Influence of Physical Exercise on Coronary Collateral Blood Flow in Chronic Experimental Two-vessel Occlusion

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SUMMARY In 45 approximately 1-year-old purebred German shepherd dogs, the left circumflex and the right coronary arteries were chronically occluded by implantation of slowly swelling ameroid constrictors. Before the operation, 27 dogs were trained on a treadmill until they could run 8 mph on a 22% incline for 1 hour, 5 days per week. Two weeks after the operation, exercise was gradually resumed and continued for 4 weeks, until the preoperative fitness level had been regained. Preoperative exercise training lasted 1–3 months; postoperative training lasted 100 ± 22 days (mean ± SD). After the dogs had trained with two chronically occluded coronary arteries, collateral and coronary blood flows were measured with tracer microspheres at maximal coronary vasodilation (adenosine infusion) in an isolated, blood-perfused Langendorff preparation at perfusion pressures of 40, 60, 80, 100, 120 and 140 mm Hg. Eighteen nonexercising dogs that also had two-vessel coronary occlusion served as controls. Nine controls and nine exercising dogs were paired littermates. Exercise of relatively high intensity (heart rates greater than 200 beats/min) before and after occlusion had no effect on coronary collaterals. Collateral conductance in trained and untrained dogs reached only slightly less than 40% of that of the replaced coronary artery. This result agrees well with earlier results in a group of nonexercising dogs with chronic two-vessel occlusion studied in an identical way. Two-vessel occlusion was associated with a 25% mortality rate. All dogs died instantaneously without warning symptoms of ventricular fibrillation. Exercise had no influence on mortality.

EXPERIMENTS conducted by Eckstein1 in dogs with a chronic coronary artery stenosis showed that treadmill running improved retrograde flow. Later experiments carried out with more refined techniques and under more nearly clinical conditions have produced conflicting results.2,6 The present study was undertaken to restudy the problem using a rigidly standardized model by testing regional blood flows with tracer microspheres during maximal vasodilation and under a wide range of perfusion pressures (40–140 mm Hg).

Methods

Forty-five purebred German shepherd dogs of either sex were studied. They were approximately 1 year old at entry into the study. After an adaptation period of 6 weeks, the dogs were anesthetized with subcutaneous piritramide.6 5 mg/kg, a synthetic morphine-like analgesic, and i.v. sodium pentobarbital, 10 mg/kg, and artificially ventilated with nitrous oxide and oxygen in a 50:50 ratio. The chest was opened at the fourth left intercostal space, the heart was cradled in the pericardium and the left circumflex and right coronary arteries were prepared and fitted with ameroid constrictors7,9 that slowly occluded the artery within 2.5 weeks.9 Penicillin and streptomycin were instilled into the chest cavity, which was thereafter closed in layers. The dogs were allowed to recover and were restudied 3 months later.

Experimental Design

Twenty-seven exercising and 18 nonexercising dogs entered the study. Nine exercising and nine nonexercising dogs were paired littermates. The exercising dogs ran at 8 mph on a treadmill with an incline of 22% for 1 hour, 5 days per week. The speed posed no problem, but the 22% grade was the main load; most dogs required 1–3 months of training preoperatively before they endured 1 full hour. Postoperative training started 2 weeks after operation and was continued for another 12 weeks (mean 100.4 ± 22.3 days). The trained and nonexercising dogs were kept in individual kennels with a 2-floor area of 8 m², equally divided between indoor and outdoor space. They were fed standard dog chow and had free access to food and water.

