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Relationship of Changes in Maximal and Submaximal Aerobic Fitness to Changes in Cardiovascular Disease and Non–Insulin-Dependent Diabetes Mellitus Risk Factors With Endurance Training: The Heritage Family Study

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The purpose of this study was to determine the relationship between changes in maximal oxygen uptake ($\dot{V}O_2$ max) and submaximal markers of aerobic fitness and changes in risk factors for cardiovascular disease (CVD) and non–insulin-dependent diabetes mellitus (NIDDM) consequent to a 20-week endurance training program. The 502 participants in this study were healthy and previously sedentary men (n = 250) and women (n = 252) of varying age (17 to 65 years) and race (blacks n =142; whites n = 360) who had completed the HERITAGE Family Study testing and training protocol. Following baseline measurements, participants trained on cycle ergometers 3 days/week for a total of 60 exercise sessions starting at the heart rate (HR) associated with 55% of $\dot{V}O_2$ max for 30 minutes/session. This was progressively increased to the HR associated with 75% of $\dot{V}O_2$ max for 50 minutes/session, which was maintained during the last 6 weeks. $\dot{V}O_2$ max, heart rate at 50 W, power output at 60% of $\dot{V}O_2$ max, lipids and lipoproteins, resting blood pressure, body composition including abdominal fat (computed tomography [CT] scan), and blood glucose and insulin at rest and at peak following an intravenous glucose tolerance test (IVGTT) were determined both before and after training. Following training, there were significant increases in $\dot{V}O_2$ max (16%) and the power output at 60% of $\dot{V}O_2$ max and a significant decrease in HR at 50 W. These changes in markers of aerobic fitness were significantly correlated only to the changes in the body composition variables and the lipids and lipoproteins. Further, there was considerable individual variation in response for all variables studied. Finally, when risk factor data were analyzed by quartile of change in $\dot{V}O_2$ max, there were few significant relationships. It is concluded that there is a significant relationship between changes in markers of aerobic fitness and changes in several risk factors for CVD and NIDDM. However, the magnitude of these relationships is small.

IT HAS NOW BEEN clearly established that physical inactivity is a significant risk factor for coronary artery disease,[1-3] hypertension,[2,4] and non–insulin-dependent diabetes mellitus (NIDDM).[2,5] An active lifestyle is being promoted in an attempt to reduce the risk of early death and disability from each of these chronic debilitating diseases.[2] Scientific evidence suggests that an active lifestyle plays an important role in risk reduction through its positive impact on specific disease risk factors.

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Historically, maximal oxygen uptake ($\dot{V}O_2$ max) has been used as a surrogate measure of the physical activity status of individuals and populations, assuming that those with high values are physically active and those with low values are not. It has also been established that aerobic endurance training substantially increases $\dot{V}O_2$ max, and that the more highly aerobically-trained the individual, the higher his or her $\dot{V}O_2$ max.[6] However, it is possible to have a moderate to high $\dot{V}O_2$ max without being physically active and to be physically active without having a high $\dot{V}O_2$ max. This is largely due to the influence of genetics on $\dot{V}O_2$ max. Bouchard et al[7] have demonstrated that there is a significant familial aggregation for $\dot{V}O_2$ max in the sedentary state, even when the data are adjusted for age, sex, body mass, and body composition. The heritability of $\dot{V}O_2$ max was estimated to be as high as 50% of the total phenotypic variance. With this in mind, investigators are now starting to distinguish between fitness and physical activity, treating them as discrete entities. Fitness is assessed by physiologic testing and is represented by such markers as $\dot{V}O_2$ max, HR response to a fixed power output, or the power output associated with a fixed percentage of one's $\dot{V}O_2$ max. Physical activity is assessed by direct observations, physical activity records, survey questionnaires and interviews, mechanical and electronic devices (eg, accelerometers, pedometers), and physiologic testing (eg, HR monitoring, doubly-labeled water).

Is the reduction in risk for various chronic diseases associated with an active lifestyle related to physical activity, physical fitness, or both? The answer appears to be both.[8] Low-intensity exercise (ie, less than that required to increase $\dot{V}O_2$ max) has been shown to decrease risk for all-cause mortality, coronary artery disease, NIDDM, hypertension, and site-specific cancers.[8] The specific effect of an increase or decrease in $\dot{V}O_2$ max on overall risk for chronic diseases or on specific risk factors for individual chronic diseases is less clear. McMurray et al[9] conducted a study of basic law enforcement employees, which incorporated both a cross-sectional and longitudinal component. They reported $\dot{V}O_2$ max levels in the untrained state (n = 1,664) and changes in $\dot{V}O_2$ max following a 9-week training program in low-fit individuals (n = 806) were more closely related than physical activity levels, as assessed by questionnaire, to cardiovascular disease (CVD) risk factors and their changes. Few longitudinal studies have looked at the relationship between changes in $\dot{V}O_2$ max and changes in risk factors for CVD and NIDDM.

Therefore, the purpose of this study was to determine the relationship between changes in maximal aerobic fitness (Δ $\dot{V}O_2$ max) and markers of submaximal aerobic fitness and changes in CVD and NIDDM risk factors consequent to a 20-week endurance training program using data from the HERITAGE Family Study. The HERITAGE Family Study is a large multicenter clinical trial investigating the possible genetic basis for the large variability in the responses of physiologic measures, as well as risk factors for CVD and NIDDM, to endurance exercise training. This study includes 4 Clinical Centers (Indiana University [formerly at Arizona State University], Laval University, Québec, Canada, the University of Minnesota, and The University of Texas at Austin) and a Data Coordinating Center (Washington University School of Medicine, St Louis, MO).

