Training Status, Resting Metabolic Rate, and Cardiovascular Disease Risk in Middle-Aged Men

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We investigated differences in resting metabolic rate (RMR) and cardiovascular disease risk factors among 86 middle-aged men (36 to 59 years) classified as resistance-trained ([RT] n = 19), aerobic-trained ([AT] n = 37), or untrained ([UT], n = 30) according to habitual exercise patterns. RMR, body composition, body fat distribution, supine blood pressure, maximal aerobic capacity ($\dot{V}O_2$max), plasma lipid levels, and fasting levels of insulin, glucose, and thyroid hormones were measured. We found that RMR, adjusted for differences in fat-free mass, showed a tendency to be greater in AT men as compared with RT men ($P = .09$) and was greater in AT men as compared with UT men ($P < .05$). No differences in RMR were noted between RT and UT men. UT men had higher values for total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-C), and the insulin to glucose ratio and lower values for high-density lipoprotein cholesterol (HDL-C) (all $P < .01$) as compared with RT and AT men, whereas no differences in these variables were noted between RT and AT men. Supine diastolic blood pressure was lower in RT men as compared with both AT and UT men. Stepwise regression analysis showed that variations in body fatness accounted for the greatest variation in fasting lipid profile, blood pressure, and the insulin to glucose ratio among groups. Furthermore, statistical control for body fatness either diminished or abolished differences in cardiovascular disease risk factors among training groups. We conclude that resting energy requirements are greater in middle-aged AT men as compared with RT and UT men. Furthermore, RT and AT men displayed a comparable cardiovascular risk profile despite large differences in $\dot{V}O_2$max. These findings suggest that attainment of low levels of body fat (via high levels of energy expenditure and/or prudent dietary practices) is an important factor associated with a favorable cardiovascular risk profile in middle-aged men.

RESTING METABOLIC RATE (RMR) constitutes the largest portion of total daily energy expenditure. RMR decreases with age[1-6] on the order of 2% to 3% per decade. Recent evidence has shown that the rate of decrease of RMR is greater during middle-age years, coincident with the loss of fat-free mass and increase in adiposity.[5,6] The decline in RMR may be one factor that contributes to the increase in adiposity and decline in daily energy requirements in older individuals. Long-term endurance exercise has been shown to increase RMR, and therefore may be one effective clinical intervention to offset the age-related decline in RMR and enhance daily energy needs.[7,8]

Resistance training for older individuals has gained increased popularity in recent years as a therapeutic intervention to increase muscular strength and enhance functional independence. However, less information is available on long-term effects of resistance training on RMR in middle-aged men. It could be hypothesized that resistance training is effective in ameliorating the age-related decline in RMR through anabolic effects on fat-free mass. Thus, the first purpose of this study was to compare RMR in middle-aged men who had a long-term participation in aerobic and resistance training with that in sedentary individuals.

Exercise also appears to have beneficial effects on decreasing cardiovascular disease risk. Longitudinal evidence suggests that individuals who participate in either aerobic-type activities[9] or intense muscular activity[10] have reduced rates of morbidity and mortality due to cardiovascular disease. However, it is unclear as to the effects of resistance training on cardiovascular disease risk factors in younger men,[11] and to our knowledge only one study has directly compared effects of aerobic and resistance training on cardiovascular risk factors in middle-aged men.[12] Unfortunately, resistance training programs frequently result in small changes in body composition that render effects on cardiovascular disease risk factors (ie, lipids, insulin resistance, and blood pressure) difficult to ascertain. Thus, in the present study an alternative approach was used in which we examined the relationship between resistance training and cardiovascular disease in individuals who have maintained high levels of resistance training over several years. Therefore, the second purpose of the present study was to examine cardiovascular risk factors in a cohort of well-characterized, resistance-trained (RT), aerobic-trained (AT), and untrained (UT) middle-aged men and to identify those physiologic factors that may explain differences in cardiovascular disease risk among individuals who vary in exercise training mode.

