Editorial Comment

Effects of Exercise on Coronary Atherosclerotic Lesions*

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The Present Study

It has long been appreciated that elements in individual life-style can have a significant impact on the development of coronary atherosclerosis. Perhaps the least explored of these factors is physical activity. The article by Hambrecht et al. (1) in this issue of the Journal carries investigation of the effect of exercise to the level of quantitative angiography. They studied 62 men with symptomatic coronary disease who had not undergone revascularization procedures or angioplasty. The patients were assigned randomly to a usual care group or to a group enrolled in a structured exercise program. Quantitative angiography was performed initially and after 1 year. In many respects, the subjects resembled most patients who present with clinical coronary disease. Their mean serum cholesterol and low density lipoprotein (LDL) cholesterol levels were about 233 mg/dl and 163 mg/dl, respectively. Mean high density lipoprotein (HDL) cholesterol levels were about 35 mg/dl and many patients had mild hypertriglyceridemia.

Whereas the control group was merely instructed in the value of regular physical exercise and diet, the intervention group was maintained three times longer on a metabolic ward where they received an American Heart Association phase 3 diet. It is therefore possible that some of the benefit attributed to exercise in this study may represent the results of more serious adherence to diet in the intervention group. Physical exercise was supervised carefully. It consisted of 1 h/day on a cycle ergometer and 2 h/week of group training sessions.

By history, compliance with the prescribed exercise was about 60%. The mean energy expenditure/week in leisure time physical activity was 1,876 kcal in the intervention group versus 1,187 in the control group. This difference is equivalent to running about 8 miles/week.

The response in mean within-patient change in minimal diameters of stenotic lesions was trichotomized on the basis of net progression, net regression or lack of change. Within the intervention group, there was a significant increase in energy expenditure from the lowest level, in the group showing progression, to an intermediate level in the group showing no net change and highest level in the group showing regression. In the aggregate, there was a significant correlation between increasing energy expenditure and decreasing diameter stenosis. The other variable that correlated highly with change in diameter stenosis was the level of LDL cholesterol during the trial. Surprisingly, HDL cholesterol and triglycerides were not significantly correlated with change in diameter stenosis.

Results of Other Studies

This study comes in the setting of impressive new evidence for protection against death from cardiovascular disease by exercise. In a study of more than 10,000 Harvard University alumni, Paffenbarger et al. (2) found a 23% lower risk of death among men undertaking moderately vigorous physical activity than in those who did not embark on such an exercise program. The most active men, who expended \( \geq 3,500 \) kcal/week, had half the risk of death of those who expended \(<500 \) kcal/week. Activities that required 4.5 metabolic equivalents (METs), that is, 4.5 times the basal energy expenditure for a 70-kg man sitting quietly, appeared to be a significant discriminator of risk. One of the most striking findings in the Harvard alumni study was that benefits of exercise in preventing mortality from coronary artery disease also accrued to previously sedentary men who did not undertake significant physical activity until middle age. Conversely, previously active men who became sedentary incurred a significantly increased risk of mortality. This is concordant with earlier observations on college athletes indicating that those who discontinued regular exercise sustained a higher mortality rate from coronary disease than their teammates who continued to exercise.

Another contemporary study, by Sandvik et al. (3), found that the risk of death from all causes in the quintile of men with the highest level of physical activity was less than half that of those in the least active quintile in a prospective study of nearly 2,000 middle-aged Norwegian men. Changes in mortality from cardiovascular disease accounted for the largest portion of these differences in all-cause mortality.

Implications

Given the virtual unanimity of findings of a cardioprotective effect of vigorous exercise, what are the mechanisms underlying this effect? Clearly, in the study of Hambrecht et al. (1), the exercise and diet intervention had an impact on LDL cholesterol levels. Data from several large intervention trials suggest that a reduction of 2% in the incidence of new coronary events can be anticipated for every 1% reduction in LDL cholesterol. Quantitative angiographic support for a significant relation between the level of LDL cholesterol during the study period and the extent of regression of stenotic lesions has been forthcoming from three interven-
In the study of Hambrecht et al., even though the HDL cholesterol levels rose proportionately in both the intervention and control groups, the control group had a simultaneous increase in LDL cholesterol of 5%, which would have canceled the effect of the increase in HDL. In contrast, the intervention group had both a 2% increase in HDL cholesterol and an 8% decrease in LDL cholesterol. On the basis of experience in the Lipid Research Clinics Followup Study, this could account for an independent decrease in mortality risk of approximately 3%. Whereas much higher levels of HDL cholesterol are often seen in persons who are committed to an extensive exercise program, individual responses are variable. Hence, the exercise-induced changes in HDL cholesterol cannot be predicted with confidence. In the present study, it is also possible that smokers in the intervention group decreased their consumption of cigarettes during their year of supervised exercise. Unfortunately, this factor was undocumented in the study. In keeping with the multifactorial etiology of coronary heart disease, virtually all studies have shown at least an additive effect of controlling smoking behavior. A further possibility is that an exercise-induced increase in lumen diameter would be interpreted by quantitative angiography as a decrease in plaque dimensions. It is likely that the observed effect of exercise cannot be fully accounted for by known mechanisms.

In sum, the findings of Hambrecht et al. are consistent with a large and convincing body of cross-sectional and prospective observations that attribute a cardioprotective effect to exercise. Taken together, those data present a persuasive argument for the incorporation of systematic exercise into a hygienic life-style directed at diminution of risk of coronary artery disease.

References