MATERIALS AND METHODS

Participants

The HERITAGE Family Study subject population consisted of families, including the natural father and mother (≤ 65 years of age) and generally 3 offspring 17 years of age or older for white families and at least 2 first-degree relatives for black families. Inclusion and exclusion criteria have been summarized in detail in a previous publication.[10] Specific criteria of importance to this report included the fact that participants were sedentary at baseline, normotensive or mildly hypertensive (<160/100) without antihypertension medication, and body mass index (BMI) was less than 40.0 kg/m^2. Participants with BMIs slightly in excess of this value (n = 5 in these analyses) who were considered by the supervising physician to be "healthy" and able to perform the required exercise prescription were included in the study. A total of 742 participants finished all HERITAGE testing and training protocols. Of this total, 502 participants constitute the sample for this study, having complete pre- and posttraining data for the fitness variables and the CVD and NIDDM risk factors. Subjects with incomplete data were excluded. Subject characteristics are presented in Table 1. Each Clinical Center's Institutional Review Board had previously approved the study protocol, and informed consent was obtained from each participant.

Experimental Design

Participants were screened by the Clinical Center's supervising physician and staff. Only those who were previously sedentary, free of pre-existing disease, and not taking medications that would affect any

Table 1. Physical Characteristics of the Subject Population

Subject Group	Age (yr)	Height (cm)	Weight (kg)	BMI (kg/m^2)
All subjects (n = 502)	34.1 ± 13.3	170.4 ± 9.3	75.3 ± 16.2	25.9 ± 4.7
	(15.9-65.9)	(148.6-196.8)	(39.6-138.0)	(17.0-43.0)
By sex				
Men (n = 250)	34.8 ± 13.9	177.3 ± 6.4	82.8 ± 14.9	26.3 ± 4.4
	(15.9-65.9)	(160.3-196.8)	(54.0-138.0)	(17.3-43.0)
Women (n = 252)	33.3 ± 12.7	163.4 ± 6.1	67.9 ± 13.8	25.4 ± 5.1
	(16.7-63.4)	(148.6-182.7)	(39.6-118.5)	(17.0-41.3)
By race				
Blacks (n = 142)	32.3 ± 10.5	169.0 ± 9.3	78.1 ± 16.2	27.3 ± 5.2
	(15.9-65.9)	(151.5-194.1)	(44.5-133.4)	(17.8-43.0)
Whites (n = 360)	34.8 ± 14.3	170.9 ± 9.3	74.2 ± 16.1	25.3 ± 4.5
	(17.0-64.3)	(148.6-196.8)	(39.6-138.0)	(17.0-41.5)

NOTE. Values are means ± SD and (range).

of the outcome variables were allowed to enter the study.[10] A comprehensive battery of tests was administered prior to starting the training program, which included the following: health, medical, and nutrition questionnaires; maximal and submaximal exercise tests; blood tests for lipids, lipoproteins, and sex steroids; intravenous glucose tolerance test (IVGTT); resting blood pressure; and body composition tests. Following the initial test battery, subjects completed a 20-week endurance training program (3 days/week for a total of 60 exercise sessions) on cycle ergometers, which were computer-controlled to maintain the participants' HRs at levels associated with fixed percentages of their $\dot{V}O_2$ max. The training program started at 55% of $\dot{V}O_2$ max for 30 minutes/session and gradually increased to 75% of $\dot{V}O_2$ max for 50 minutes/session during the last 6 weeks of training. Skinner et al[11] have provided details of the training program. The full test battery was administered again at the conclusion of the training program. For both resting blood pressure and blood lipid and lipoprotein measures, posttraining values were obtained at 24 hours and 72 hours after the last exercise bout. This was done in an attempt to differentiate the acute effects associated with the last exercise bout from the chronic adaptations to the 20-week training program.

Methodology for CVD and NIDDM Risk Factors

Resting blood pressure was taken using the Colin STBP-780 automated blood pressure unit (San Antonio, TX), as described in detail in a previous publication.[12] Participants reported to the laboratory before 11:00 AM, having refrained from tobacco and caffeine products for at least 2 hours, and having performed no formal exercise in the previous 12 hours. They were seated in a reclining chair in a semirecumbent position (legs supported parallel to the floor and the back support reclined at a 45° angle from the floor), with the arms relaxed and supported. The laboratory was quiet, with little or no light and a room temperature between 23°C and 26°C. A sheet or blanket was available if requested. A series of 4 to 8 blood pressure measurements were obtained on each of 2 separate days, both pre- and posttraining.

For the body composition assessment, participants reported to the laboratory at least 4 hours postprandial, having performed no formal exercise in the previous 4 hours. The entire body composition test battery was usually administered on a single day, with the exception of the computed tomography (CT) scan for abdominal visceral adipose tissue, which was usually scheduled on a different day. Hydrostatic weighing was used to assess body density according to the method of Behnke and Wilmore.[13] Residual lung volume was assessed using the oxygen- or helium dilution techniques. Percent body fat was estimated from body density using the equations of Siri[14] for white men, Lohman[15] for white women, Schutte et al[16] for black men, and Ortiz et al[17] for black women. CT was used to provide an estimate of abdominal visceral adipose tissue at the level of the vertebral disc between the 4th and 5th lumbar vertebrae (L4-L5 space), using either a Siemens Somatom DRH scanner (Erlangen, Germany) or a General Electric CT 9800 scanner (Waukesha, WI). The general procedures described by Sjöström et al[18] were followed. Total and visceral fat areas were calculated by delineating those areas with an electronic graph pen and then computing the adipose tissue surfaces using an attenuation range of -30 to -190 Hounsfield units. Subcutaneous abdominal fat area was calculated as the difference between total and visceral fat areas. Full details of all body composition procedures have been published previously.[19]

