Coronary Artery Size and Dilating Capacity in Ultradistance Runners

William L. Haskell, PhD; Chris Sims, MD; Jeff Myll, MS; Walter M. Bortz, MD; Frederick G. St. Goar, MD; and Edwin L. Alderman, MD

Background. Increases in coronary artery size and dilating capacity have been observed in some animals after endurance training, and at autopsy, active men appear to have enlarged epicardial coronary arteries. This cross-sectional study was designed to test the hypothesis that highly trained endurance runners have larger epicardial coronary arteries and greater dilating capacity than inactive men.

Methods and Results. The subjects, ages 39–66 years, included 11 male volunteers who had participated in ultradistance running during the past 2 years and 11 physically inactive men who had been referred for arteriography but had no visible coronary artery disease. The internal diameter of the proximal segments of each major epicardial coronary artery was measured before and after nitroglycerin administration using a computer-based quantitative arteriographic analysis system. Measurements also included maximal oxygen uptake, plasma lipoprotein concentrations, body composition, and cardiac mass by echocardiography. Before nitroglycerin, the sum of the cross-sectional areas for the proximal right, left anterior descending, and circumflex arteries was not different for the runners and the inactive men: 22.7±4.79 versus 21.0±7.97 mm² (p=0.57), respectively. However, the increase in the sum of the cross-sectional area for the proximal right, left anterior descending, and circumflex arteries in response to nitroglycerin was greater for the runners (13.20±4.76 versus 6.00±3.02 mm²; p=0.002). Left ventricular mass index (152±21 versus 116±41 g/m²; p<0.05) but not left ventricular mass (284±40 versus 246±91 g; p=0.22) was significantly greater for the runners. Among the runners, dilating capacity was positively correlated with aerobic capacity and negatively related to adiposity, resting heart rate, and plasma lipoprotein concentrations.

Conclusions. Highly trained, middle-aged endurance runners demonstrated a significantly greater dilating capacity of their epicardial coronary arteries in response to nitroglycerin compared with inactive men. The causes of this greater dilating capacity and its clinical significance need to be determined.

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Key Words • coronary circulation • exercise • vasodilation

Physically active persons tend to experience fewer clinical manifestations of coronary artery disease (CAD) than less-active men and women,1–4 and several recent reports document that endurance exercise capacity is inversely related to all-cause and CAD mortality.5,6 Also, two meta-analyses of the effects of exercise training on morbidity and mortality in patients after myocardial infarction concluded that exercise favorably influenced mortality but not infarction.7,8 The lower mortality associated with greater physical activity or exercise capacity could be mediated by various biological changes induced by regular exercise that increase myocardial oxygen supply, decrease myocardial oxygen demand, or enhance intrinsic myocardial contractility.9

One way that habitual activity might reduce the clinical manifestations of CAD is to increase coronary blood flow by increasing the diameter of the coronary arteries. During the past 50 years, studies using various animal models, from rats to monkeys, have demonstrated enlargement in the diameter of coronary arteries of animals performing vigorous endurance-type exercise.10–15 The results from a few human autopsy studies also indicate that habitual physical activity is related to a larger cross-sectional area of the major epicardial arteries.16–19

The development of quantitative coronary arteriography and the relative safety of the procedure permit direct measurement of the relation between coronary artery size and physical activity status in humans. Using computer-assisted arteriographical measurement, we compared the diameter of the major epicardial coronary arteries at rest and after nitroglycerin administration in ultradistance runners versus inactive men. We hypothesized that the runners would demonstrate larger epi-
cardiac arteries at rest and greater vasodilation in response to nitroglycerin.

