Functional Development of the Coronary Collateral Circulation During Coronary Artery Occlusion in the Conscious Dog

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We studied changes in the coronary collateral circulation during coronary artery occlusion in 14 conscious dogs by: a) determining simultaneous changes in peripheral coronary pressure (PCP) and retrograde flow (RF) after abrupt coronary artery occlusion; b) correlating these functional indices with quantitative anatomic indices (AI) of coronary collateral development (Menick *et al*: Am Heart J 82:503–510, 1971); and c) observing changes in these indices after repeated reocclusions of a coronary artery. These dogs were subjected to left circumflex coronary artery (LCCA) occlusions for 2 hours to 8 days; pressure tubes were implanted in the aorta and LCCA, the latter tube placed distal to an occlusive cuff for PCP and RF measurements. Afterwards the animals were sacrificed, their hearts injected with a modified Schlesinger's gelatin mass, and AI determined. During 2 to 24 hour LCCA occlusions (11 dogs) mean PCP rose to levels 50 to 80% of prevailing aortic pressure. During repreated 2- to 24-hour occlusions (2 dogs) in the same dog, the rate at which PCP rose increased. Retrograde flow was unchanged during 2- to 24-hour occlusions. Anatomic indices of these dogs were in the same range as those observed in unoccluded controls. When LCCA occlusion was maintained for more than 4 days (3 dogs), mean PCP rose during the first 24 hours and then remained stable; RF did not change until 4 days into occlusion and then increased. Anatomic indices of dogs occluded for more than 4 days were significantly greater ($P < 0.001$) than those of the 2- to 24-hour occlusion groups. Our study shows that: a) the early PCP rise after occlusion is not associated with an increase in RF, b) RF is a better index of collateral function and c) RF correlated well with the anatomic development of the collateral bed (Am J Pathol 67:483–500, 1972).

IN PREVIOUS STUDIES in the anesthetized dog, using peripheral coronary pressure, retrograde flow and isotope clearances as indices of coronary collateral blood flow,[1–5] no evidence was found for increased function of the coronary collateral circulation during the first few days after the onset of acute coronary artery occlusion. These studies were in agreement with earlier morphologic studies,[6–8] which showed no increase in the size or number of intercoronary collaterals

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until at least 4 to 5 days after the onset of coronary artery occlusion. However, recent studies of the coronary collateral circulation in the conscious dog suggest that a marked increase in coronary collateral circulation can occur within a few days after coronary artery occlusion.[9,10] These latter studies used indirect indices of collateral flow—*ie*, peripheral coronary pressure and augmented coronary blood flow through the unoccluded coronary artery, which may account for their variance with earlier investigators. In acute experiments involving ligation of the anterior descending branch in dogs, Rees and Redding[5] followed xenon clearances for 10 days in the closed-chest state and observed a lag of 3 to 4 days after infarction before the clearances started to rise, a finding consistent with previous morphologic studies.[6–8] A recent study in our laboratory showed the feasibility of measuring and correlating retrograde flow in the conscious dog with a quantitative anatomic index of coronary collateral circulatory development.[11] Thus, our study intends to: a) determine simultaneous changes in peripheral coronary pressure and retrograde flow after abrupt coronary artery occlusion; b) correlate these functional indices with a quantitative anatomic index of coronary collateral development; and c) observe changes in these parameters after repeated reocclusion of a coronary artery.

Materials and Methods

Our studies were made in 14 healthy dogs weighing 20 to 35 kg.* These animals were trained to lie quietly and unrestrained for several hours on a padded table, before and after surgery. We anesthetized the dogs with intravenous sodium pentobarbital (30 mg/kg) and performed a left thoracotomy at the fifth left intercostal space while maintaining the animal on intermittent positive pressure breathing with a Harvard respirator. The heart was exposed and supported in a pericardial sling. The main branches of the left coronary artery were identified and 1.5-cm segments of the left anterior descendens and the left circumflex branch were dissected free. In 6 dogs, a pneumatic occlusive cuff [12] was placed on the left circumflex branch. An intracoronary tube [9,13] was implanted in the left circumflex branch distal to the cuff for measuring peripheral coronary pressure. In 8 dogs a pneumatic occlusive cuff [12] was placed on the left anterior descendens branch and a silastic T-tube [11] inserted into the same branch distal to the cuff. The T-tube allowed continuous coronary blood flow until the time of occlusion. Then measurements of peripheral coronary pressure and retrograde flow were obtained from the T-tube. In all animals a polyvinyl catheter was inserted into the distal aortic arch to obtain aortic blood pressure. These devices were tunneled subcutaneously and attached to appropriate skin connectors.[12] Patency of the intracoronary tube was maintained by flushing once or twice daily with 20,000 USP

* In conducting the research described, the investigators adhered to the Guide for Laboratory Animal Facilities and Care as promulgated by the Committee on the Guide for Laboratory Animal Facilities and Care of the Institute of Laboratory Animal Resources, National Academy of Science–National Research Council.

units ml of heparin; the aortic tube was flushed daily with 1000 USP units ml of heparin. Fibrinolysin was occasionally needed to obtain free backflow of blood. Aortic and coronary phasic pressures were measured with Elema-Schonander transducers. Records of phasic pressure were recorded on an Elema-Schonander Mingograf 81 ink-jet recorder. Mean aortic and coronary blood pressures were determined on a number of representative heart beats by planimetric integration using calibration factors. Tension-time index [14] was equal to the product of mean systolic aortic pressure during systolic ejection times the duration of systole and was expressed in mm Hg-sec/beat.