Blood lipid and lipoprotein concentrations were determined from blood samples obtained from an antecubital vein into vacutainer tubes containing EDTA. Subjects arrived in the early morning following a 12-hour overnight fast. Blood samples were drawn after the subject had been seated for a minimum of 5 minutes in a semirecumbent position. Samples were obtained on 2 different days, both before and after training. Cholesterol and triglyceride concentrations were determined in plasma and lipoproteins by enzymatic methods using a Technicon RA-500 analyzer (Bayer, Tarrytown, NY). Plasma very–low-density lipoproteins (VLDLs) were isolated by ultracentrifugation. High-density lipoprotein (HDL) was obtained after precipitation of low-density lipoprotein (LDL) in the infranatant by the heparin-manganese chloride method. Selective precipitation was used to isolate HDL_2 and HDL_3 subfractions using dextran sulfate. The apolipoprotein (Apo) A-1 concentration was measured in the infranatant and Apo B in the plasma and infranatant fraction by the rocket-immunoelectrophoretic method. Please see the article by Leon et al[20] for details.

The IVGTT was conducted in the morning following an overnight fast. Fasting samples were obtained from a venous catheter inserted into an antecubital vein after a 15-minute rest in a semirecumbent position. Glucose was then injected through an anticubital vein in the other arm at a dose of 20 g/m^2 of body surface area followed by 10-mL saline rinse. Blood samples for the measurement of plasma glucose, insulin, and C-peptide were taken at 1, 3, 5, 10, 15, 20, 30, 45, 60, 75, 90, 120, 150, and 180 minutes after the end of the glucose injection. Plasma glucose was measured enzymatically, and plasma insulin was measured by radioimmunoassay with polyethylene glycol separation. C-peptide was measured by using polyethylene glycol precipitation. A full description of these techniques has been published previously.[10]

Methodology for Exercise Tests

Subjects completed a total of 3 exercise tests, each on different days, both pre- and posttraining: a maximal test (Max), a submaximal test (Submax), and a submaximal to maximal test (Submax/Max). All exercise tests were conducted on a cycle ergometer (SensorMedics Ergo-Metrics 800S, Yorba Linda, CA). The details have been provided in previous publications.[21,22] Briefly, subjects completed the initial maximal exercise test using a graded exercise test protocol, starting at 50 W for 3 minutes. The rate of work was then increased by 25 W every 2 minutes thereafter to the point of exhaustion. For older, smaller, or less fit subjects, the test was started at 40 W and increased by 10 to 20 W increments. Using the results of this initial maximal test, subjects then performed the Submax exercise test on a second day at 50 W and at 60% of their initial $\dot{V}O_2$ max. The Submax/Max exercise test was then performed on a third day, starting with the Submax protocol, ie, 50 W and 60% of the initial $\dot{V}O_2$ max, and progressing to a maximal level of exertion. The results of the 3 exercise tests were used to establish the endurance training program work rates and to quantify the magnitude of the training response.[10]

For the Submax and Submax/Max tests, 2 HR values were obtained and averaged at 50 W, and the power output at 60% of the initial and final $\dot{V}O_2$ max was recorded. Subjects exercised for approximately 12 to 15 minutes at each work rate, with a 4-minute period of seated rest between work rates. The values presented in this report represent the mean of the responses for the 2 submaximal tests (ie, Submax and Submax/Max) and for the 2 maximal tests (ie, Max and Submax/Max), both before and after training.

For all exercise tests, $\dot{V}O_2$, $\dot{V}CO_2$, expiratory minute ventilation ($\dot{V}_E$), and the respiratory exchange ratio (RER) were determined every 20 seconds and reported as a rolling average of the 3 most recent 20-second values, using a SensorMedics 2900 metabolic measurement cart (MMC, Yorba Linda, CA). $\dot{V}O_2$ max was defined as the peak value obtained during the test. HR was determined by electrocardiogram (ECG) and the Colin STBP-780 instrument, and values were recorded during the last 15 seconds of each stage of the maximal test, and once steady state had been achieved at each of the submaximal work rates during the Submax and Submax/Max tests.

Quality Assurance, Quality Control, and Statistical Methodology

Important quality assurance and quality control procedures were instituted across all 4 Clinical Centers, as described by Gagnon et al.[23]

Staff from all Clinical Centers were trained centrally on several occasions, and all staff from each Clinical Center had to attain certification on each technique for which they were responsible. A detailed Manual of Procedures (MOP) was developed, and staff were required to review those sections of the MOP for which they were responsible every 6 months. Additional quality assurance and quality control procedures were implemented as described by Gagnon et al[23] in detail.

All data were analyzed using the SAS statistical package (version 6.12; SAS Institute, Cary, NC). Change values (posttraining score minus pretraining score) were generated for both the variables indicative of aerobic fitness status and the variables related to CVD and NIDDM risk. Because one of the primary variables of interest, change in $\dot{V}O_2$ max, was found not to be normally distributed, Spearman rank order correlation was used to determine relationships among variables.[24] Correlations were computed for the total sample, as well as for men, women, blacks, and whites as separate groups. Minimal significance was set at the .05 level. To further analyze the relationship between changes in fitness and changes in CVD and NIDDM risk factors, the total sample was divided into quartiles on the basis of the change in $\dot{V}O_2$ max. The mean changes for the CVD and NIDDM risk factors, as well as submaximal fitness estimates, were then compared across quartiles using the General Linear Model procedures to test for differences in quartiles. Duncan's Multiple Range Test was used to identify differences across groups.