SUBJECTS AND METHODS

Subjects

A total of 86 healthy male volunteers (36 to 59 years) participated in the present study. Each subject met the following criteria: no clinical signs or symptoms of heart disease, resting blood pressure less than 160/90 mm Hg, normal resting ECG, normal 12-lead ECG response to an exercise stress test, absence of any

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prescription or over-the-counter medication that could affect cardiovascular function, and weight stability (± 2 kg) by medical history within the past year. Subjects were categorized according to the type of exercise they regularly performed. UT subjects were those individuals who did not participate in a regular exercise program. The RT group consisted of subjects who had regularly participated in a resistance training program for at least 5 years before testing. It was required that their training regimen be at least 3 days per week and consist of exercises for both the upper and lower portion of the body performed at a moderate intensity (~70% to 85% of one-repetition maximum). RT subjects used both free weights and exercise machines and reported no prior steroid use. The AT group consisted of runners who reported participation in endurance training exercise at least four times per week for the 5 years before testing for an average distance of 45 ± 10 km/wk. The nature, purpose, and possible risks of the study were carefully explained to each subject before obtaining consent to participate.

RMR

The reliability and a detailed description of this procedure have previously been reported.[7] Briefly, RMR was measured after an overnight fast (10 to 12 hours) by indirect calorimetry using the ventilated-hood technique. Energy expenditure was calculated using the equation of Weir.[13] RMR was measured after an overnight stay in the clinical research center because inpatient measures of RMR yield lower values than those measured on an outpatient basis.[14] Subjects who normally participated in exercise were told to refrain from exercise for 48 hours before the measurement to eliminate the residual effect of exercise on RMR and plasma determinations.[15,16] Recent test-retest data in 17 male volunteers yielded an intraclass correlation of .91 and a coefficient of variation of 3.9%.[17]

Measurement of Maximal Aerobic Capacity

Maximal aerobic capacity ($\dot{V}O_2max$) was assessed by a progressive and continuous test to exhaustion on a treadmill as previously described.[7] Briefly, a comfortable initial walking or jogging speed was determined for each individual and maintained throughout the test. After the first 3 minutes, the incline was increased by 2.5% every 2 minutes. $\dot{V}O_2max$ was defined as attainment of age-predicted maximal heart rate and a respiratory exchange ratio greater than 1.0. Test-retest conditions (within 1 week) for $\dot{V}O_2max$ in a group of male volunteers yielded an intraclass correlation of .94 and a coefficient of variation of 3.8%.[7]

Body Composition, Anthropometrics, and Blood Pressure

Body density was estimated using the equation reported by Brozek et al[18] by underwater weighing with simultaneous measurement of lung volume by helium dilution. The Keys-Brozek equation[19] was used to estimate body fat from body density. Fat-free mass was estimated as total body weight minus fat weight. Reproducibility of percent body fat was examined using test-retest conditions (within 1 week). The intraclass correlation and coefficient of variation in a previous group of male volunteers (N = 25) for the estimation of percent body fat were .98 and 4.9%, respectively.[7] The means of three consecutive measurements of nine separate skinfold sites (abdomen, axillary, biceps, calf, chest, subscapular, suprailiac, triceps, and thigh) were obtained by the same investigator and are represented as the sum of nine skinfolds. The waist to hip ratio was obtained using a plastic measuring tape. The waist circumference was obtained by placing the tape around the waist at the minimal circumference (approximately at the umbilicus) and around the hips at the greatest protrusion of the buttocks. Supine systolic and diastolic blood pressures were measured as an average of the last four of five readings (one per minute) on the right arm using an automated-cuff machine (Dinamap, Critikon, Tampa, FL) after the subject was in a supine position for at least 10 minutes. Mean arterial pressure was calculated as two-thirds diastolic blood pressure plus one-third systolic blood pressure.

Plasma Determinations

All blood was withdrawn after a 10- to 12-hour overnight fast and after RMR was determined. Plasma glucose concentrations were determined using a glucose analyzer (Yellow Springs Instrument, Yellow Springs, OH). A modification of the radioimmunoassay technique reported by Starr et al[20] was used to determine plasma concentrations of immunoreactive insulin. As previously described,[7] a Clinical Assay kit (Baxter, Cambridge, MA) was used to quantify free (F) and total thyroxine (T_4) and total 3,5,3'-triiodothyronine (T_3) levels. An analog assay (Diagnostic Products, Los Angeles, CA) was used to determine plasma concentrations of FT_3. Enzymatic processes were used to determine both total cholesterol[21] and triglyceride.[22] High-density lipoprotein cholesterol (HDL-C) levels were determined after removal of low-density lipoprotein cholesterol (LDL-C) and very–low-density lipoprotein cholesterol by a procedure using dextran sulfate.[23] LDL-C levels were calculated using the formula reported by Friedewald et al,[24] LDL-C = total cholesterol − (HDL-C + [triglycerides/5]), since all volunteers had fasting plasma triglyceride levels less than 400 mg/dL.