Methods

Subjects

The study sample consisted of 11 healthy ultradistance runners (ages 40-52 years) and 11 physically inactive men (ages 39-66 years). To be considered eligible for the study, a runner must have run an average of 40 miles or more per week and completed at least two marathons or other ultradistance running events in the past 2 years. They were recruited from a register of long-distance runners living in northern California. The physically inactive men were free of any arteriographic evidence of CAD, and had cardiac catheterization because of atypical anginal symptoms, and most often had a borderline or abnormal exercise ECG or radionuclide test. By interviewer-administered physical activity questionnaire, we determined that the control subjects had not participated in any type of exercise training program during the past year. Echocardiography in all subjects demonstrated no evidence of cardiac structural or functional abnormalities, including mitral valve prolapse or cardiomyopathy. No subject was taking any cardiac or antihypertensive medication. The study received approval by the Panel on Human Subjects in Medical Research at Stanford University, and written informed consent was obtained from each participant after a detailed discussion of the protocol.

Clinical Evaluation

The runners were interviewed regarding their medical status, general health habits, and exercise training regimen. They underwent a cardiovascular-oriented physical examination including fasting blood samples for plasma lipoproteins, chemistries, and hematology. Plasma was separated from venous blood within 2 hours, and blood and plasma were kept at 4°C until processed. Plasma total cholesterol and triglycerides were measured according to enzymatic procedures (Abbott ABA 200 instrument), high density lipoprotein cholesterol (HDL-C) was determined by the dextran sulfate-magnesium precipitation procedure, and low density lipoprotein cholesterol (LDL-C) was calculated using the following equation: total cholesterol-[HDL=C+(triglycerides+5)].

Two-dimensional echocardiography was performed in subjects at rest in the left lateral decubitus position. Measurements of wall thickness and cardiac mass were made according to the Penn convention. Hydrostatic weighing was performed to measure lean and fat body mass using the equation of Siri. A maximal treadmill exercise test was performed with recording of a 12-lead ECG, blood pressure, and oxygen uptake each minute of exercise. The test consisted of 2-minute stages increasing in speed from 3 to 6 miles per hour over the first three stages with a 3% increase in grade at each subsequent stage. Oxygen uptake was measured continuously with maximum oxygen uptake being the highest value obtained during the past 2 minutes of exercise. Each of the control subjects received these evaluations except for maximal exercise testing and hydrostatic weighing.

Coronary Arteriography

Both the runners and inactive men had outpatient coronary arteriography using the percutaneous femoral approach. Identical selective coronary artery visualizations were recorded on cine film before and 3 minutes after sublingual nitroglycerin (0.4 mg). Films were recorded at 30–45 frames per second. Multiple projections, including cranial and caudal angulated views, were obtained for all patients. In the basal or prenitroglycerin condition, two projections of the left coronary artery and two of the right coronary artery (RCA) were selected for exact replication after nitroglycerin. Only the left main (LM) coronary artery and the most proximal portions of the right coronary artery (p-RCA), the left anterior descending (p-LAD), and the circumflex artery (p-CIRC) were quantitated for this study to reduce subject-to-subject variability. In general, the p-RCA was quantitated from a left anterior oblique projection, and the LM, p-LAD, and p-CIRC were quantitated from a caudal right anterior oblique projection. A catheter with a distal cylindrical metallic marker provided calibration for computer-assisted quantitation.

All coronary cineangiographic films were analyzed using a computer-assisted edge-detection system mounted on a movable stage (Vanguard Instruments, Melville, N.Y.). End-diastolic cine frames, identified by an ECG-triggered mark on the frames, were selected and magnified (×3.5). Coronary segments were centered in the image field, and the image was digitized with a computer-controlled video processor (model 5524 DeAnza Systems, Fremont, Calif.) controlled by a Hewlett Packard 2100 computer (Andover, Mass.). The digitized image was displayed on a graphic computer terminal linked to a light pen. The margins of either the ring on the catheter or coronary segment were traced manually using the light pen. Using these lines as initial search locations, the automatic edge-finding algorithm drew and smoothed the edges, defining the edge at the peak of the first derivative of the gray-scale density gradient perpendicular to the long axis of the catheter or vessel as estimated from the initial manual tracings. When the computer algorithm was unable to resolve vessel boundaries in areas of noise or vessel crossings, manual editing of short segments of boundary with the light pen was used to correct the computer-generated boundary. At no time did the length of a manually entered margin exceed 20% of the total length of the quantitated segment.