RESULTS

Compliance to the training program was a major issue in the design of the HERITAGE Family Study. Subjects had to complete at least 95% of all training sessions (≥ 57 of 60 sessions) to be included in any training response data analyses. Of the 742 subjects who completed the training program, 90.2% completed all 60 training sessions. Of the remaining 9.8%, 0.6% missed 3 sessions, 2.0% missed 2 sessions, and 7.3% missed only 1 session. Of those who didn't complete all 60 training sessions, most were women who had to start their posttraining testing early to assure testing during the appropriate phase of their menstrual cycle.

The training program led to significant improvements in the markers of aerobic fitness, with increases in $\dot{V}O_2$ max (0.39 L/min, or 16.4%) and the power output at 60% of $\dot{V}O_2$ max (25.8 W, or 28.1%) and a decrease in the HR response at 50 W (-11 beats/min, or -9.4%) as can be seen in Table 2. There was

Table 2. Changes in Markers of Aerobic Fitness and CVD and NIDDM Risk Factors Consequent to 20 Weeks of Endurance Training for the Total Population (n = 502)

Risk Factor	Pretraining Values	Posttraining Values	Absolute Change	Relative Change %	Min/Max*
Aerobic fitness marker					
$\dot{V}O_2$ max (L/min)	2.44 ± 0.73	2.83 ± 0.80	0.39 ± 0.21	16.4†	−0.11/+1.10
HR at 50 W (beats/min)	118.5 ± 18.2	107.4 ± 13.9	−11.1 ± 10.0	−9.4†	+13.5/−44.5
PO at 60% $\dot{V}O_2$ max (W)	91.8 ± 36.4	117.6 ± 41.7	25.8 ± 15.4	28.1†	−20/+100
Body composition					
BMI (kg/m^2)	25.9 ± 4.8	25.8 ± 4.7	−0.1 ± 0.8	−0.4‡	+2.4/−3.5
Body fat mass (kg)	20.7 ± 10.4	20.0 ± 10.2	−0.7 ± 1.9	−3.4†	+4.7/−12.5
Body fat (%)	26.7 ± 9.9	25.8 ± 9.8	−0.9 ± 1.9	−3.4†	+6.0/−8.3
Fat-free mass (kg)	54.6 ± 11.1	55.1 ± 11.0	0.5 ± 1.2	0.9†	−4.5/+4.8
Waist/hip ratio	0.87 ± 0.08	0.86 ± 0.08	−0.01 ± 0.02	−1.1†	+0.1/−0.1
CT total fat (cm^2)	334.8 ± 173.5	321.1 ± 169.6	−13.7 ± 34.1	−4.1†	+69/−158
CT visceral fat (cm^2)	82.1 ± 53.9	77.1 ± 50.2	−5.0 ± 15.1	−6.1†	+43/−76
CT subcutaneous fat (cm^2)	252.7 ± 139.2	244.0 ± 137.6	−8.7 ± 26.6	−3.4†	+58/−136
Lipids and lipoproteins					
Cholesterol (mg/dL)	171.4 ± 36.8	173.1 ± 36.3	1.7 ± 16.1	1.0§	+66.5/−42.5
HDL-C (mg/dL)	40.8 ± 10.7	42.2 ± 11.3	1.4 ± 4.7	3.4†	−19.5/+22.8
HDL_2-C (mg/dL)	13.6 ± 7.5	14.6 ± 8.1	1.0 ± 4.3	7.4†	−13.1/+20.5
LDL-C (mg/dL)	114.1 ± 31.2	114.2 ± 30.6	0.1 ± 14.2	0.1	+59.5/−47.0
VLDL-C (mg/dL)	16.3 ± 13.7	16.2 ± 13.6	−0.1 ± 6.9	−0.6	+28.2/−32.3
Triglycerides (mg/dL)	114.4 ± 69.4	113.9 ± 70.6	−0.5 ± 37.8	−0.4	+262/−148
Apo B (mg/dL)	84.3 ± 23.7	85.2 ± 23.2	0.9 ± 10.7	1.1	−39.0/+40.0
Resting blood pressure					
Systolic (mm Hg)	117.7 ± 11.8	117.1 ± 11.4	−0.6 ± 6.7	−0.5§	+26.0/−27.5
Diastolic (mm Hg)	67.2 ± 8.7	67.2 ± 8.7	0.0 ± 5.7	0.0	+23.3/−18.2
MAP (mm Hg)	84.0 ± 9.1	83.8 ± 8.9	−0.2 ± 5.3	−0.2	+18.8/−16.3
IVGTT					
Glucose-rest (mmol/L)	5.0 ± 0.6	5.0 ± 0.6	0.0 ± 0.5	0.0	+2.0/−2.3
Insulin-rest (pmol/L)	64.4 ± 55.1	57.2 ± 48.6	−7.2 ± 45.9	−11.2†	+457/−360
Glucose-peak (mmol/L)	19.8 ± 4.4	20.7 ± 4.6	0.9 ± 4.9	4.6†	+25.1/−19.8
Insulin-peak (pmol/L)	809.8 ± 859.0	783.8 ± 751.5	−26.0 ± 460.9	−3.2	+2,664/−3,203

NOTE. Values are mean ± SD.