Dietary Intake

Dietary energy and macronutrient intake was determined using a 3-day, self-report diary (2 weekdays and 1 weekend day) as previously described.[25] Each subject was supplied with a 5-lb metabolic scale and instructed on the accurate measurement and recording of intake. Subjects were strongly encouraged not to change their dietary habits during measurement of food intake, although it is likely that volunteers underreport their level of habitual food intake.[26]

Leisure Time Physical Activity Questionnaire

The Minnesota Leisure Time Activity Questionnaire[27] was completed for each subject using a structured interview. In the interview, frequency and duration of subject participation in various recreational activities over the previous 12-month period was assessed. Each activity was then assigned an intensity code that was multiplied by the total estimated minutes in the year spent performing this activity. The cumulative energy cost for leisure time physical activity (LTA) over the past year was averaged and expressed as kilocalories per day. A recent study in our laboratory has shown that LTA is highly correlated with the energy expenditure of physical activity (r = .83) as measured by doubly labeled water in older individuals.[28]

Statistics

A one-way ANOVA examined differences in dependent variables among groups. If a significant group effect was found, Duncan's multiple-comparison test identified the location of differences among groups. Stepwise regression analysis identified independent correlates of cardiovascular disease risk factors. Independent variables used as possible predictors were those variables that have previously been shown to be associated with cardiovascular risk factors: body composition, body fat distribution, physical activity and fitness level, dietary variables, and hormone levels.

Analysis of covariance was used to determine if differences existed in dependent variables among groups after statistical control for variables identified in the stepwise regression procedure. All values are expressed as the mean ± SD, unless otherwise specified.

RESULTS

Physical characteristics of the subjects are listed in Table 1. No differences in age were noted among groups. RT men were shorter than both UT and AT men. UT weighed more ($P < .01$) than their trained counterparts due to a higher level of fat mass ($P < .01$). No differences in fat-free mass were noted among groups. UT men therefore exhibited a greater percent fat mass relative to AT and RT men ($P < .01$). AT men reported higher LTA values than UT men ($P < .01$), but had a lower level as compared with RT men ($P < .05$). $\dot{V}O_2$max was greater in AT men ($P < .01$) than in UT and RT men both in absolute terms (liters per minute) and after adjustment for fat-free mass. The sum of nine skinfolds, an index of subcutaneous fat, was higher ($P < .01$) in UT men relative to RT and AT men. UT men had a greater waist to hip ratio ($P < .01$) than either trained group.

Table 2 lists differences in dietary intake data among the three groups. Dietary energy intake was greater in RT men as compared with UT men ($P < .01$), but was not different from that in AT men. RT and AT men had a higher absolute and relative intake of carbohydrates ($P < .01$) than UT men. RT individuals reported a lower fat intake (absolute and relative amounts, as well as polyunsaturated and saturated fractions) and higher protein intake (absolute and relative amounts) than UT and AT men (all $P < .01$). Dietary cholesterol intake was not different among groups.

Figure 1 illustrates group differences in absolute RMR. AT men had a higher RMR (1.33 ± 0.11 kcal/min, $P < .05$) as compared with UT men (1.27 ± 0.10 kcal/min) and a trend for a higher RMR as compared with RT men (1.28 ± 0.10 kcal/min, $P = .09$). Adjustment for fat-free mass did not change the aforementioned results. This would be expected, since no mean differences in fat-free mass were noted among groups.