Evaluation of Collateral Development

Three months after the ameroid constrictor was implanted, the dogs were again anesthetized and artificially ventilated as described. The chest was opened and the heart quickly excised and connected to a Langendorff-type perfusion apparatus,10 which was fed with arterial blood from an anesthetized support dog. The venous effluent was continuously returned to the support dog. Perfusion pressure in the Langendorff circuit was kept at any desired level by a servocontrolled roller pump. The arterial inflow was measured with an electromagnetic flowmeter during autoregulation as well as during maximal coronary vasodilation produced with adenosine. Peripheral coronary pressure was obtained by needle puncture of the occluded left circumflex coronary artery. Arterial inflow, perfusion pressure and peripheral coronary
Regional coronary blood flow was determined by injecting 9-μ tracer microspheres during maximal vasodilation at perfusion pressures of 40, 60, 80, 100, 120 and 140 mm Hg. Two hundred thousand beads were injected into the aortic inflow cannula through a catheter with six sideholes to ensure adequate mixing at every pressure level and to ensure a tissue content of about 500 beads per 500-mg tissue sample of a 200-g heart. The isotopes used were 141Ce, 61Cr, 113Sn, 85Sr, 89Nb and 43Sc. At the end of the experiment, the heart was sliced into 8-mm-thick rings parallel to the apex-base axis. Each ring was cut into about 25 wedges of adjacent myocardium and each wedge was subdivided into subepicardial, endomural and subendocardial samples. Dissection of the occluded arteries showed that complete occlusion was produced by the amerdoid device in all dogs. Myocardium unrelated to the topic under study (part of the right ventricle, the atria, aorta and pulmonary artery) was cut into 2-g pieces and assayed for radioactivity. The sum of all counts/min from all tissue samples of the entire heart was then equated with the metered inflow into the heart. In this way, a calibration factor was obtained with which counts/min and counts/unit sample weight could be translated into ml/min/100 g fresh tissue weight according to equations 1 and 2.

Blood flow of an individual tissue sample (Fi) is

$$F_i = A_i \cdot C$$  \hspace{1cm} (1)

where C is a calibration factor with

$$C = \frac{F}{\sum_{i=1}^{n} A_i \cdot G_i}$$  \hspace{1cm} (2)

and $A_i$ = activity of tissue sample i (counts/min • g$^{-1}$), $G_i$ = weight of tissue sample i (g), n = total number of tissue samples and $F$ = total arterial inflow into the heart measured by electromagnetic flowmeter.

Radioactivity was assayed in a computer-based gamma spectrometer (ND-810) coupled to a 3-inch NaI scintillation crystal with 8% resolution. Spectra were separated by storing background and calibration samples of each isotope into seven stacks of 256 channels. Window setting and stripping procedures were carried out as described previously.11,12 "Maps" of regional blood flow distribution per ring of myocardium were obtained by recombination of flow values of the adjacent myocardial wedges by an interactive computer program.12 A map of regional blood flows for a given myocardial ring and for a given isotope is shown in figure 1. On the basis of these maps — which show a sharp demarcation between normally and collateral-perfused myocardium, especially at high flow rates — and on the basis of the known anatomic origin of each sample, average values for collateral blood flow and for normally perfused myocardium were computed by calculating averages of values between cursors using the interactive computer program. In this way, coronary and collateral blood flows were obtained for each pressure level between 40 and 140 mm Hg. Pressure-flow relationships were then constructed for normal coronary, collateral, subepicardial and subendocardial flow. Collateral resistance was calculated by constructing a pressure-flow curve for collateral blood flow vs aortic perfusion pressure minus peripheral coronary pressure. Steepness of pressure-flow relationships and the y-intercept were obtained by linear regression analysis.

**Results**

Mortality

Eleven of the 45 dogs (24%) with chronic two-vessel occlusion died. Five of 18 nonexercising controls

![Blood flow map of a ring of left ventricular myocardium at five pressure levels. Ordinate: blood flow at perfusion pressure of 40, 60, 80, 100 and 120 mm Hg. Abscissa: adjacent wedges (samples) of left ventricular myocardium. Note the canyon-like depression of blood flow in the area perfused by collaterals. LAD = left anterior descending coronary artery; EPI = epicardium.](image-url)
(28%) and six of 27 runners (22%) died suddenly. All of them collapsed unexpectedly, probably from ventricular fibrillation, which was recorded in a few instances. One dog died instantaneously during treadmill exercise. Another dog died shortly after exercise. The difference in mortality between exercising and nonexercising dogs is not statistically significant. The death rate of about 25% has remained unchanged in the author’s laboratory for 16 years. Autopsy of these dogs always revealed absence of a developed collateral circulation associated either with premature arterial closure (early deaths) due to a constrictor fitted too tightly at operation or to thrombus formation inside the stenosed artery.

In accordance with previous experience, the sedentary dogs died a mean of 14.8 ± 3.4 days (±SD), after implantation of the ameroid constrictor. The exercising dogs died a mean of 18.6 ± 4.6 days after the operation (NS). The dog that died during exercise died 43 days after operation; it appeared to be well trained and died unexpectedly. Postmortem arteriography revealed complete occlusion of both arteries and no visible collaterals. Arterial occlusion by the ameroid constrictor was unusually late in this case.