Two to three days after recovery from surgery aortic and coronary pressures and coronary collateral indices were measured, with the dog lying on its right side. Two methods were used to study coronary collateral circulation. First, estimates of residual pressure (peripheral coronary pressure) were obtained by measuring it in the coronary branch distal to the point of its temporary or permanent occlusion, using the pneumatic cuff.[9] During control runs (*ie*, before permanent vessel occlusion) the peripheral coronary pressure was arbitrarily defined as the residual pressure at the end of a 10-second occlusion. Second, retrograde flow was measured from the peripheral end of the anterior descendens branch [11] by collecting it for at least 30 seconds in a graduate. After the control runs in the normal dog, either the circumflex or anterior descendens branch was occluded abruptly by the pneumatic cuff for periods of 2 hours to 8 days. Changes in coronary collateral indices during permanent coronary occlusion were monitored as frequently as technically feasible, usually at 5-to 15-minute intervals.

In 2 dogs, the occlusion was released after 2 hours and coronary collateral indices measured 1 minute later. After 2 days recovery, the 2-hour occlusion was repeated. This procedure was repeated twice more. In 1 of these dogs, 24-hour occlusion of the circumflex artery was later repeated in like manner at 4-day intervals.

After the experimental studies were completed, the animals were killed with an overdose of sodium pentobarbital, the hearts removed and placed in cold saline in a refrigerator for 24 to 36 hours until rigor mortis subsided.

Gelatin Injection Method

The hearts were warmed to room temperature, the atria removed and the left coronary branches cannulated with polyethylene tubing. Both major left coronary branches were injected with a modified Schlesinger mass, according to the procedure of Menick *et al.*[11] After appropriate fixation and clearing, the number and diameters of intercoronary collaterals were recorded and the quantitative anatomic anastomotic index determined for each heart, according to Menick *et al.*[11] Representative sections were taken from the injected specimen for histologic examination.

Results

Systemic and coronary data before and during coronary artery occlusion are summarized in Tables 1 and 2. Due to the complicated nature of the experiments, not all of the desired measurements were obtained in each dog. Four dogs (7, 9, 10 and 13) developed ventricular fibrillation during coronary artery occlusion. This occurred at 2 to 25 hours after the onset of occlusion. Nine days after occlusion car-

Table 1—Summary of Systemic and Coronary Data for Control Period and During Coronary Artery Occlusion

Dog No.	Body wt (kg)	Heart wt (g)	Occlusion duration (hr)	Heart rate (beats/min)		Mean aortic pressure (mmHg)		Peripheral coronary mean pressure (mmHg)		Retrograde flow (ml/min)		Tension-time index (mmHg sec/beat)	
				Control	Occlusion peak*	Control	Occlusion range	Control	Occlusion peak*	Control	Occlusion range	Control	Occlusion range
1	22	152	1	103	128	95	93–95	10	23	—	—	14.0	11.0–14.0
2	17	128	72	82	150	110	97–116	21	50	—	—	—	—
3	24	156	24	83	111	92	92–105	15	62	—	—	15.6	12.4–15.6
4	23	157	2	122	122	125	101–125	15	22	—	—	—	—
5	20	170	240	158	158	92	92–103	32	103	4.3	4.0–6.4	18.4	14.4–21.6
6	41	225	1	118	137	102	102–105	14	20	—	—	—	—
7	28	191	4	128	148	116	116–121	15	27	1.8	1.0–1.8	—	—
8	38	250	120	138	145	95	86–100	15	58	2.6	2.2–3.1	—	—
9	24	169	25	137	187	103	90–138	15	35	5.5	2.1–5.8	22.3	13.8–22.3
10	21	165	70	120	173	125	75–134	21	52	4.0	1.0–4.8	23.5	10.0–23.5
11	23	161	4	150	180	98	98	28	28	3.3	3.3	—	—
12	28	194	216	150	157	92	86–96	12	51	2.4	—	20.0	10.0–22.2
13	21	145	2	108	108	88	88–92	13	16	1.8	1.8	—	—
14	25	178	2	119	154	100	93–112	10	19	—	—	19.0	16.1–19.0
Mean±SE	25 ± 2	174 ± 8		122 ± 6		103 ± 3		18 ± 2		3.0 ± 0.3		18.9 ± 1.2	

* Occlusion peak is the highest peak observed for these parameters during occlusion

Table—2 Summary of Coronary Collateral Indices for Control Period and During Coronary Artery Occlusion