Abbreviations: PO, power output; MAP, mean arterial pressure; IVGTT, intravenous glucose tolerance test.

*Minimum/maximum change values (least favorable change/most favorable change).

† < .001.

‡ < .01.

§ < .05.

a wide variation in the $\dot{V}O_2$ max response, with improvement varying from -4.7% to +47.8%, or from -0.11 to +1.10 L/min. With respect to the CVD and NIDDM risk factors, the BMI, fat mass, relative body fat (%), waist/hip ratio, and CT scan measures of total, subcutaneous, and visceral abdominal fat decreased significantly with training, while fat-free mass increased.[25] While there were no significant changes in LDL cholesterol (LDL-C), VLDL-C, triglycerides, and Apo B, there were significant increases in total cholesterol (TC), HDL-C, and HDL_2-C.[20] There were significant reductions in resting systolic, diastolic, and mean arterial pressure posttraining, but these reductions occurred at either 24 hours posttraining or 72 hours posttraining, not across the average of these 2 posttraining measurement periods as used in this study except for systolic blood pressure.[12] With respect to the changes in resting and peak glucose and insulin values from the IVGTT pre- and posttraining, resting glucose and peak insulin values were unchanged, but resting insulin decreased and peak glucose increased. While the mean changes in risk factors were generally small, there was large variability in response as indicated by both the standard deviations of the change scores and the minimum and maximum change values.

The intercorrelations between the markers of aerobic fitness were significant, but generally low to moderate, with one exception. The correlation between Δ $\dot{V}O_2$ max (L/min) and Δ $\dot{V}O_2$ max (%) was high (r = .83); but the correlations between Δ $\dot{V}O_2$ max (L/min) and Δ HR 50 W and Δ power output at 60% of $\dot{V}O_2$ max were only low to moderate (r = -.13 and r = .53), respectively, as were the correlations between Δ $\dot{V}O_2$ max (%) and Δ HR 50 W and Δ power output at 60% of $\dot{V}O_2$ max (r = -.32 and r = .36, respectively). The correlation between Δ HR 50 W and Δ power output at 60% of $\dot{V}O_2$ max was only -.18.

The correlations between the changes in aerobic fitness measures and the changes in the CVD and NIDDM risk factors are presented in Table 3. For the group as a whole, significant correlations with the changes in aerobic fitness were found only among the body composition variables and the lipids and lipoproteins. The changes in fat mass, relative body fat, and fat-free mass had the greatest association with the changes in the fitness measures among the body composition variables and HDL-C and HDL_2-C among the lipids and lipoproteins. There were several other significant correlations, but they were not consistent across the fitness measures.

The correlations between fitness and risk factor variables within each subgroup are not reported, although those correlations that were statistically significant are noted in Table 3. While the subgroup correlations were similar to the group as a whole, they did exhibit several differences. When examining these relationships in men and women, the changes in fat mass, relative body fat, and fat-free mass were significantly related to the change in fitness measures in men, but to a lesser extent in women. The change in the waist/hip ratio was significantly related to the changes in fitness measures in women, but not men. Further, there were significant correlations between the changes in resting systolic, diastolic, and mean arterial blood pressure and Δ HR 50 W in women, but not men. When comparing blacks and whites, the changes in fitness measures were associated more with body composition variables in whites and more with lipids and lipoproteins in blacks.

The analyses of these submaximal fitness and risk factor data grouped by quartiles on the basis of the subjects' changes in $\dot{V}O_2$ max are presented in Table 4. The first quartile is composed of the low responders in $\dot{V}O_2$ max and the fourth quartile is composed of the high responders. With respect to submaximal fitness, there were no differences in Δ HR 50 W among the 3 highest quartiles, but the lowest quartile had a significantly smaller reduction in HR posttraining. The change in power output at 60% of $\dot{V}O_2$ max was closely related to the change in $\dot{V}O_2$ max. With respect to changes in body composition, the highest quartile had greater losses in fat mass and in percentage body fat than the other 3 quartiles, and the lowest quartile had the least change in fat-free mass. There were several minor differences in the magnitude of change in the risk factors for CHD and NIDDM, but they were of little significance.

DISCUSSION

The results of this study indicate that changes in the 4 markers of aerobic fitness were primarily related to changes in body composition variables and lipids and lipoproteins. Where relationships were established, they were generally of low magnitude. The changes observed in the 4 measures of aerobic fitness were all significant and substantial, although there was considerable individual variation in response, with changes in $\dot{V}O_2$ max varying from -4.7% to +47.8%. This variation in response was not the result of differences in adherence to the study protocol, because over 90% of the subjects completed all 60 training sessions, and all subjects completed at least 57 training sessions. Further, relative intensity and duration were identical for all subjects. Most of the changes in the CVD and NIDDM risk factors were also significant, but of lesser magnitude. However, they too were characterized by considerable individual variation in response, as indicated by the standard deviations of the change scores and the large range between the minimum and maximum change scores. Thus, it is not likely that the lack of substantial change in the risk factor values consequent to training would attenuate the correlations between risk factors and fitness values. Grouping the data into quartiles on the basis of the magnitude of change in $\dot{V}O_2$ max provided essentially the same results, in that the high responders (those in the fourth quartile) did not have more favorable changes in risk factors, with the exception of fat mass and percentage of body fat.