After operation, the exercising dogs were allowed to recover for 13 ± 5 days before training was gradually resumed. Although this is the time around which death is most frequent, no ill effect of exercise on death rate was observed.

General Effects of Exercise

Implantation of coronary constricting devices was scheduled when the dogs could run for 1 hour on the treadmill. This was achieved on the average after 53 ± 39 days (±SD) of exercise. Evaluation of the collateral circulation was scheduled when the preoperative performance level had been regained and maintained for 1 month. Final evaluation of collateral flow was carried out 100 ± 22 days after the operation. Physical conditioning was achieved by the training program, as demonstrated by three observations: 1–3 months of training were necessary to reach the projected level of performance; the heart rates for given levels of external work (treadmill incline) decreased by as much as 50 beats/min; and the body weight of the sedentary dogs increased by a factor of 1.46 within approximately 150 days, whereas the weight of the runners increased only by a factor of 1.11 (p < 0.05).

During the last 4 weeks before the final experiment, the dogs were able to run 7.2 ± 1.0 mph (11.5 km/hour, mean ± SD) at a treadmill incline of 20.4 ± 2.1% for 1 hour. This represents an external work of 4.7 W/kg and an energy expenditure of 12 kcal/kg/hour, or 320 kcal/dog. The heart weight of the runners was slightly higher than that of the controls (262 g vs 223 g, NS). Dividing heart weights by body weight resulted in 9.65 g heart/kg body weight in runners and 9.2 g heart/kg body weight in controls (NS). The heart weight/body weight ratios of both groups differ from that reported in the literature (7.9 g/kg) and from our own data base (8.0 g/kg). Comparing only matched pairs, the runners were of equal weight and had slightly heavier hearts, on the average, but the difference was not statistically significant.

Influence on Coronary and Collateral Flow

The relationship between aortic perfusion pressure and coronary blood flow is linear (correlation coefficients close to unity) (fig. 2, table 1). These data were obtained under maximal coronary vasodilation with adenosine. Collateral blood flow (fig. 2) also shows a linear relationship with perfusion pressure, though significantly less steep. These pressure-flow relationships follow the general function \( y = Ax + B \). When coronary and collateral pressure-flow relationships (or pressure-flow relationships between runners and non-runners) are compared, the difference of steepness (A) of the pressure-flow curves (or slope) can be compared by calculating the A/A ratio (the slope ratio). Comparison between collateral and coronary conductance reveals a ratio of slopes (A in table 1) of 0.39. This implies that collaterals in exercising dogs replace only slightly less than 40% of the conductance of the bypassed artery before its occlusion. In computer-generated flow maps (fig. 1) from radiomicrosphere distributions, the "trough-like" flow depression indicates a flow deficit at loads requiring a high blood flow. In the control group, the ratio of slopes was similar (0.38). Comparison with a larger control group studied previously in an identical fashion revealed the same difference in slopes.

If we compare pressure-flow relationships (i.e., slope ratios) only for subendocardial regions, we find that the ratio of collateral to left anterior descending flow is 0.31 in runners, 0.32 in controls and 0.29 in the earlier controls. Figures 3–7 show that coronary flow to the unimpeded left anterior descending region, collateral blood flow and subepicardial and suben-
Table 1. Results of the Regression Analysis of Pressure Flow Curves*

<table>
<thead>
<tr>
<th></th>
<th>Runners</th>
<th></th>
<th></th>
<th>Controls</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
<td>B</td>
<td>r</td>
<td>R</td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>AoP vs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD_{tot}</td>
<td>6.15</td>
<td>-132</td>
<td>0.99</td>
<td>0.21</td>
<td>7.05</td>
<td>-131</td>
</tr>
<tr>
<td>LAD_{epi}</td>
<td>5.34</td>
<td>-78</td>
<td>0.99</td>
<td>0.22</td>
<td>5.78</td>
<td>-79</td>
</tr>
<tr>
<td>LAD_{endo}</td>
<td>6.63</td>
<td>-184</td>
<td>0.99</td>
<td>0.21</td>
<td>7.70</td>
<td>-177</td>
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<tr>
<td>Coll_{tot}</td>
<td>2.59</td>
<td>-43</td>
<td>0.99</td>
<td>0.46</td>
<td>2.51</td>
<td>-4.4</td>
</tr>
<tr>
<td>Coll_{epi}</td>
<td>2.55</td>
<td>-28</td>
<td>0.98</td>
<td>0.44</td>
<td>2.12</td>
<td>14.6</td>
</tr>
<tr>
<td>Coll_{endo}</td>
<td>2.05</td>
<td>-31</td>
<td>0.98</td>
<td>0.58</td>
<td>2.43</td>
<td>-21.2</td>
</tr>
<tr>
<td>AoP - PCP vs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coll_{tot}</td>
<td>4.17</td>
<td>5.53</td>
<td>0.99</td>
<td>0.24</td>
<td>3.50</td>
<td>27.1</td>
</tr>
<tr>
<td>PCP vs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coll_{tot}</td>
<td>6.44</td>
<td>-113.2</td>
<td>0.99</td>
<td>0.19</td>
<td>6.86</td>
<td>-84</td>
</tr>
<tr>
<td>AoP vs</td>
<td>0.39</td>
<td>11.04</td>
<td>0.99</td>
<td></td>
<td>0.33</td>
<td>11.0</td>
</tr>
</tbody>
</table>