	Time after onset of coronary artery occlusion (hr)								
	Control	1	2	6	24	48	72	96	>96
Heart rate (beats/min)	122 ± 6	136 ± 5†	132 ± 9*	156 ± 12†	148 ± 8†	145 ± 4*	131 ± 22	125 ± 11	110 ± 10
No. dogs	14	10	7	5	6	5	4	2	3
Mean aortic blood pressure (mm Hg)	103 ± 3	102 ± 5	111 ± 5	109 ± 9	94 ± 4	91 ± 4	103 ± 3	92 ± 1	102 ± 3
No. dogs	14	10	7	5	6	5	4	2	3
Peripheral coronary mean pressure (mmHg)	18 ± 2	19 ± 2	24 ± 2†	33 ± 5†	34 ± 6†	37 ± 3†	56 ± 7†	61 ± 6†	71 ± 13†
No. dogs	14	10	7	5	6	5	4	2	3
Retrograde flow (ml/min)	3.0 ± 0.3	3.0 ± 0.4	3.3 ± 1.0	3.2 ± 0.4	2.5 ± 0.4	2.6 ± 0.7	2.4 ± 0.7	3.7 ± 0.9	4.8 ± 1.2
No. dogs	8	4	4	4	5	3	3	2	2
Tension-time index (mm Hg-sec/beat)	18.9 ± 1.2	16.7 ± 1.4†	16.8 ± 2.0†	18.8 ± 1.6	15.0 ± 0.8†	11.9 ± 1.5†	18.7 ± 2.1	17.5 ± 0.3	19.3 ± 2.1
No. dogs	7	6	3	2	4	3	2	2	2

Values = mean ± SE

Significance of differences between control mean and experimental means was tested using Student's paired t test

* $P < 0.05$

† $P < 0.01$

diac arrest occurred immediately after fibrinolysin was injected into the heart to unplug the silastic intracoronary tube of dog 12.

Control Data

A typical peripheral coronary pressure tracing is shown in Text-figure 1. This tracing resembles the ventricular pressure wave—*ie*, a rapid increase at the beginning of systole and a rapid decline in the latter half of systole with no runoff during diastole. During the control period, heart rate and aortic blood pressure averaged 122 ± 6 beats/min and 103 ± 3 mm Hg, respectively. These values are similar to those obtained by Pasyk *et al*[15] in the unanesthetized dog. Retrograde flows during the control period averaged 3.0 ± 0.3 ml/min. Retrograde flow has not been measured previously in the intact unanesthetized dog, but this value was similar to that obtained by other investigators in the open chest anesthetized animal.[1,2]

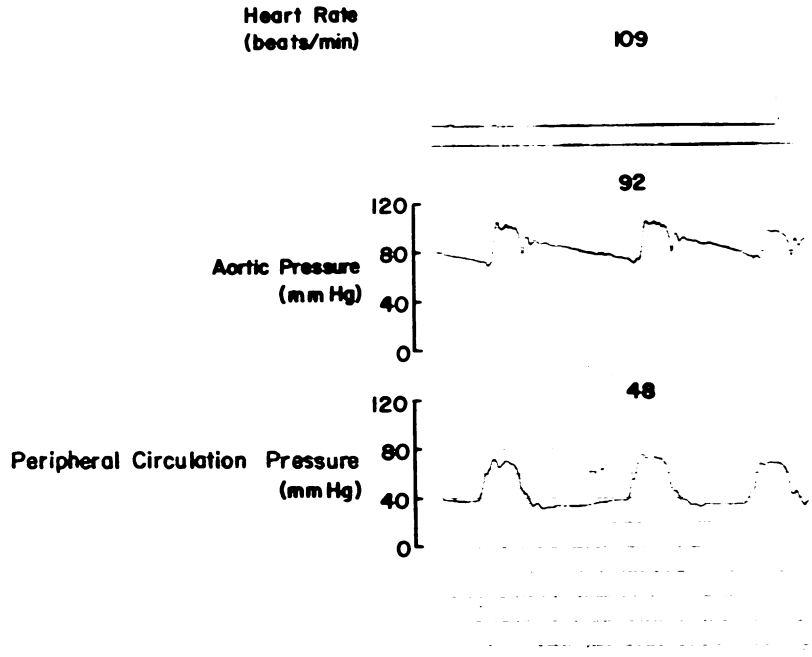
Responses During Coronary Artery Occlusion

Systemic and General Changes

At some time within the first few minutes, and often within the first minute, after coronary artery occlusion, heart rate increased. As the occlusion continued, heart rate increased further. The peak rate, varying from 108 to 187 beats/min, was reached some 6 to 24 hours after the onset of occlusion (Tables 1 and 2). Aortic pulse pressure decreased progressively throughout the occlusion period, while mean aortic pressure did not decrease significantly. Tension-time index (Table 2) decreased significantly ($P < 0.01$) at 1 to 48 hours after the start of occlusion and then returned to control levels.