McMurray et al[9] investigated the relationship between changes in $\dot{V}O_2$ max and changes in risk factors in 576 low fit basic law enforcement trainees in North Carolina. Subjects completed a 9-week exercise program composed of 27 1-hour blocks of supervised exercise training, including a warm-up, aerobic training, resistance training, and a cool down. The investigators compared those subjects who had increased $\dot{V}O_2$ max by $\geq$ 3 mL $\cdot$ kg^{-1} $\cdot$ min^{-1} with those who had not increased $\dot{V}O_2$ max. The group that had increased $\dot{V}O_2$ max by $\geq$ 3 mL $\cdot$ kg^{-1} $\cdot$ min^{-1} had more favorable changes in body weight, relative body fat, and TC, and there was a trend for a more favorable blood pressure response. Correlations among the fitness and risk factor variables were not reported.

Sedgwick et al[26] reported the relationship between changes in aerobic fitness and changes in blood pressure and plasma lipids in men and women who had participated for 4 years in a fitness program that emphasized vigorous exercise of an aerobic nature. The subjects were segregated into 1 of 2 groups,

Table 3. Correlations Between Changes in Aerobic Fitness and Risk Factors for CVD and NIDDM for the Total Sample (n = 502)

Risk Factor	Δ $\dot{V}O_2$ max (L/min)	Δ $\dot{V}O_2$ (max %)	Δ HR at 50 W (beats/min)	Δ 60% $\dot{V}O_2$ (max W)
Body composition				
Δ BMI (kg/m^2)	−0.01	0.02	−0.04	−0.01
Significant subgroups	None	Bl	None	None
Δ Body fat mass (kg)	−0.11*	−0.08	0.03	−0.12†
Significant subgroups	W	W	None	Bl; BlM
Δ Body fat (%)	−0.14†	−0.12†	0.07	−0.12†
Significant subgroups	M; Wh	W; Wh; WhM	None	Bl; BlM
Δ Fat-free mass (kg)	0.20‡	0.19‡	−0.11*	0.12†
Significant subgroups	M; W; Bl; Wh	M; W; Bl; Wh	Bl	M; Wh
Δ Waist/hip ratio	−0.10*	−0.12†	0.02	−0.04
Significant subgroups	Wh; WhW	Wh; WhW	None	None
Δ CT total fat (cm^2)	−0.06	−0.03	0.04	−0.10*
Significant subgroups	Wh	None	M	None
Δ CT visceral fat (cm^2)	−0.04	−0.01	−0.01	−0.08
Significant subgroups	None	None	None	None
Δ CT subcutaneous fat (cm^2)	−0.05	−0.03	0.05	−0.08
Significant subgroups	None	None	M	M
Lipids and lipoproteins				
Δ Cholesterol (mg/dL)	−0.01	0.03	0.08	−0.08
Significant subgroups	None	None	Bl; BlM	None
Δ HDL-C (mg/dL)	0.05	0.09*	−0.04	0.07
Significant subgroups	W; Bl	W; Bl	None	None
Δ HDL_2-C (mg/dL)	0.02	0.10*	−0.17‡	0.00
Significant subgroups	None	None	M; W; Wh	None
Δ LDL-C (mg/dL)	0.01	0.02	0.09*	−0.05
Significant subgroups	None	None	M; Bl	None
Δ VLDL-C (mg/dL)	−0.06	−0.03	−0.03	−0.04
Significant subgroups	WhW	W	None	None
Δ Triglycerides (mg/dL)	−0.08	−0.05	−0.01	−0.07
Significant subgroups	W; Wh	W	None	None
Δ Apo B (mg/dL)	−0.02	0.04	0.00	0.11*
Significant subgroups	None	None	None	Wh
Resting blood pressure				
Δ Systolic (mm Hg)	−0.01	−0.01	0.07	0.03
Significant subgroups	None	None	BlW	None
Δ Diastolic (mm Hg)	−0.02	−0.01	0.06	0.05
Significant subgroups	None	None	W	None
Δ MAP (mm Hg)	−0.01	−0.01	0.07	0.05
Significant subgroups	None	None	W	None
IVGTT				
Δ Glucose-rest (mmol/L)	0.03	0.04	−0.01	0.06
Significant subgroups	None	None	None	None
Δ Insulin-rest (pmol/L)	0.02	0.05	−0.06	−0.03
Significant subgroups	None	None	W	None
Δ Glucose-peak (mmol/L)	0.03	0.06	−0.12†	0.02
Significant subgroups	None	None	Bl	None
Δ Insulin-peak (pmol/L)	0.06	0.07	−0.05	0.04
Significant subgroups	Bl	Bl	None	None

Abbreviations: Subgroups: M, men; W, women; Wh, white; Bl, black; WhM, white men; WhW, white women; BlM, black men; BlW, black women.

*< .05.

†< .01.

‡< .001.

fitness "gainers" and "nongainers." For men, comparisons of the 2 groups and multiple regression analyses were unable to identify a relationship between changes in aerobic fitness (estimated $\dot{V}O_2$ max) and changes in blood pressure and plasma lipids. For women, gainers improved resting systolic blood pressure, triglycerides, and the HDL/TC ratio more than nongainers. Only the correlation between change in aerobic fitness and change in systolic blood pressure in men (r = .13) was statistically significant (note: while this was reported as a positive correlation, there was an increase in $\dot{V}O_2$ max and a decrease in systolic blood pressure).