Segment fiducial points, replication of angiographic projections, and specification of identical lengths ensured equivalence of the prenitroglycerin and postnitroglycerin segments. Single-plane quantititation was performed on those cine frames that were closest to end diastole, best elongated the vessel of interest, were at least 0.5 cm in length, and exhibited good-to-excellent visualization without substantial vessel overlap. The p-RCA, p-LAD, and p-CIRC measurements were obtained proximal to any major bifurcation or branches. The mean diameter of the full length of the available segment was used for the analysis. The mean diameter of segments was computed from perpendiculare constructed through the length of a computer-generated center line. The operator was not blinded to the patient identity or group; however, all measurements are based
TABLE 1. Subject Characteristics in the Study Groups

<table>
<thead>
<tr>
<th></th>
<th>Runners (n=11)</th>
<th>Inactive men (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>21.4±2.9</td>
<td>19.8±1.5</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>71.4±10.9</td>
<td>72.0±10.1</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>23.2±2.3</td>
<td>23.7±2.7</td>
</tr>
<tr>
<td>LVMI (g/m²)</td>
<td>152±21</td>
<td>167±41</td>
</tr>
<tr>
<td>LVM (g)</td>
<td>284±40</td>
<td>246±91</td>
</tr>
</tbody>
</table>

LVMI, left ventricular mass index; LVM, left ventricular mass. "p<0.01, "p<0.05. Values are mean±SD.

Table 2. Heart Disease Risk Factors and Exercise Status in Ultrardistance Runners and Inactive Men

<table>
<thead>
<tr>
<th></th>
<th>Runners</th>
<th>Inactive men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure (mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>123±8</td>
<td>139±18</td>
</tr>
<tr>
<td>Diastolic</td>
<td>77±7</td>
<td>82±11</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>51±8</td>
<td>75±16</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>10.4±4.2</td>
<td></td>
</tr>
<tr>
<td>Plasma lipid concentrations (mmol/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triglycerides</td>
<td>0.78±0.23</td>
<td>2.21±1.81*</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>4.95±0.52</td>
<td>6.39±0.92†</td>
</tr>
<tr>
<td>Low density lipoprotein cholesterol</td>
<td>3.06±0.60</td>
<td>4.12±0.66†</td>
</tr>
<tr>
<td>High density lipoprotein cholesterol</td>
<td>1.55±0.39</td>
<td>1.22±0.20‡</td>
</tr>
<tr>
<td>Years running</td>
<td>13±5.6</td>
<td></td>
</tr>
<tr>
<td>Training distance 1989 (km)</td>
<td>4,002±1,155</td>
<td></td>
</tr>
<tr>
<td>Best 100-mile race (hours:minutes)</td>
<td>19:55±2:33</td>
<td></td>
</tr>
<tr>
<td>Maximal VO₂ (mL/kg/min)</td>
<td>59.7±4.9</td>
<td></td>
</tr>
</tbody>
</table>

"p<0.05, "p<0.01, "p<0.01 for runners versus controls. Values are mean±SD.

Results

Characteristics of Runners and Inactive Men

Presented in Table 1 are selected characteristics of the runners and inactive men. The runners were on average 7 years younger and substantially leaner. The left ventricular mass index calculated from two-dimensional echocardiography was larger in the runners than the inactive men (152±21 versus 116±41 g/m²; p<0.05) and was similar to that reported for other distance runners. However, left ventricular mass was not significantly different between the two groups: 284±40 versus 246±91 g for runners versus inactive men, respectively (p=0.22). The runners had a coronary artery disease risk profile similar to what we have previously reported for endurance runners with normal blood pressure at rest; low resting heart rate, percent body fat, and plasma triglycerides; relatively low plasma total and LDL-C concentrations; and an elevated HDL-C concentration (Table 2). The inactive men had somewhat elevated plasma cholesterol, LDL-C, and triglyceride concentrations and average HDL-C compared with Lipid Research Clinics standards (Table 2). None of the inactive men reported participating in vigorous exercise on a regular basis during the year before angiography. In contrast, the runners reported serious training for an average of 13 years, with an average running distance of 4,002 km (2,501 miles) in 1989. Their average best time for running a 100-mile race was 19 hours and 55 minutes (all had run the Western States 100 Mile Trail Run) and had a maximal oxygen uptake (VO₂max) of 59.7 mL/kg/min, which is excellent for men with a mean age of 45 years.