Peripheral Coronary Pressure Changes

Within the first few minutes of coronary artery occlusion, mean peripheral coronary pressure rose. A significant increase ($P < 0.01$) of mean peripheral coronary pressure occurred within 2 hours of the onset of occlusion (Table 2) and pressure continued to rise throughout the duration of occlusion. At the same time, there was a marked increase in peripheral coronary pulse pressure in both its systolic and diastolic levels. Although mean peripheral coronary pressure reached a level that was approximately 66% of the prevailing aortic blood pressure during the first 96 hours of coronary artery occlusion, the peripheral coronary pressure trace retained a ventricular pressure wave form like that shown in Figure 1. In the 3 dogs (5, 8, 12) occluded for longer than 96 hours, mean peripheral coronary pressure

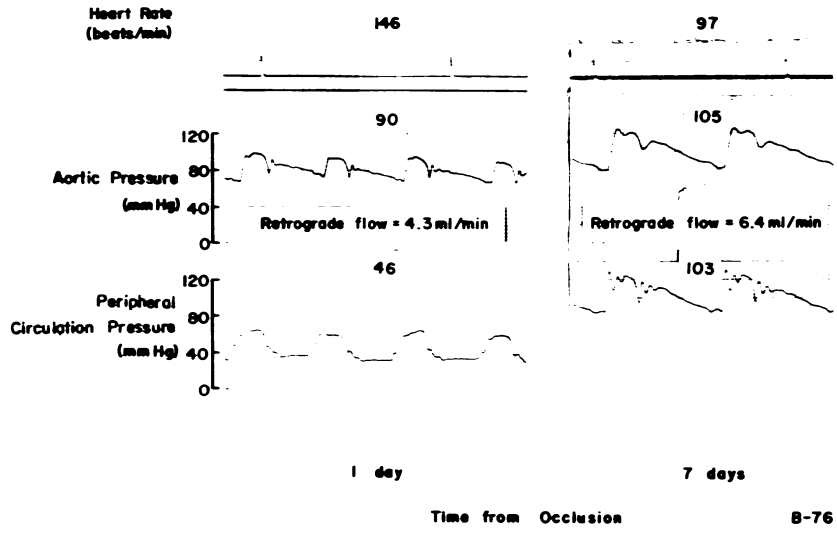


TEXT-FIG 1—Phasic tracing from Dog 3 six hours after the onset of coronary occlusion. Traces from *top* to *bottom* are time (1-second intervals), aortic blood pressure (*AP*) and left circumflex peripheral coronary pressure (*PCP*). Mean values for heart rate, AP and PCP are given in bold numerals. Recording speed = 50 mm/sec.

continued to rise; in dog 5, at 10 days after the onset of occlusion, it was nearly identical to the prevailing aortic blood pressure (Text-figure 2). A striking alteration of wave form occurred in the peripheral coronary pressure trace when the duration of occlusion exceeded 96 hours. The tracing was similar to the aortic pressure trace—*ie*, the appearance of diastolic runoff and a dicrotic notch, and no longer resembled a ventricular pressure curve. These features of the pressure curve indicate the presence of large intercoronary collaterals.[9]

Retrograde Flow Changes

Typical changes observed in retrograde flow before and after coronary artery occlusion are shown in Tables 2 and 3. Control values for retrograde flow averaged 3.0 ± 0.3 ml/min. In the 5 dogs that developed ventricular fibrillation or cardiac arrest (7, 9, 10, 12 and 13) retrograde flow decreased from control values (Table 3). Dogs 7 and 13, which had the lowest control values for retrograde flow, developed ventricular fibrillation the earliest—*ie*, within 2 hours of the onset of



TEXT-FIG 2—Phasic tracing from Dog 5 one day (*left panel*) and 7 days (*right panel*) after the onset of coronary occlusion. Description same as for Text-figure 1. At 7 days peripheral coronary pressure trace has a wave form similar to the aortic blood pressure trace.

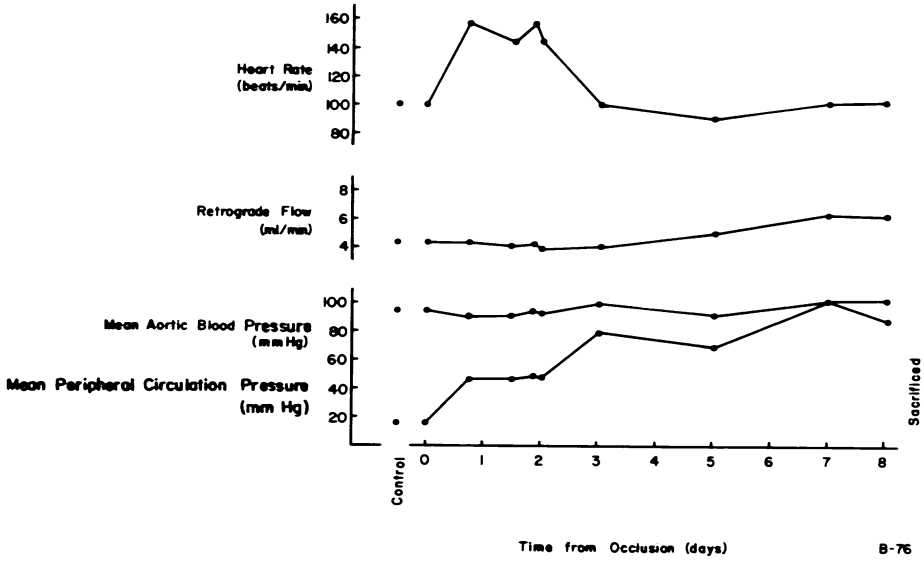
coronary artery occlusion. In the remaining 3 dogs, there was no significant change in retrograde flow from control values during the first 96 hours of occlusion, although mean peripheral coronary pressure rose to high levels. When the duration of occlusion exceeded 96 hours, retrograde flow increased above control levels. Dog 5, occluded for 240 hours, and dog 8, occluded for 120 hours, showed a 49 and 19% increase, respectively, in retrograde flow. This rise was secondary to an increase in the size and number of intercoronary collaterals, since heart rate and mean aortic blood pressure of these 2 dogs were not significantly different from control values (Table 1).

