number of large hearts above median to large hearts below median. It thus appears that retrograde flow is relatively fixed and independent of heart weight. A similar lack of correlation exists between retrograde flow and either dog weight or weight of muscle supplied by the circumflex artery. (Plots not shown.)

The individual dogs showing minor electrocardiographic changes following circumflex occlusion are indicated in figure 1 as P (protected). It is evident that the protected dogs are in general small dogs having high retrograde flows.

Since the effectiveness of collateral flow depends upon the flow per unit weight of ischemic muscle, the results of calculating

\[ \text{retrograde flow in cc./minute} \times 100 \]
\[ \text{wt. of muscle supplied by circumflex artery (injected wt.)} \]

were plotted against the injected weight. The results are displayed in figure 2. Horizontal and vertical lines were constructed as before. There is a significant difference in the numbers of hearts in the four quadrants (P < 0.01). This indicates that the volume of retrograde circumflex flow and hence its capacity for benefit is less per unit muscle weight in the hearts with the greater weights of muscle normally supplied by the circumflex artery.

There are likewise significantly less hearts with large collateral flows per unit weight of perfused muscle among the heavy hearts than among the light hearts (P < 0.05). (Plot not shown.) Although a similar decrease in collateral flow per unit weight of muscle was expected in the large dogs as compared with small dogs, statistically the results are not significant (0.2 > P > 0.1).

Response of Interarterial Anastomoses to Myocardial Ischemia. In an effort to determine the effect of progressive myocardial ischemia on retrograde flow, the first flow measurements

![Response of Interarterial Anastomoses to Myocardial Ischemia](http://circres.ahajournals.org/)

**Fig. 2.** Retrograde flows per minute per 100 Gm. of muscle injected with India ink via circumflex artery plotted against the weight of the injected muscle. P indicates "protected" dogs; 1, 2, 3 and 4 designate the pups. Lines constructed as in figure 1.
were compared with maximum flow after several 30-second periods of free bleeding of the peripheral circumflex artery. In measurements from 27 dogs, average retrograde flow increased from 3.5 cc. per minute to a maximum of 4.8 cc. per minute. Further periods of ischemia up to 12 minutes did not appreciably alter the maximum value.

**Injection Studies.** Successful barium injections were made into the circumflex arteries of 25 dog hearts. The amount of barium in branches of the ramus descendens anterior, right and septal arteries was estimated as none, slight, moderate and large. Table 2 is a summary of the relationship between injection, retrograde flow and electrocardiographic findings. There is general agreement between the demonstration of anastomoses by injection, the volume of retrograde flow and the electrocardiographic findings. However, a considerable overlap of flows exists (figs. 1 and 2) and there are exceptions to the general agreement.

For example, a survey of the entire series including those without satisfactory injections reveals the existence of minor (+) electrocardiographic changes with retrograde flows as small as 8.5 cc. per 100 Gm. per minute, while in one instance +++ electrocardiographic changes occurred with a retrograde flow of 15.3 cc. per 100 Gm. per minute. Although differences in the ratio of injected circumflex weight to heart weight may be expected to influence the degree of electrocardiographic changes following circumflex occlusion, such differences were not observed in these instances. These ratios were 33.9 per cent for the flow of 8.5 cc. and 32.9 per cent for the flow of 15.3 cc., respectively, and may be compared with the average ratio of 36 per cent for the entire series (range 47.3 per cent to 26 per cent).

**Relation of Retrograde Flow to Peripheral Coronary Pressure (P.C.P.).** A priori reasoning, as well as experiments with a model, indicate that the peripheral coronary pressure is directly related to the volume of interarterial anastomotic flow into an occluded artery, and inversely related to the magnitude of runoff through the capillary bed. In addition, the heart rate, as it modifies vascular resistance by compression, may play a role. The variability of the size of the runoff may be minimized by the expression of retrograde flow per unit muscle weight. Figure 3 shows such calculated flows plotted against mean peripheral coronary pressure. The regression line (peripheral coronary pressure on retrograde flow) has a significant slope ($P < .01$).

The variability of the peripheral coronary pressure with identical retrograde flows is not understood. In these experiments there is no relationship to heart rate or to hemoglobin levels. (Plots not shown.)

**DISCUSSION**

These results, based on direct measurements in beating hearts, indicate that young pigs
have minimal functional coronary collateral vessels. This agrees essentially with the anatomic findings of Blumgart. It is noteworthy that the injection technic reported here, while differing markedly from that employed by Blumgart, leads to the identical conclusion in the dead pig heart. Since anastomotic channels are not injected when small retrograde flows exist, it is probable that injection technics, employing fluids with high viscosity, underestimate the function of small collateral vessels. This same situation applies to 14 of the 25 dogs listed in table 2.

The magnitude and variability of anastomoses in dogs were correctly predicted by Blumgart. It is believed that the large retrograde flows found in two of the four pups rules out the possibility that the age of mongrel dogs can fully explain the more extensive collateral formation in comparison with pigs. In addition, the four pups were from two litters of different breeds, one pair being from each. A high retrograde flow was found in one member of each pair. This suggests that collateral development is not a characteristic of litters.

The fact that the volume of retrograde flow, and hence the magnitude of interarterial anastomotic development, bears no relationship to dog weight, heart weight, or unit muscle mass supplied by the circumflex artery, is significant. Furthermore, communicating vessels in small and large hearts exhibit similar patterns by barium injection. It may be concluded that collaterals are independent of heart weight and limited both in number and in size in normal hearts. The existence of large retrograde flows in the pups leads to the speculation that the fundamental collateral pattern is established very early in life and remains relatively unchanged during growth, even though the size of the large vessels increases and the number of capillaries is multiplied. This observation has a practical bearing on experimental deductions in normal dogs based on mortality rates following coronary occlusion. Since both mortality and infarct size are intimately related to collateral blood supply per unit muscle weight, it is predicted that coronary ligation in large dogs may be accompanied by more serious consequences than in small dogs.

The cause of the occasional very large retrograde flow in this series is not clear. Careful examination of the arteries for evidence of disease revealed no abnormalities. The age of the dog with a retrograde flow of 17.1 cc. per minute was estimated to be 9 years, but other dogs of this age had flows within the lower range. None of these animals had an anemia of sufficient degree to produce collaterals of this extent (unpublished data). Although predictions are hazardous, it is suggested that small pressure differences may exist between terminal branches of coronary arteries at birth which are equalized by intercoronary anastomotic flow. Attempts are being made to study this possibility.

**Summary**

Coronary interarterial anastomoses in young pigs have been compared with those existing in dogs of various weights and ages. The results consist of measurements of retrograde circumflex flow and pressure, electrocardiographic findings after circumflex occlusion, and x-ray appearance following barium injection.

Postmortem injection technics predict that young pigs have minimal functional intercoronary anastomoses. The coronary flow, myocardial oxygen consumption and physiologic behavior of the coronary arteries in the pig are similar to those in the dog. Functional and anatomic intercoronary arterial anastomoses in dogs are variable and occasionally of a magnitude to allow major coronary occlusion with but minor electrocardiographic changes. The degree of such collateral development and function bears no statistical relationship to dog or heart weight.

It is believed that interarterial anastomoses are formed at an early age and remain relatively fixed in normal hearts. Following coronary ligation these anastomoses are most beneficial in the smaller hearts.

**Acknowledgment**

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REFERENCES


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