Angiographic Results

The group means and standard deviations for the calculated cross-sectional area in square millimeters of

TABLE 3. Cross-sectional Area of Proximal Epicardial Coronary Arteries Before and After Nitroglycerin for Ultrardistance Runners and Inactive Men

<table>
<thead>
<tr>
<th></th>
<th>Pre nitroglycerin</th>
<th>Post nitroglycerin</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Inactive men</td>
<td>Runners</td>
<td>p</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14.61±6.88 (3)</td>
<td>12.87±3.57 (8)</td>
<td>0.59</td>
<td>18.14±5.96</td>
</tr>
<tr>
<td>5.80±1.60 (8)</td>
<td>8.10±1.83 (11)</td>
<td>0.01</td>
<td>8.22±2.75</td>
</tr>
<tr>
<td>7.72±3.38 (11)</td>
<td>8.04±2.86 (11)</td>
<td>0.81</td>
<td>8.97±3.30</td>
</tr>
<tr>
<td>7.45±4.11 (14)</td>
<td>6.57±2.32 (11)</td>
<td>0.55</td>
<td>9.14±4.81</td>
</tr>
<tr>
<td>21.00±7.97 (8)</td>
<td>22.71±4.11 (11)</td>
<td>0.57</td>
<td>25.79±9.97</td>
</tr>
</tbody>
</table>

p-RCA, p-LAD, and p-CIRC, proximal portions of right coronary artery, left anterior descending coronary artery, and circumflex artery. No. of segments contributing to each measurement is given in parentheses. Sum of p-RCA, p-LAD, and p-CIRC (n=8 for inactive men and 11 for runners). Values for comparison of inactive men versus runners.

*p<0.05, "p<0.01 for change within group. Values are mean±SD mm².
the LM, p-LAD, p-CIRC, and p-RCA arteries before and after nitroglycerin for the 11 ultradistance runners and 11 inactive men are presented in Table 3. Also included in this table are the changes in mean cross-sectional area from before to after nitroglycerin for each artery. In 11 subjects (eight inactive men and three runners), the LM artery was too short (<0.5 cm) to obtain accurate measurements, and in three of the inactive subjects the p-RCA was of inadequate length (<0.5 cm) proximal to a major branch. To obtain a global measure of coronary artery size, the cross-sectional areas for the p-RCA, p-CIRC, and p-LAD for each subject were added and expressed as the total cross-sectional area. The rami vessels were not included in these analyses.

In the basal condition, the cross-sectional area of the arteries was not consistently different between the two groups, with the runners having only a significantly larger p-RCA (8.1 versus 5.8 mm²; p<0.01) (Table 3). The mean total cross-sectional area before nitroglycerin was not different between the inactive men and runners: 21.0±7.97 versus 22.7±4.79 mm² (p=0.57), respectively. After nitroglycerin, the mean cross-sectional area increased significantly in both groups for all arteries except for the LM in the inactive men (n=5) (Table 3 and Figure 1). The mean increase in cross-sectional area for the p-LAD (p<0.001) and p-CIRC arteries (p=0.006) was greater for the runners than for the inactive men. For the p-RCA, the increase in the runners was approximately 50% greater than for the inactive men, but this difference was not significant (p=0.15) (Figure 1). The increase in mean total cross-sectional area after nitroglycerin was 13.20 mm² for the runners versus 6.00 mm² for the inactive group, a 2.2-fold greater increase in the runners (p=0.002). When expressed as a percent of prenitroglycerin values, the increase in total cross-sectional area was 32% for the inactive men and 58% for the runners (p<0.01). The values for total cross-sectional area before and after nitroglycerin for each subject are displayed in Figure 2.