Text-figure 3 shows the changes in collateral indices observed in Dog 5 during 8 days of coronary artery occlusion. During the initial 24 hours of occlusion there were rapid rises in heart rate and peripheral coronary pressure, while mean aortic blood pressure and retrograde flow were unchanged. The tachycardia persisted for an additional 24 hours before heart rate returned to control values 3 days after the onset of occlusion. Peripheral coronary pressure continued to rise throughout occlusion and was nearly equal to the prevailing aortic blood pressure 7 to 8 days after the start of occlusion. By this time the configuration of the peripheral coronary pressure wave was similar to that of the aortic pressure wave (Text-figure 2). Retrograde flow remained constant during the first 4 days of occlusion; on the fifth day, retrograde flow

began and continued to rise throughout the remaining observation times. The time-interval before retrograde flow began to increase was similar to the minimum time interval, indicated by others,[6-8] necessary for the size or number of intercoronary anastomoses to increase.

Effects of Repeated Occlusions on Peripheral Coronary Pressure

In dogs 2 and 3, the coronary artery was repeatedly occluded (2 to 24 hours duration) to observe effects on collateral indices and on the anastomotic index. In both dogs, peripheral coronary pressure was the sole collateral index available. Dog 3 was subjected to four 2-hour and two 24-hour occlusions with 2- to 6-day recovery intervals. The observed data are shown in Figures 4 and 5. During the first 2-hour occlusion, peripheral coronary pressure rose from a control value of 18 to 38 mmHg. Heart rate was unchanged and mean aortic pressure varied during occlusion. One minute after the 2-hour occlusion was released, the coronary artery was reoccluded for 10 seconds to obtain peripheral coronary pressure. Within this brief interval, peripheral coronary pressure fell to the control level and remained there during the 4-day recovery interval. During the second 2-hour occlusion, peripheral coronary pressure rose to a level higher than before, but fell back to the control level within 1

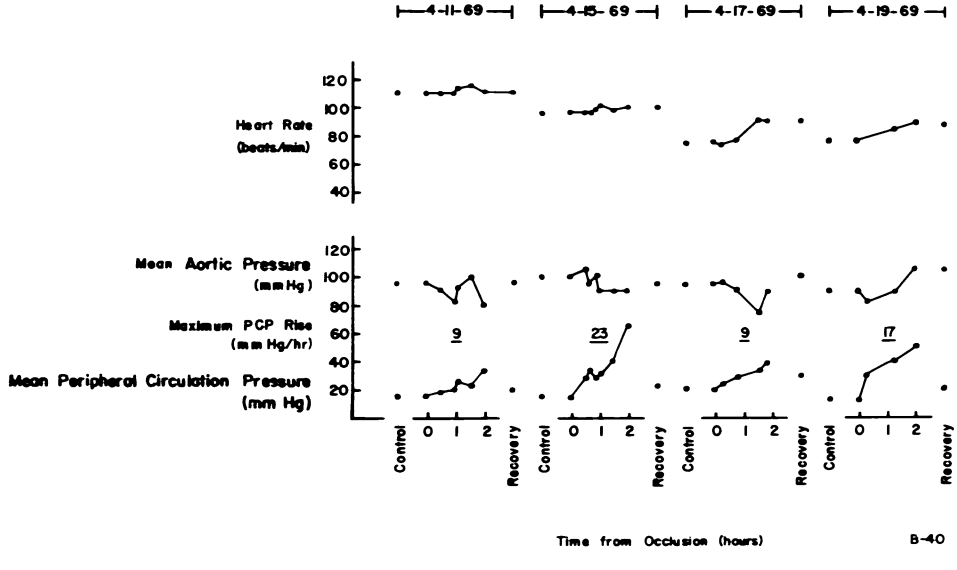


TEXT-FIG 3—Changes in heart rate, retrograde flow, mean aortic blood pressure and peripheral circumflex pressure observed in dog 5 during the initial 8 days of coronary occlusion. Control values before occlusion are given for all parameters. Onset of coronary occlusion was at time 0.