Table 1. Physical Characteristics of UT, RT, and AT Middle-Aged Men

Variable	UT	RT	AT	Difference
n	30	19	37	
Age (years)	46 ± 5	44 ± 5	44 ± 7	NS
Height (cm)	179 ± 7	173 ± 7	178 ± 8	UT, AT > RT*
Body mass (kg)	85 ± 16	74 ± 8	75 ± 9	UT > AT, RT†
Fat mass (kg)	18 ± 8	9 ± 4	10 ± 4	UT > AT, RT†
Fat-free mass (kg)	67 ± 10	65 ± 6	65 ± 8	NS
Fat mass (%)	21 ± 6	12 ± 5	13 ± 5	UT > AT, RT†
LTA (kcal/d)	292 ± 132	695 ± 401	538 ± 250	RT > AT*
				RT, AT > UT†
$\dot{V}O_2$max (L/min)	3.6 ± 0.6	3.6 ± 0.7	4.3 ± 0.6	AT > UT, RT†
Adjusted $\dot{V}O_2$max (L/min)‡	3.4 ± 0.6	3.6 ± 0.7	4.2 ± 0.5	AT > UT, RT†
Sum of skinfolds (mm)	156 ± 59	76 ± 29	95 ± 34	UT > AT, RT†
Waist to hip ratio	0.93 ± 0.1	0.88 ± 0.1	0.87 ± 0.04	UT > AT, RT†

NOTE. All values are expressed as the mean ± SD.
*$P < .05$.
†$P < .01$.
‡$\dot{V}O_2$max values were adjusted for fat-free mass according to recent recommendations.[29]

Table 2. Self-Reported Dietary Intake Data for UT, RT, and AT Middle-Aged Men

Variable	UT	RT	AT	Difference
Energy (kcal/d)	2,502 ± 726	3,331 ± 1,185	2,959 ± 780	RT > UT*
Carbohydrate g/d	307 ± 96	448 ± 145	417 ± 147	RT, AT > UT*
%	48 ± 7	55 ± 12	54 ± 8	RT, AT > UT*
Fat g/d	91 ± 35	65 ± 26	97 ± 35	UT, AT > RT*
%	32 ± 5	19 ± 9	29 ± 7	UT, AT > RT*
Protein g/d	104 ± 30	225 ± 227	108 ± 29	RT > UT, AT*
%	17 ± 4	25 ± 13	15 ± 4	RT > UT, AT*
Polyunsaturated fat (g)	14 ± 8	8 ± 4	14 ± 8	UT, AT > RT*
Saturated fat (g)	26 ± 11	15 ± 11	27 ± 13	UT, AT > RT*
Cholesterol (mg/d)	247 ± 127	327 ± 243	286 ± 148	NS

NOTE. All values are expressed as the mean ± SD.
*$P < .01$.

Measured and adjusted values for fasting plasma lipid levels and supine blood pressure for the three groups are listed in Table 3. Table 4 lists results from stepwise regression analysis. Independent variables identified by stepwise analysis that explained the greatest source of variation in the dependent variable were then used to adjust measured cardiovascular disease risk factor variables.

Both AT and RT men showed a lower measured plasma cholesterol level than UT men ($P < .01$). Variation in plasma cholesterol was best predicted by three factors (total $R^2 = 41\%$): percent fat mass ($R^2 = 27\%$), fat-free mass ($R^2 = 9\%$), and the sum of nine skinfolds ($R^2 = 5\%$). Statistical control for percent fat mass, fat-free mass, and

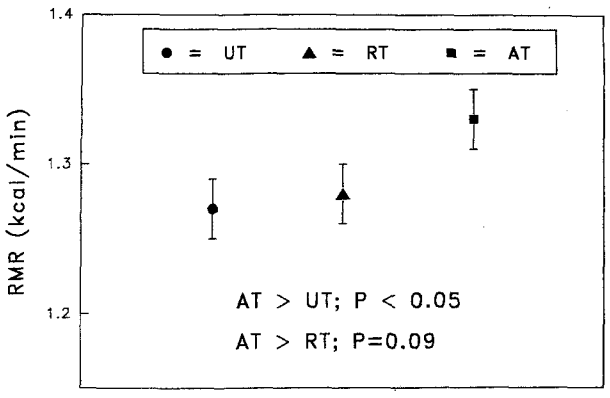

Fig 1. Mean absolute RMR in AT, RT, and UT middle-aged men. Group measured RMR values did not change when controlled for differences in fat-free mass. Values are the mean ± SE.