*Pressure-flow curves conforming to the general equation \( y = Ax + B \), where \( A \) = steepness of the curve, \( B \) = \( y \)-intercept at zero pressure, and \( R \) = coronary resistance units (mm Hg/ml/min/100 g).

Abbreviations: LAD_{tot} = PF relationship for the normally perfused LAD region; Coll_{tot} = PF relationship for collateral-dependent myocardium; AoP = aortic perfusion pressure; PCP = peripheral coronary pressure.

docordial blood flows are all slightly higher in the control group. These differences are not statistically significant.

Analysis of pairs of littermates did not reveal any beneficial effects of physical exercise. About half of the pairs showed lower and the other half higher collateral flows in the exercising dogs. Calculated total collateral resistance (aortic perfusion pressure vs total collateral blood flow at 100 mm Hg) was 0.39 coronary resistance units (mm Hg/ml/min/100 g) for both trained and control littermates. The slopes of individual pressure-flow relationships for matched pairs were steeper for runners in only four of seven pairs. Calculated total coronary resistance was lower for runners in only two matched pairs, equal in one pair and larger in four pairs. The analysis of matched pairs shows that if four runners of seven matched pairs react to exercise with higher resistance values, a continuation of the study with additional matched pairs appears meaningless because neither a beneficial nor a detrimental effect of exercise can be ascertained. Two-tailed binomial analysis shows that at least 11 additional matched pairs of littermates should react in one direction without a single exception, which is extremely unlikely.

Collateral resistance was calculated by relating collateral blood flow to the pressure difference over the collateral bed (i.e., aortic perfusion pressure minus peripheral coronary pressure) (fig. 7). In contrast to pressure-flow relationships using only aortic perfusion pressure (fig. 2), the collateral conductance exhibits no noticeable pressure intercept, i.e., it is a straight line \( r = 0.999 \) that goes through the origin. Figure 7 shows that the standard deviations of the peripheral cor-

![Coronary (LAD) blood flow (transmural)](image)

**Figure 3.** Comparison of exercised and sedentary dogs for normal coronary (left anterior descending artery [LAD]) and collateral blood flows as a function of aortic perfusion pressure (AoP) and in maximal coronary vasodilation. Sedentary dogs had insignificantly higher flows at almost all pressure levels. Mean values ± SD are shown.
Exonory pressure are much smaller than those of the collateral blood flow. This indicates that in view of the strict linearity of the collateral conductance, the ratio of peripheral coronary pressure and aortic perfusion pressure provides a fairly accurate estimate of collateral conductance during maximal coronary vasodilation.

Comparison of collateral conductance in exercising and sedentary dogs showed a slightly steeper slope for the sedentary dogs (NS) (table 1). Comparison of collateral conductance with that of a larger group of sedentary dogs studied identically also showed no significant differences.