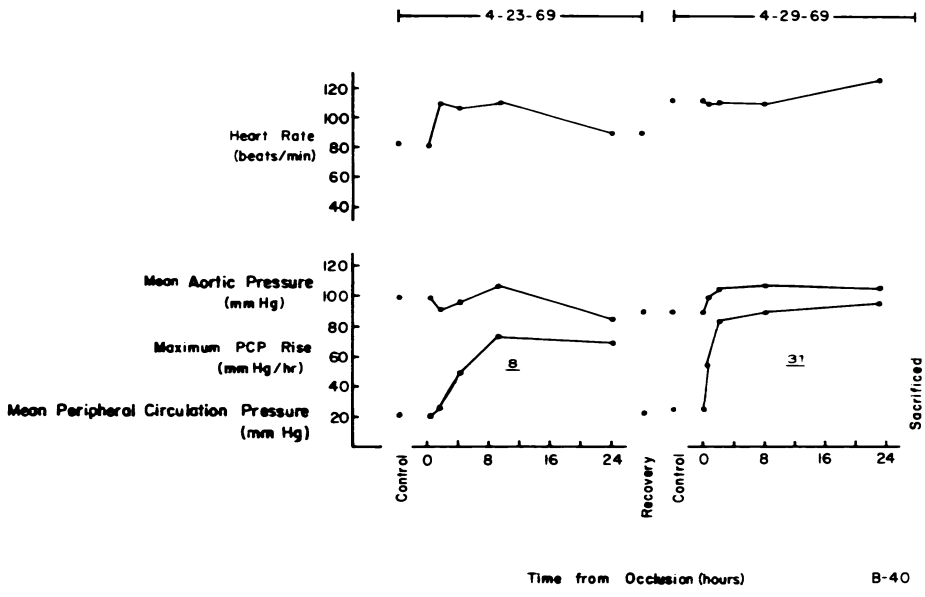
minute after the occlusion was released. The maximum rate of rise of peripheral coronary pressure (mmHg/hr) during occlusion increased with repeated occlusion (Text-figure 4). When repeated occlusions were longer (24 hours), similar results occurred (Text-figure 5). Control values for peripheral coronary pressure were the same as before (15–18 mmHg). With the longer duration of occlusion, peripheral coronary pressure increased to higher levels, approximating 77 to 90% of prevailing aortic blood pressure. The maximum rate of rise of peripheral coronary pressure was greater during the second 24-hour occlusion. A surprising finding was the fall of peripheral coronary pressure to control level within 1 minute after the 24-hour occlusion was released. After the second 24-hour occlusion it was maintained and the dog killed with an overdose of sodium pentobarbital. Postmortem studies (Table 4) showed that the repeated peripheral coronary pressure rises in dogs 2 and 3 were not associated with an increase in the size or number of intercoronary anastomoses.

Postmortem Studies (Anastomotic Indices)

The distribution of coronary collaterals in each heart is given in Table 4. In dogs occluded for less than 96 hours, the ranges of values



TEXT-FIG 4—Changes in heart rate, mean aortic blood pressure and peripheral circumflex pressure observed in dog 3 during four repeated 2-hour occlusions of the left circumflex coronary artery. Control values before each occlusion are given for all parameters. Onset of each occlusion was at time 0. Recovery values for all parameters were obtained 1 minute after the release of coronary occlusion.



TEXT-FIG 5—Changes in heart rate, mean aortic blood pressure and peripheral circumflex pressure observed in dog 3 during two repeated 24-hour occlusions of the left circumflex artery. Description same as for Text-figure 4.

for anastomotic indices of coronary collateral development were similar to those observed before.[11] The average value for this group (dogs 1–4, 6, 7, 9–11, 13 and 14) was 909 ± 134. Dogs 5, 8 and 12 ,which were occluded for longer than 96 hours, had higher anastomotic indices, ranging from 2275 to 3994. Their average value (2915 ± 543) was significantly greater ($P < 0.001$) than that for the other group, indicating that coronary occlusion lasting more than 96 hours leads to an increase in the size and number of intercoronary collaterals.

Figures 6 and 7 demonstrate gelatin injection specimens from a representative dog from each occlusion group. Dog 3 (Figure 1) had repeated occlusions of the coronary artery, but never for more than 24 hours at any one time. Although its peripheral coronary pressure rose to high levels on several occasions (Text-figure 4 and 5), relatively few intercoronary collateral vessels were present. Those present were small in size—*ie*, one-half of them were less than 100 μ in diameter (Table 4). In dog 5 the left circumflex coronary was occluded for 240 hours. Peripheral coronary pressure rose to levels approximating the prevailing aortic blood pressure, while a significant increase in retrograde flow occurred after 96 hours of coronary occlusion. The gelatin specimen from dog 5 (Figure 2) had an increased number of inter-

Table 3—Retrograde Flow Values for Control Period and During Coronary Artery Occlusion

Dog No.	Time after onset of coronary artery occlusion (hr)								
	Control	1	2	6	24	48	72	96	>96
5	4.3	—	—	—	4.3	4.2	4.0	5.0	6.4
7	1.8	—	1.0	—	—	—	—	—	—
8	2.6	—	—	—	2.5	2.2	2.2	2.4	3.1
9	5.5	5.5	5.8	4.0	2.1	—	—	—	—
10	4.0	3.8	4.8	3.6	2.0	1.3	1.0	—	—
11	3.3	—	—	3.3	—	—	—	—	—
12	2.4	2.4	—	1.8	1.5	—	—	—	—
13	1.8	1.8	1.8	—	—	—	—	—	—
Mean ± SE	3.0 ± 0.3	3.0 ± 0.4	3.3 ± 1.0	3.2 ± 0.4	2.5 ± 0.4	2.6 ± 0.7	2.4 ± 0.7	3.7 ± 0.9	4.8 ± 1.2