Table 3. Measured and Statistically Adjusted Values for Fasting Plasma Lipid Levels and Blood Pressure in UT, RT, and AT Middle-Aged Men

Variable	UT	RT	AT	Difference
Cholesterol (mg/dL)	213 ± 35	167 ± 41	179 ± 34	UT > AT, RT†
Adjusted cholesterol (mg/dL)‡	204 ± 36	178 ± 35	184 ± 14	UT > AT, RT*
Triglycerides (mg/dL)	145 ± 55	104 ± 46	88 ± 33	UT > AT, RT†
Adjusted triglycerides (mg/dL)#	127 ± 44	111 ± 48	103 ± 55	NS
HDL-C (mg/dL)	44 ± 8	52 ± 9	63 ± 9	RT, AT > UT†
Adjusted HDL-C (mg/dL)§	45 ± 12	51 ± 10	52 ± 10	AT > UT*
LDL-C (mg/dL)	137 ± 34	94 ± 34	99 ± 34	UT > AT, RT†
Adjusted LDL-C (mg/dL)‖	124 ± 38	106 ± 35	105 ± 30	UT > AT*
MAP (mm Hg)	89 ± 8	84 ± 11	88 ± 8	NS
SBP (mm Hg)	116 ± 10	120 ± 16	118 ± 11	NS
DBP (mm Hg)	75 ± 8	66 ± 11	73 ± 8	UT, AT > RT†
Adjusted DBP (mm Hg)¶	73 ± 11	68 ± 9	74 ± 9	NS

NOTE. Variables were adjusted using analysis of covariance for predictor variables (Table 4). All values are expressed as the mean ± SD.
Abbreviations: MAP, mean arterial pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure.
*$P < .05$.
†$P < .01$.
‡Adjusted for % fat mass, fat-free mass, and sum of nine skinfolds.
§Adjusted for fat mass.
‖Adjusted for % fat mass, fat-free mass, and LTA.
¶Adjusted for % fat mass.
#Adjusted for % fat mass and adjusted $\dot{V}O_2$max.

the sum of nine skinfolds diminished differences in cholesterol among groups, but a higher ($P < .05$) adjusted cholesterol in the UT group persisted relative to AT and RT groups. Triglycerides were higher in UT men than in AT and RT men ($P < .01$). Thirty-two percent of the variation in triglycerides was explained by percent fat mass ($R^2 = 21\%$) and adjusted $\dot{V}O_2$max ($R^2 = 11\%$). No significant differences among groups for fasting triglycerides were found after controlling for percent fat mass and adjusted $\dot{V}O_2$max. HDL-C was higher in both AT and RT men than in UT men ($P < .01$). HDL-C was best predicted (total $R^2 = 9\%$) by differences in fat mass. The AT group showed a higher plasma HDL-C level ($P < .05$) as compared with the UT group after controlling for differences in fat mass.

Table 4. Stepwise Multiple Linear Regression Predicting Cardiovascular Risk Factor Variables in the Total Group (N = 86)

Dependent Variable	Step	Independent Variable	R^2	P
Cholesterol	1	%Fat mass	.27	<.01
	2	Fat-free mass	.36	<.01
	3	Sum of skinfolds	.41	<.05
Triglyceride	1	%Fat mass	.21	<.01
	2	Adjusted $\dot{V}O_2$max*	.32	<.01
HDL-C	1	Fat mass	.09	<.01
LDL-C	1	%Fat mass	.27	<.01
	2	Fat-free mass	.32	<.05
	3	LTA	.37	<.05
DBP	1	%Fat mass	.21	<.01
I/G ratio	1	Sum of skinfolds	.38	<.01

NOTE. R^2 represents the amount of explained variance provided by each variable to the regression model, with the final-step R^2 representing the cumulative R^2.
Abbreviations: DBP, supine diastolic blood pressure; I/G ratio, insulin to glucose ratio.
*$\dot{V}O_2$max values were adjusted for fat-free mass according to recent recommendations.[29]

AT and RT men had a lower LDL-C level than UT men. LDL-C was predicted (total $R^2 = 37\%$) by percent fat mass ($R^2 = 27\%$), fat-free mass ($R^2 = 5\%$), and LTA ($R^2 = 5\%$). After statistical control for these variables, a higher ($P < .05$) LDL-C level persisted in UT as compared with AT men.