Thompson et al[27] observed a 13.5% increase in HDL-C

Table 4. Changes (posttraining-pretraining) in Markers of Aerobic Fitness and CVD and NIDDM Risk Factors After 20 Weeks of Endurance Training by Quartiles of Improvement in VO_{2max} (mL/min)

Risk Factor	Quartile 4 (highest 25%) N = 126	Quartile 3 N = 125	Quartile 2 N = 126	Quartile 1 (lowest 25%) N = 125	Significance
Aerobic fitness marker					
Δ $\dot{V}O_2$ max (mL/min)	671 ± 145	449 ± 40	318 ± 38	153 ± 72	All differences significant
Δ HR at 50 W (beats/min)	−11.8 ± 10.1	−12.9 ± 10.1	−11.2 ± 9.2	−8.3 ± 10.1	Q1 < Q4, Q3, Q2
Δ PO at 60% $\dot{V}O_2$ max (W)	38.1 ± 15.6	26.0 ± 11.8	22.7 ± 12.0	16.5 ± 13.6	Q4 > Q3, Q2, Q1 Q3 > Q1, Q2 > Q1
Body composition					
Δ BMI (kg/m^2)	−0.2 ± 0.8	−0.0 ± 0.9	0.0 ± 0.8	−0.2 ± 0.7	None
Δ Body fat mass (kg)	−1.2 ± 2.1	−0.5 ± 2.0	−0.6 ± 1.8	−0.6 ± 1.7	Q4 > Q3, Q2, Q1
Δ Body fat (%)	−1.3 ± 1.8	−0.7 ± 2.1	−0.7 ± 1.8	−0.6 ± 1.9	Q4 > Q3, Q2, Q1
Δ Fat-free mass (kg)	0.7 ± 1.3	0.5 ± 1.3	0.6 ± 1.2	0.0 ± 1.1	Q1 < Q4, Q3, Q2
Δ Waist/hip ratio	−0.01 ± 0.02	−0.00 ± 0.02	0.00 ± 0.03	−0.00 ± 0.02	Q4 > Q1
Δ CT total fat (cm^2)	−19.8 ± 35.5	−9.4 ± 35.2	−14.3 ± 33.5	−11.2 ± 31.6	Q4 > Q3
Δ CT visceral fat (cm^2)	−6.2 ± 13.3	−3.1 ± 15.4	−6.6 ± 15.6	−4.0 ± 15.8	None
Δ CT subcutaneous fat (cm^2)	−13.8 ± 27.7	−6.3 ± 28.7	−7.7 ± 24.4	−7.2 ± 24.9	Q4 > Q3
Lipids and lipoproteins					
Δ Cholesterol (mg/dL)	1.6 ± 16.1	1.8 ± 15.1	0.5 ± 16.4	2.8 ± 16.9	None
Δ HDL-C (mg/dL)	1.6 ± 4.2	1.5 ± 3.9	2.0 ± 5.7	0.7 ± 4.7	Q2 > Q1
Δ HDL_2-C (mg/dL)	0.9 ± 3.9	1.1 ± 3.9	1.9 ± 4.7	0.3 ± 4.4	Q2 > Q1
Δ LDL-C (mg/dL)	0.3 ± 13.7	0.8 ± 13.4	−1.5 ± 14.0	1.1 ± 15.8	None
Δ VLDL-C (mg/dL)	−0.4 ± 7.3	−0.6 ± 6.4	−0.5 ± 6.6	1.1 ± 7.1	None
Δ Triglycerides (mg/dL)	−1.3 ± 40.9	−4.6 ± 33.2	−0.3 ± 41.8	4.1 ± 34.5	None
Δ Apo B (mg/dL)	0.6 ± 9.6	1.3 ± 11.3	−0.2 ± 11.1	2.1 ± 10.8	None
Resting blood pressure					
Δ Systolic (mm Hg)	−0.6 ± 5.8	−0.7 ± 6.7	−0.7 ± 7.0	−0.3 ± 7.2	None
Δ Diastolic (mm Hg)	−0.2 ± 5.9	−0.5 ± 5.9	0.5 ± 5.2	−0.0 ± 5.9	None
Δ MAP (mm Hg)	−0.3 ± 5.0	−0.6 ± 5.4	0.1 ± 4.9	−0.1 ± 5.7	None
IVGTT					
Δ Glucose-rest (mmol/L)	0.1 ± 0.5	0.1 ± 0.4	0.0 ± 0.5	−0.0 ± 0.5	None
Δ Insulin-rest (pmol/L)	−2.5 ± 58.3	−7.5 ± 29.4	−7.7 ± 39.0	−10.9 ± 51.5	None
Δ Glucose-peak (mmol/L)	0.8 ± 5.0	1.4 ± 4.9	1.1 ± 4.7	0.4 ± 5.2	None
Δ Insulin-peak (pmol/L)	8.0 ± 488	25.8 ± 383	6.0 ± 406	−144.2 ± 534	Q1 > Q4, Q3, Q2

NOTE. Values are mean ± SD.

(corrected for plasma volume changes) and a 26% increase in $\dot{V}O_2$ max with aerobic training of up to 48 weeks duration. The changes in HDL-C were unrelated to changes in $\dot{V}O_2$ max, although there were only 8 subjects in this study. Després et al[28] found no significant correlations between changes in $\dot{V}O_2$ max (%) and cholesterol, triglycerides, Apo B, LDL-C, HDL-C, and the plasma glucose and insulin areas under the curve (oral glucose tolerance test) following 22 consecutive days of aerobic training in 6 pairs of monozygotic twins, and the actual correlations were similar to those obtained in the present study. In a second study, Després et al[29] found no significant relationship between changes in $\dot{V}O_2$ max (15.1% increase) and cholesterol, triglycerides, LDL-C, HDL-C, HDL_2-C, and glucose and insulin areas under the curve (oral glucose tolerance test) following 14 months of aerobic training in 13 obese premenopausal women. CT estimates of abdominal fat (visceral and subcutaneous) were also not significantly correlated with the changes in $\dot{V}O_2$ max.