Characteristics Related to Artery Size and Dilating Capacity

For the runners, we calculated Spearman's correlation coefficients for selected characteristics and their total cross-sectional area. Included in Table 4 are variables that were significantly correlated with total cross-sectional area before or after nitroglycerin or with the change in total cross-sectional area. The basal total cross-sectional area was positively correlated with age (r=0.64), and left ventricular mass index (r=0.73) and negatively related to percent body fat (r=−0.76) and resting heart rate (r=−0.65) (all p<0.05). After nitroglycerin, these same variables, except for age, remained significantly correlated with cross-sectional area. Being lean and fit (low resting heart rate and high VO₂max) and having low LDL-C and triglycerides were all strongly associated with an increased vasodilating response.

Stepwise multivariate regression analyses were performed in runners only to partially sort out which of these variables might be more independently associated with coronary artery size and vasodilating response. When all of the variables that by univariate analysis were significantly correlated with total cross-sectional area in the basal condition (Table 4) were entered in the analysis, only advancing age made a significant independent contribution. When the change in total cross-sectional area was the dependent variable, LDL-C and percent body fat were found to be independent predic-

TABLE 4. Correlations Between Selected Variables and Three-Vessel Cross-sectional Area in Ultradistance Runners

<table>
<thead>
<tr>
<th></th>
<th>Before nitroglycerin</th>
<th>After nitroglycerin</th>
<th>Change*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.64†</td>
<td>0.49</td>
<td>−0.07</td>
</tr>
<tr>
<td>Percent body fat</td>
<td>−0.76†</td>
<td>−0.88†</td>
<td>−0.61†</td>
</tr>
<tr>
<td>Resting heart rate</td>
<td>−0.65†</td>
<td>−0.62†</td>
<td>−0.62†</td>
</tr>
<tr>
<td>Maximal oxygen uptake</td>
<td>0.51</td>
<td>0.64†</td>
<td>0.68†</td>
</tr>
<tr>
<td>LDL-C</td>
<td>−0.25</td>
<td>−0.44</td>
<td>−0.77†</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>−0.12</td>
<td>−0.27</td>
<td>−0.66†</td>
</tr>
<tr>
<td>LVMI</td>
<td>0.73†</td>
<td>0.71†</td>
<td>0.46</td>
</tr>
</tbody>
</table>

LDL-C, low density lipoprotein cholesterol concentration; LVMI, left ventricular mass index.

*Change, change in cross-sectional area from before to after nitroglycerin.

†p<0.05, ‡p<0.01.
tors with a multiple $R^2$ of 0.84. No other variable significantly contributed to the analysis.

**Discussion**

The internal diameter of mammalian arteries generally are correlated with luminal blood flow during their development, and this relation continues throughout life.29 Also, experimental changes in local blood flow alter vessel diameter,30 with decreases in flow producing significant reductions in artery diameter,31 whereas sustained increases in flow increase the size of healthy arteries.32 These changes appear to be due more to structural modifications of the arterial wall than to changes in vascular tone.31 The ultradistance runners in this study averaged 400–800 hours of running per year at a cardiac output at least twofold to threefold resting values. Thus, coronary arteries of the runners frequently were exposed to a substantial increase in blood flow, which could be responsible for their greater cross-sectional area after nitroglycerin.

**Coronary Artery Size Before Nitroglycerin**

The hypothesis that the runners would have disproportionately larger diameter arteries at rest was based on human studies demonstrating that coronary artery diameter increases in response to increases in cardiac mass due to valvular disease and exercise training studies in animals and humans demonstrating coronary vessel enlargement. For example, Lewis and Gotsman34 found left ventricular wall mass determined by echocardiography to be significantly correlated with the sum of the cross-sectional area of the proximal left and right coronary arteries ($r=0.84, p<0.001$) in 27 patients with various cardiac abnormalities. O'Keefe et al35 reported a correlation of 0.79 ($p<0.001$) between left ventricular mass and proximal coronary artery cross-sectional area in 40 patients with valvular heart disease or normal valvular and ventricular function. Similar results have been reported by other investigators based on angiographical36 and autopsy37 observations. Recently, Pelliccia and colleagues38 reported that coronary artery diameter measured by echocardiography was significantly correlated with training-induced myocardial hypertrophy ($r=0.69$ with left ventricular wall thickness and 0.50 with left ventricular mass) in highly trained athletes.