**Discussion**

The high level of physical endurance fitness achieved by dogs in the present study did not improve collateral blood flow above levels achieved spontaneously in nontrained sedentary controls. These results are at variance with other studies, which suggest a beneficial effect of exercise on collaterals. However, Heaton et al. showed only a trend toward a redistribution in favor of subendocardial collateral-dependent perfusion; total collateral blood flow was not significantly altered by exercise training. Neill and Oxendine reported that exercise can promote coronary collateral development without improving perfusion of ischemic myocardium. Scheel et al. found the most impressive improvement of collateral function by physical training even though the intensity of training was one of the lowest reported (table 2) and the one-vessel occlusion used in their study is unlikely to produce an exercise-related stimulus for continued vascular growth at these low training intensities. Lambert et al. showed that one-vessel ameroid occlusion leads to development of collaterals that do not produce flow deficits during graded treadmill exercise tests. The study of Scheel et al. suffers from two disadvantages: The retrograde flow method, although perfected by Scheel et al. to an impressive degree of precision, does not allow inferences about true tissue perfusion by collaterals and the nonexercised group had significantly more scar formation in collateral-dependent myocardium as judged by the significantly higher coronary resistance under conditions of antegrade perfusion. Earlier studies indicate that collateral development is a function of the myocardial mass to be perfused. Reduction of the bed size by

![Figure 4](image4.png)

**FIGURE 4.** Normal coronary (left anterior descending artery [LAD]) and collateral blood flows in exercised dogs as a function of aortic perfusion pressure (AOP) during maximal coronary vasodilation. Comparison of subendocardial and subepicardial flows shows that the endo/epi ratio (numbers above columns) is dependent on perfusion pressure.

![Figure 5](image5.png)

**FIGURE 5.** Comparison of exercised and sedentary dogs for subendocardial and subepicardial blood flow (normal left anterior descending artery [LAD] flow) as a function of aortic perfusion pressure (AOP) during maximal coronary vasodilation. Sedentary dogs tend to have insignificantly higher flows in both layers at all pressure levels. Mean ± SD are shown.
scar formation significantly curtails development of collaterals.\textsuperscript{12} Accidental allocation of dogs with more scar tissue into the nonexercising group might have suggested better development of collaterals in the exercised group. Also, physical training might significantly increase collateral blood flow in the presence of a stenosis that becomes critical during physical stress.\textsuperscript{1, 18} Cohen et al.\textsuperscript{15} clearly showed that the beneficial effect of exercise in dogs with one-vessel stenosis is significant, but collateral blood flow augmented by training does not come close to levels found in stable chronic coronary occlusion without infarction.

The advantages of this study are that the intensity of the exercise was by far the highest reported (table 2), that the dogs were already well-conditioned before the operation and resumed training early after the operation, that the duration of postoperative training is the longest reported so far and that the total mileage covered after the operation is more than twice as high as the highest reported in the literature (table 2).

Further, conclusions on collateral conductance or resistance are based on pressure-flow relationships encompassing a wide range of pressures (40–140 mm Hg) and blood flows (100–1000 ml/min/100 g). The significant pressure intercepts\textsuperscript{21, 22} at zero flow on some of these relationships invalidate all studies that measure resistance or conductance from only one pair of pressure-flow measurements.

**Critique of Method**

In chronic experimental coronary occlusion or stenosis, resting coronary and collateral blood flows are equal.\textsuperscript{12} Therefore, it is pointless to study these hearts unstressed. The physiologic stresses of exercise or cardiac pacing do not tax the entire reserve of the coronary system\textsuperscript{18} and they increase extravascular resistance considerably through tachycardia.\textsuperscript{19} This increase in extravascular resistance is felt much more by the collateral-dependent area because of the considerably decreased intravascular pressure; i.e., there is less force to counteract increased tissue pressure.\textsuperscript{20} Pharmacologic stresses such as specific drug-induced coronary vasodilation\textsuperscript{10} are therefore preferable. The disadvantage is that maximal coronary vasodilation cannot be produced in the intact dog without some decrease in perfusion pressure and increase in heart rate. Further, the pressure-flow relationships of the coronary circulation exhibit significant pressure intercepts at zero flow,\textsuperscript{21, 22} which invalidates calculations of coronary resistance or conductance based on one pair of pressure-flow values. Therefore, blood flow must be measured over a wide range of pressures to construct pressure-flow curves that will be correct expressions of resistance or conductance. These conditions cannot be obtained experimentally in the intact animal. We therefore used a Langendorff preparation with blood from a support dog, as previously described.\textsuperscript{10} Transfer of the hearts from the anesthetized and artificially ventilated dogs to the Langendorff apparatus takes only about 1 minute, so the hearts behave normally under a variety of test conditions: They develop isovolumic pressures greater than 250 mm Hg at filling pressures of 8 mm Hg and the coronary circulation autoregulates within a few minutes after being connected to the perfusion apparatus, vasodilates upon infusion of adenosine and resumes autoregulation after adenosine. The ATP content is normal, especially after infusion of adenosine.