No differences in mean arterial pressure or supine systolic blood pressure were noted among groups. However, UT and AT individuals showed a higher supine diastolic blood pressure as compared with RT men ($P < .01$). Variation in percent fat mass accounted for 21% of the variation in diastolic blood pressure. No group differences in diastolic blood pressure were found after adjustment for percent fat mass.

Table 5 lists fasting plasma thyroid hormones, insulin, glucose, and the measured and adjusted values for the

Table 5. Measured and Statistically Adjusted Fasting Plasma Thyroid Hormone, Insulin, and Glucose Levels in UT, RT, and AT Middle-Aged Men

Variable	UT	RT	AT	Difference
T_3 (ng/dL)	127 ± 32	117 ± 30	128 ± 38	NS
T_4 (μg/dL)	7.3 ± 1.7	7.1 ± 1.9	7.2 ± 1.7	NS
FT_3 (pg/mL)	2.1 ± 1.2	2.9 ± 0.9	2.0 ± 0.8	RT > UT, AT†
FT_4 (ng/dL)	1.7 ± 0.7	1.4 ± 0.6	2.0 ± 0.7	AT > RT†
Insulin (pmol/L)	71 ± 45	41 ± 19	48 ± 23	UT > RT, AT†
Glucose (mg/dL)	103 ± 7	96 ± 5	100 ± 7	UT, AT > RT†
I/G ratio	0.7 ± 0.4	0.4 ± 0.2	0.5 ± 0.2	UT > RT, AT†
Adjusted I/G ratio‡	0.6 ± 0.3	0.5 ± 0.3	0.5 ± 0.3	NS

NOTE. Adjusted variables were adjusted using analysis of covariance for predictor variables (Table 4). All values are expressed as the mean ± SD.
Abbreviation: I/G ratio, insulin to glucose ratio.
*$P < .05$.
†$P < .01$.
‡Adjusted for sum of nine skinfolds.

insulin to glucose ratio in the three groups. No differences among groups were noted in plasma concentrations of T_3 or T_4. RT men showed a greater plasma FT_3 level as compared with AT and UT men ($P < .01$). However, RT men had a lower FT_4 as compared with AT men ($P < .01$). UT men showed a higher fasting plasma insulin level ($P < .01$) as compared with the two trained groups. Furthermore, both UT and AT men had a higher fasting glucose level as compared with RT men ($P < .01$). Together, this contributed to a higher fasting insulin to glucose ratio ($P < .01$) in the UT group as compared with the AT and RT men. Variation in the insulin to glucose ratio was predicted by the sum of nine skinfolds (total $R^2 = .38$). Groups did not differ in the insulin to glucose ratio after adjustment for differences in the sum of nine skinfolds.

DISCUSSION

This study was undertaken to examine differences in RMR and cardiovascular disease risk factors in middle-aged men who participate in either an aerobic or resistance training regimen. The major findings are as follows: (1) AT men showed a higher RMR relative to UT men and a trend toward a higher RMR relative to RT men; (2) RT middle-aged men showed a cardiovascular risk profile comparable to that of AT men despite large differences in $\dot{V}O_2$max; and (3) a low level of adiposity is an important variable associated with a favorable cardiovascular risk profile in middle-aged men.

RMR

This study was prompted by earlier studies from our laboratory in which younger AT and RT men showed a higher RMR for their metabolic size as compared with UT men.[30] However, it is unknown whether these metabolic adaptations persist into the middle-aged years.

This study adds new information by comparing resting energy requirements in middle-aged men who primarily train anaerobically (ie, resistance training) with those in AT individuals. We noted a higher RMR (5%) in middle-aged AT men as compared with UT middle-aged men and a tendency for a higher RMR in AT men as compared with RT men. These differences persisted whether RMR was compared on an absolute basis or normalized for differences in fat-free mass. Because subjects were asked to refrain from exercise for at least 48 hours before measurement of RMR, it is likely that differences in RMR among groups reflect long-term adaptations to exercise rather than the short-term effect of the last bout of exercise.[15,16] The magnitude of this difference in RMR in middle-aged men who vary in training status is comparable to previous results from our laboratory in which younger[30] and older[31] AT individuals exhibited a higher RMR relative to their age-matched UT counterparts.