Larger coronary artery trees have been reported for physically active rats compared with sedentary litter mates.11–14 Short-term exercise training by dogs produced a significant increase in the diameter of their epicardial coronary arteries,15 and 42 months of endurance training by monkeys resulted in increased cardiac mass and larger coronary artery size compared with sedentary controls.14 Men who reportedly had physically active occupations8,33 or generally active lifestyles16,17 had larger-than-expected coronary arteries. Frequently cited is the case report based on the autopsy of the marathon runner Clarence De Mar, in which his epicardial vessels were found to be “two or three times the normal size.”16 Mann and colleagues17 found that physically active Masai tribesmen dying of noncardiovascular causes with no clinical evidence of coronary disease had as much coronary atherosclerosis at autopsy as US men but had patent arterial lumens because of the large size of their epicardial vessels. Rose et al18 studied the hearts at autopsy of a group of men and women with and without infarction and found an association between increasing physical activity of occupation and increasing coronary artery diameter. Based on these autopsy data where the coronary arteries were observed or measured to be larger in more active men (when there was no myocardial oxygen demand or coronary flow), it might be expected that the ultradistance runners would have demonstrated a significantly larger coronary artery diameter at rest than the sedentary men.

In our subjects, in the basal condition, there were no systematic differences in the cross-sectional area of the coronary arteries between the runners and inactive men. Left ventricular mass index expressed as grams per square meter was larger for the runners than for inactive men. However, total left ventricular mass (g) was slightly but not significantly larger for the runners. The enhanced left ventricular mass index in the runners reflected the fact that body weight for the runners was 16.9 kg less than for the inactive men. Thus, based just on the relation of left ventricular mass to the total cross-sectional area of proximal coronary arteries, the runners and sedentary controls in this study would be expected to have proximal coronary arteries of somewhat similar size. Using the Penn procedure for calculating left ventricular mass, other investigators38,39 have reported smaller left ventricular mass index for sedentary men than we observed here (116 g/m²), usually closer to 90–100 g/m². It could be that several of the controls had had hypertension in the past that was not detected at the time of their evaluation. Even at a similar left ventricular mass or mass index, coronary artery size in the basal condition might not be increased in the runners because of their lower myocardial oxygen demand due to their lower heart rate and mean arterial pressure. Thus, in the basal state, the coronary arteries of runners may exhibit greater vascular tone.

**Vasodilation Response to Nitroglycerin**

After the administration of nitroglycerin, the cross-sectional area of all artery segments in both groups increased, with the average magnitude of increase being greater for the runners. The mean increase in total cross-sectional area of 32% for the inactive men is greater than the 18% increase after 0.4 mg sublingual nitroglycerin in proximal coronary arteries reported by Brown and colleagues43 but similar in magnitude to that reported by Vita et al44 and Yasue et al.45 The increase in the total cross-sectional area for the runners was 2.2-fold greater than for the inactive men.

We are unaware of any published studies reporting the effects of exercise training on the vasodilating capacity of coronary arteries in humans. The results of several cross-sectional46,47 and exercise training studies48,49 have demonstrated a significantly greater hyperemic blood flow in the calf and forearm after ischemic exercise to fatigue in trained men and women. These results are consistent with a greater capacity for vasodilation in trained skeletal muscle and are not related to muscle hypertrophy. They appear to be due to adaptation of the vascular structure, possibly an increase in the caliber and/or number of resistance arterioles. Whether these exercise-induced changes in skeletal muscle vascularity relate to any changes in the coronary arteries is not known.
Factors Associated With Artery Size