All hearts were studied at perfusion pressures of 40, 60, 80, 100, 120 and, if possible, 140 mm Hg, which
greatly facilitated statistical analysis. All hearts were studied in electrically induced ventricular fibrillation for the following reasons:

1. Langendorff-perfused empty fibrillating hearts show the same radionuclide distribution across the left ventricular wall as hearts beating under normal circulatory load in vivo and in situ. As in normal hearts, the endo-epi ratio of blood flow increases over unity above a certain perfusion pressure level (fig. 4).
2. Fibrillating isolated perfused hearts exhibit a more stable myocardial oxygen consumption than empty beating hearts, which often show variable heart rates.
3. For calculating collateral resistance proper (aortic perfusion pressure minus peripheral coronary pressure vs collateral flow) (fig. 7), it is immaterial whether the heart beats, fibrillates or is arrested in diastole. The functional state of the myocardium into which blood drains after flowing through collaterals does not change collateral resistance proper.

Flow Limitation by Collaterals

The present study is acceptably accurate in terms of fluid dynamics. Measurement of regional blood flows over a wide range of perfusion pressures showed linear pressure-flow relations; collateral blood flow approximates only 40% of normal left anterior descending flow at the same perfusion pressure. We do not know with the same degree of accuracy whether this flow deficit is significant under the varying conditions of life or during the heavy exercise to which the dogs were subjected. Because of technical difficulties, lactate production was not measured during exercise; but we did inject tracer microspheres in a few dogs during treadmill exercise and found similar flow deficits, especially subendocardial. We therefore believe that the dogs exercised with subendocardial ischemia. Dogs do not exhibit pain reactions to myocardial ischemia as human patients commonly do. The redundantly large heart of the dog (8 g heart/kg body weight vs 4–5 in humans) apparently prevents performance limitation, which is common in human coronary heart disease. The high level of energy expenditure — 4 W/kg for 1 hour in dogs with chronic two-vessel occlusion — contrasts with the 2 W/kg occasionally found in well-trained human postcoronary runners. However it is difficult to measure external work output for treadmill work in dogs because the commonly used equation predicts zero external work with level running. Our calculated values agree well with those directly measured in dogs by Stegemann for the same speed and inclination.

Table 2. Comparison of Exercise Regimen in Four Studies of Chronic Stable Coronary Artery Occlusion in Dogs

<table>
<thead>
<tr>
<th>Study</th>
<th>Running speed</th>
<th>Treadmill incline</th>
<th>Exercise intensity</th>
<th>Total running distance</th>
<th>Effect of training on collateral circulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scheel et al.</td>
<td>3.6</td>
<td>97</td>
<td>25</td>
<td>326</td>
<td>Positive</td>
</tr>
<tr>
<td>Neill and Oxendine</td>
<td>5.0</td>
<td>134</td>
<td>15</td>
<td>475</td>
<td>Positive trend (NS)</td>
</tr>
<tr>
<td>Heaton et al.</td>
<td>3.0</td>
<td>81</td>
<td>5</td>
<td>106</td>
<td>Positive trend (NS)</td>
</tr>
<tr>
<td>Present study</td>
<td>7.0</td>
<td>188</td>
<td>22</td>
<td>837</td>
<td>No effect</td>
</tr>
</tbody>
</table>

The Cause of Failure of Collaterals to Respond to Training

The failure of dog collaterals to respond favorably to endurance training is no surprise to many students of human coronary heart disease. The few studies of repeat coronary angiography in human patients not undergoing coronary artery bypass surgery showed usually only an increase in collaterals with progression of coronary lesions regardless of the level of physical activity. Improvement of angina threshold that can be achieved in patients undergoing physical reconditioning can be explained on the basis of peripheral adaptation rather than central (cardiac) changes. Although in the present study physical exercise was severe enough to increase heart rate to more than 200 beats/min, probably only subendocardial ischemia would have developed. Collateral blood flow, although limited, should have been able to increase fivefold above normal and may thereby have prevented subepicardial ischemia. Collateral blood vessels, which are known to respond to ischemia with growth by cellular proliferation, lie on the epicardial surface of the heart and the ischemic stimulus does not reach them. This explanation probably does not fully apply for human hearts, in which collateral connections are also found in the subendocardium and it may also not apply to dogs with intramyocardial collaterals that originate from the septal artery and connect with the posterior branch of the left circumflex coronary artery.

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References

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