Others have reported no significant relationship between changes in $\dot{V}O_2$ max and changes in plasma lipids and lipoproteins following varying periods of aerobic training.[30-33] However, several studies have noted significant relationships between the change in $\dot{V}O_2$ max and the changes in TC (Whaley et al[34] [r = -.16]) and HDL-C (Santiago et al[35] [r = +.34]). Kumagai et al[36] reported very high correlations between changes in $\dot{V}O_2$ max and changes in HDL-C (r = +.68) and HDL_2-C (r = +.68) in 10 obese women who trained for 6 months at lactate threshold for 1 hour/day, 3 times/week for 6 months. It is difficult to explain the magnitude of this correlation considering those reported in other studies and the relative small mean change in $\dot{V}O_2$ max (L/min) of 4.9%. There was a decrease in body mass of 4.0 kg, which would suggest that the subjects were also restricting food intake. Posttraining energy intake was greater than 1,000 kJ/day lower (-12.7%) compared with pretraining values, but this difference was not statistically significant. It is possible that these high correlations were the result of both changes in dietary intake, as well as in $\dot{V}O_2$ max. Williams et al[37] reported an interactive effect of diet and exercise on changes in HDL mass and 5 HDL mass subclassifications, and the correlations between changes in $\dot{V}O_2$ max and in HDL mass subclassifications varied from r = +.35 to r = +.41).

Several studies have reported low, but statistically significant correlations between changes in $\dot{V}O_2$ max and changes in resting and/or ambulatory blood pressure,[38,39] while others have not.[40] Filipovsky et al[39] reported correlations of r = -.28

and r = -.29 for resting systolic and diastolic blood pressure, respectively, following a 5-week physical training course. Blumenthal et al[38] reported a significant correlation of r = +.29 between changes in $\dot{V}O_2$ max and changes in diastolic blood pressure following a 4-month exercise training program (note: it appears that this should have been a negative correlation because $\dot{V}O_2$ max increased and diastolic blood pressure decreased). They also found a significant effect for diastolic blood pressure when the subjects were classified by tertiles on the basis of their change in $\dot{V}O_2$ max, with those with the greatest increase in $\dot{V}O_2$ max having the greatest decrease in diastolic blood pressure. A similar trend was noted for systolic blood pressure, but the results were not statistically significant.

Studies have evaluated the relationship between changes in $\dot{V}O_2$ max and changes in glucose disposal rate,[41] insulin response,[42] and sensitivity.[43] Tonino,[41] using the euglycemic 2-step hyperinsulinemic clamp technique, found no significant relationship between changes in $\dot{V}O_2$ max and glucose disposal rate in subjects 60 to 80 years of age who had completed 12 weeks of aerobic training, even though there was a strong relationship (r = .69) between baseline values for glucose disposal rate and $\dot{V}O_2$ max. Soman et al[43] reported a correlation of r = .81 between changes in glucose uptake, as a marker of insulin sensitivity, and changes in $\dot{V}O_2$ max following 6 weeks of aerobic training. Lovelady et al[42] found a correlation of r = -.34 between changes in insulin response and changes in $\dot{V}O_2$ max following a 12-week aerobic training program.

In looking at the 4 markers of aerobic fitness, 2 maximal and 2 submaximal, there was no obvious marker that was consistently a better correlate of the changes in the risk factors when the risk factors are considered as a group. This was true not only for the total sample, but also for each of the subgroups.

It is now recognized that exercising at intensities of physical activity insufficient to increase $\dot{V}O_2$ max can have substantial health benefits (ie, reduction in disease risk through improvement in risk factors), including reducing the risk for chronic degenerative diseases, such as CVD and NIDDM. The health benefits of physical activity appear to accrue in approximate proportion to the total amount of activity performed[44] and are not limited to higher intensity exercise, ie, exercise of sufficient intensity to increase $\dot{V}O_2$ max. This fact has been emphasized by statements from the Centers for Disease Control and Prevention and the American College of Sports Medicine,[44] the American Heart Association,[1] the National Institutes of Health,[45] and by the US Surgeon General.[2]

Considering the above, it is not totally surprising in the present study that changes in markers of aerobic fitness were not highly related to changes in risk factors for CVD and NIDDM consequent to a 20-week endurance training program. The magnitude of change following aerobic training in both aerobic fitness markers and in the risk factors for CVD and NIDDM is similar to the average change reported in meta analyses and review articles addressing these variables. Further, the variation in response from the highest to lowest response for each of the measured variables was quite large. As just one example, when comparing the change in $\dot{V}O_2$ max with the change in HLD-C, the range of response in $\dot{V}O_2$ max varied -.11 to +1.10 L/min, and the range of response in HDL-C varied from -19.5 to +22.8 mg/dL. Thus, the fact that the actual magnitude of the mean change in HDL-C was small should not have attenuated the correlation between the changes in these 2 variables. It must also be considered that a 20-week training period might not be of sufficient duration to demonstrate the true relationship between change in $\dot{V}O_2$ max, or other markers of aerobic fitness, and change in risk factors.

Thus, from the present study, it is concluded that there are statistically significant relationships between changes in markers of aerobic fitness and changes in several risk factors for CVD and NIDDM. However, the magnitude of these relationships is relatively small.

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