Among the runners, left ventricular mass index was significantly correlated with total cross-sectional area both before ($r=0.73$, $p<0.01$) and after nitroglycerin ($r=0.71$, $p<0.01$). The magnitude of this relation was less for left ventricular mass versus total cross-sectional area ($r=0.53$, $p=0.10$ and $r=0.50$, $p=0.12$ for before and after nitroglycerin, respectively). This higher correlation for cross-sectional area with left ventricular mass index than with left ventricular mass in the runners could be due to left ventricular mass index being more related to endurance capacity than is left ventricular mass. Among the controls, the correlations between total cross-sectional area and left ventricular mass index before and after nitroglycerin were less than for the runners but similar for left ventricular mass and total cross-sectional area ($r=0.43$, $p=0.40$). The relation between left ventricular mass index and total cross-sectional area did not remain significant when left ventricular mass index was entered in a stepwise multiple regression analysis with age, percent body fat, and resting heart rate, all of which were independently correlated with total cross-sectional area.

Other personal characteristics correlated with coronary artery size have included age, sex, history of cigarette smoking, and alcohol consumption. The results are variable regarding the relation of age to artery size, with some studies reporting no relation, an increase, or a decrease in artery size with increasing age. Because the runners on average were 7 years younger than the sedentary men, the runners could have slightly larger arteries based on age alone. However, among the runners, age was positively correlated ($r=0.64$, $p<0.05$) with cross-sectional area before nitroglycerin. In one study, a history of cigarette smoking was associated with smaller artery diameter, whereas a history of alcohol use was associated with larger-diameter coronary arteries. The runners reported consuming limited amounts of alcohol, so it is unlikely that this accounts for their greater dilating capacity, and cigarette-smoking history was similar for the two groups.

In the runners, the change in total cross-sectional area in response to nitroglycerin was significantly correlated with several measures of physical fitness (resting heart rate, $V_{\text{O}_2\text{max}}$, and percent body fat) but not with left ventricular mass index ($r=0.46$, $p=0.15$). In addition, plasma LDL-C ($r=-0.77$, $p<0.01$) and triglyceride ($r=-0.66$, $p<0.05$) concentrations were negatively correlated with the change in cross-sectional area. In any multiple regression analyses that included LDL-C, it always demonstrated the strongest independent relation to the change in artery size. Several studies have demonstrated that elevated plasma cholesterol concentration, especially LDL-C, inhibits vasodilatation in vitro using coronary arteries from rabbits and in vivo in the coronary arteries and resistance vessels in the forearm of men.

Study Limitations

This preliminary study of the possible role of exercise in determining epicardial coronary artery size and dilating capacity is limited by its cross-sectional design, method of subject selection, and that angiography provides a silhouette of the artery lumen but no visualiza-

tion of the artery wall. It is not possible to determine how much genetic or environmental factors other than running contributed to the differences in the dilating response between the marathoners and inactive men. Also, we cannot rule out the possibility that the inactive men had a suppressed vasodilating response due to atherosclerosis not observed on angiography or preatherosclerotic artery wall dysfunction. There were differences in both LDL-C and HDL-C between the long-distance runners and inactive men, consistent with known effects of a physically active and weight- and diet-conscious lifestyle. We cannot differentiate whether the greater dilation observed in the runners was due to flow-mediated remodeling of the runners’ coronary vasculature or an adverse vascular effect of higher LDL-C or lower HDL-C in the inactive men. However, the percent increase in TCA of the inactive men in response to nitroglycerin was within the range reported for coronary artery segments that appear normal by angiography.

Implications

These results demonstrate for the first time that the coronary arteries of highly trained, middle-aged men have a greater dilating capacity in response to nitroglycerin than those of men who generally are sedentary. Given the cross-sectional nature of this study, it is not possible to know if this difference was caused by the running or is due to some other acquired trait or to genetic selection. Also, this study does not provide data on how much exercise would be needed to produce enhanced coronary artery dilation or whether exercise training would produce increased dilation in the coronary arteries of patients with coronary atherosclerosis. One could speculate whether pharmacological agents, such as those that activate endothelium-derived relaxing factors, would produce a similar result. Additional research is needed to determine the causes of the greater dilating capacity of epicardial coronary arteries in highly trained runners and if any clinical benefit is provided by this increased capacity.

References

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