Values are ml/min

Significance of differences between control mean and experimental means tested using Student's paired t test; differences were not significant at the 5% level

Table 4—Incidence and Size of Intercoronary Collaterals

Dog No.	Duration of occlusion (hr)	Size of intercoronary collaterals*			Anastomotic index
		40–100μ	100–200μ	200–300μ	
1	1	3	4	8	1219
2	72	8	6	3	875
3	24	4	3	1	500
4	2	8	3	—	350
5	240	7	15	14	3994
6	1	9	4	—	456
7	4	14	5	3	1112
8	120	10	5	11	2475
9	25	10	10	4	1763
10	70	10	7	—	762
11	4	24	8	3	1469
12	216	4	12	6	2275
13	2	16	5	—	600
14	2	18	6	1	888

* Values represent the number of anastomotic connections in each size category between left anterior descending and left circumflex coronary arteries.

coronary collaterals, 39% of which were greater than 200 μ in diameter. These were located predominantly in the epicardial surface, although some were located within the midportions of the myocardium. In either instance, their morphologic characteristics suggested that they represented physical expansion of preexisting vessels—*ie*, thin walls and large lumens with the absence of mitoses in the vessel walls.

Discussion

This study was undertaken to detect the rapidity with which coronary collateral circulation developed after abrupt coronary artery occlusion. In previous studies in unanesthetized animals coronary occlusion was gradual [9,10,15,16] or only peripheral coronary pressure observed [9,10,15,16] without correlating physiologic indices with morphologic indices. In our study, an anastomotic index of coronary collateral circulation established in this laboratory [11] was correlated with both peripheral coronary pressure and retrograde flow.

Although we know of no method for measuring collateral flow through a coronary bed directly, the physiologic indices we used are thought to represent the functional state of coronary collateral connections.[9,10,17] However, the discrepancies between changes in peripheral coronary pressure and retrograde flow during the initial 24 to 48 hours after abrupt coronary occlusion suggest that peripheral coronary pressure has

limitations as an index of collateral development during this period. Our findings of a rapid rise in peripheral coronary pressure with retention of a ventricular pressure wave form after abrupt coronary occlusion, particularly on repeated occlusion, are in agreement with those of Pasyk *et al*[17] and Khouri *et al.*[10] However, in all instances, in our study when occlusion was maintained for less than 96 hours, the size or number of intercoronary anastomoses did not increase (Table 4). Since the aforementioned studies[9,10,17] did not conduct similar postmortem injection studies, one must have reservations about the interpretations offered. Our results indicate that change in peripheral coronary pressure during the initial 24 to 48 hours of abrupt coronary occlusion is a poor index of changes in the anatomic development of coronary collateral circulation. The insensitivity of peripheral coronary pressure as an index of collateral blood flow after abrupt coronary occlusion has been well documented by Schaper.[18]

The rapid rise in peripheral coronary pressure after the onset of coronary occlusion may reflect other changes. For example, after the onset of coronary occlusion, the ischemic myocardium, which contains the collateral channels that transmit the peripheral coronary pressure pulse, ceases to contract and bulge.[19] As time passes, it regains contractile function and slowly increases its contractility.[20–22] Since the collateral channels initially are small, peripheral coronary pressure may largely reflect effects of extravascular compression on collateral channels. Thus, when the ischemic myocardium reaches its minimum contractile level immediately after occlusion,[22] peripheral coronary pressure is low. As contractility of the ischemic myocardium increases, extravascular compression of collateral channels would increase and peripheral coronary pressure would rise. If the collateral channels remained small, the ventricular wave form would be retained. Thus, the wave form change of peripheral coronary pressure to that resembling the aortic pressure wave would occur when the intercoronary collaterals increased in size. This is consistent with our findings and with the earlier study by Elliot *et al.*[9]

Our observation of the rapid regression of peripheral coronary pressure to control level after the occlusion is released, and its rapid rise on reocclusion resembles the observations of Khouri *et al.*[10] However, if peripheral coronary pressure is an insensitive index of collateral blood flow in this situation,[18] peripheral coronary pressure changes probably do not represent changes in the functional status of coronary collateral channels, as Khouri *et al*[10] suggest. Rather, it may reflect changes in the contractility of that part of the myocardium made ischemic by occlusion.[19–22]

Retrograde flow is an indirect index of perfusion flow since it is collected against atmospheric pressure and without the normally supplied impedance of the bed. However, our previous study showed a linear relationship between retrograde flow and a quantitative anatomic anastomotic index.[11] Our present findings that there was no change in retrograde flow during the initial 96 hours of occlusion, associated with the lack of significant increase in the size or number of intercoronary collaterals, suggest that retrograde flow is a better index than peripheral coronary pressure for determining the functional status of the coronary collateral circulation due to its anatomic development.

In our experiments, changes in retrograde flow and anastomotic index after abrupt closure of a major coronary branch in the unanesthetized dog did not occur until more than 96 hours of occlusion had passed, contrary to the suggestion by Pasyk *et al*[17] that coronary collateral function improves during the first 24 to 34 hours of coronary occlusion. Our findings are in agreement with the isotope studies by Rees and Redding,[5] the physiologic studies by several investigators [1–5] and the morphologic studies by Blumgart, Zoll *et al*.[6–8] The experimental model used in our study demonstrates the feasibility of combining physiologic and morphologic approaches to determine coronary collateral development. Extension of this approach to determine whether coronary collaterals, once formed, regress or reappear, and what interventions affect their development, seems appropriate.

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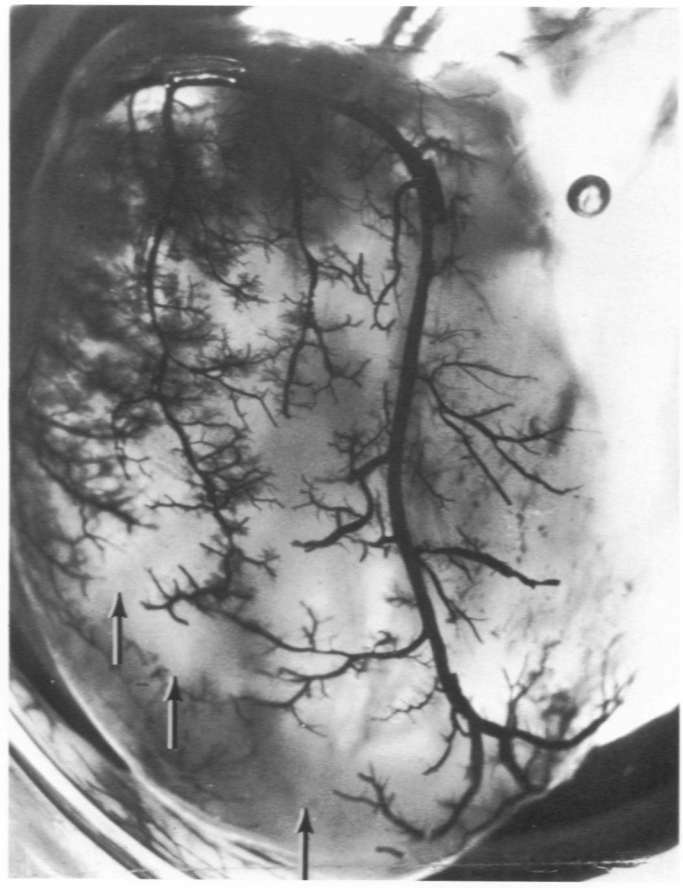
Fig 1A—Macrophotograph of gelatin injected specimen from dog 3. Posterolateral view of heart shows the posterior descending circumflex artery coursing toward the apex *(bottom)*. At the margin between the terminal branches of the anterior descending and circumflex branches *(arrows)* no intercoronary anastomoses are visible (× 1). **B**—High power view of same specimen at the margin between terminal brances of the left anterior descending branch *(LAD)* and the left circumflex branch *(right margin)*. An occasional intercoronary collateral *(arrow)* less than 100 μ in diameter is present (× 10).



A

B

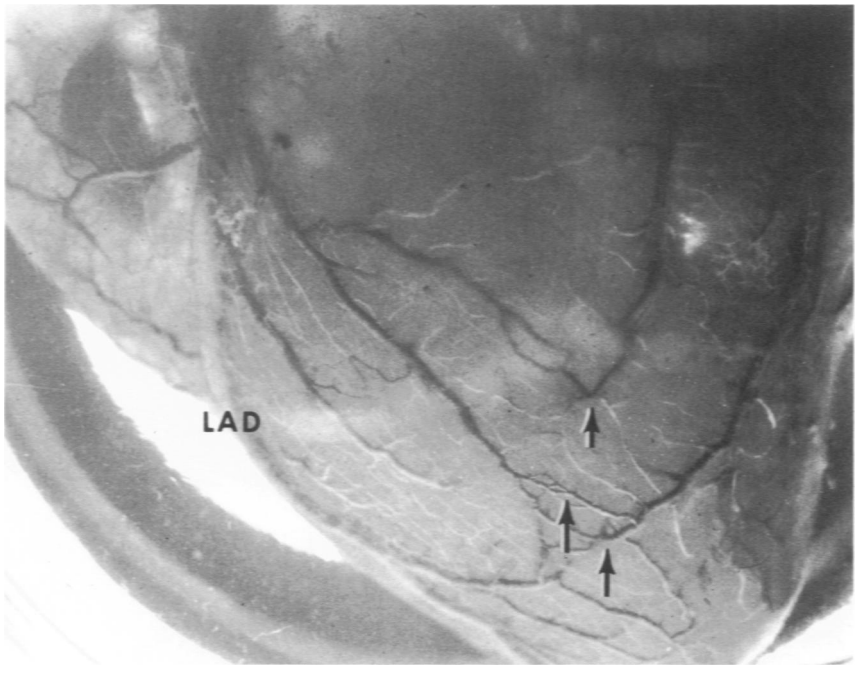


Fig 2—Macrophotograph of gelatin injected specimen from Dog 5. Anterolateral view of heart shows the left anterior descending branch (*LAD*) coursing toward the apex (*bottom*). Along the lateral margin of the heart several large intercoronary collaterals (*arrows*) are present on the epicardial surface, joining terminal branches of the anterior descending and circumflex vascular beds (× 1).