Contrary to our previous study performed in younger individuals,[30] we noted no difference in RMR between RT men and UT middle-aged men. In our earlier study, it is possible that the higher $\dot{V}O_2$max in younger RT men as compared with younger UT men may partially explain their higher RMR, as we have shown that increased aerobic fitness is related to a higher RMR.[5] In absolute terms, AT middle-aged men in the present study would expend an additional 79 kcal/d in basal conditions as compared with both RT and UT counterparts. Thus, it is possible that in addition to the direct energy cost of aerobic training, the higher levels of basal energy expenditure may contribute to the low body fat reserves in AT men. There is still much debate as to the regulatory mechanism(s) involved in the increase in RMR in response to training. We have shown that the increase in RMR after a 2-month aerobic training regimen was related to an increased appearance rate of norepinephrine into the circulation in older individuals.[8] This finding suggests that the training-induced increase in RMR may occur through activation of the sympathetic nervous system. Unfortunately, a measure of sympathetic nervous system activity was not performed in the present study. Thyroid hormones are known modulators of RMR.[32,33] In the present study, plasma FT_3 was higher in RT men as compared with AT and UT men. Also, plasma FT_4 was higher in AT men as compared with RT men. However, it is unlikely that these differences explain the observed differences in RMR, since plasma concentrations of FT_3 and FT_4 were not related to RMR.

Cardiovascular Disease Risk Factors

The second purpose of the present study was to compare cardiovascular disease risk factor variables in RT and AT middle-aged men. In general, RT middle-aged men showed a cardiovascular risk profile comparable to that of AT men but more favorable than that of UT men.

It is widely accepted that increased plasma cholesterol and LDL-C levels are related to a higher incidence of cardiovascular disease.[34] Although it has been suggested that these factors are modifiable through aerobic training,[35] the efficacy of resistance training in reducing plasma cholesterol and LDL-C remains controversial.[11] We found comparable plasma cholesterol and LDL-C levels between the training groups and higher levels in the UT group. Percent fat mass was identified as the best predictor of differences in both plasma cholesterol and LDL-C among groups. Statistical control for percent fat mass and other predictor variables diminished but did not abolish differences in cholesterol or LDL-C among groups, which suggests that variables not measured in the present study contribute to variation in plasma cholesterol and LDL-C levels. These results are different from those of our previous study in younger male volunteers, in which percent dietary intake of fat was found to be the strongest predictor of plasma cholesterol and LDL-C.[30] However, the reasons for age-related differences with regard to the impact of dietary fat versus percent fat mass on plasma cholesterol and LDL-C levels are not readily apparent.

Elevated plasma triglyceride levels are an independent predictor of cardiovascular disease.[36] In the present study, AT and RT groups did not differ in plasma triglycerides, whereas the UT group exhibited higher levels of plasma triglycerides as compared with either training group. We found that differences in percent fat mass and $\dot{V}O_2$max accounted for the greatest source of variation in plasma

triglyceride levels. Furthermore, differences in triglyceride levels among groups were diminished after statistical control for these variables. This finding suggests that decreased triglyceride levels associated with training are associated with lower body fat reserves. Wood et al[37] found that reductions in body fat mass were significantly related to changes in plasma triglyceride levels in overweight men after 7 months of aerobic exercise training. However, an increase in $\dot{V}O_2$max may also be an independent factor that contributes to a lower level of plasma triglycerides, as previously shown in women.[38] Collectively, these results imply that exercise training that induces reductions in body fat mass and enhances $\dot{V}O_2$max may have additive benefits on decreasing plasma triglyceride levels.

Despite findings that suggest an increased plasma HDL-C is protective against cardiovascular disease,[39] the mechanism responsible for elevations in HDL-C after aerobic exercise training is unclear. Observations from the present study show that AT and RT middle-aged men display similar plasma HDL-C levels. Furthermore, higher HDL-C levels in trained as compared with UT men are partially related to differences in fat mass between groups, although statistical control for fat mass did not completely diminish differences among groups. The lower HDL-C noted in UT subjects may be explained by differences in lipoprotein lipase activity, the primary enzyme responsible for production of HDL-C from very-low-density lipoprotein and chylomicrons.[40] Després et al[41] found that exercise-induced reductions in fat mass are associated with increases in lipoprotein lipase activity. Thus, it is possible that the lower body fat reserves in AT and RT men influence HDL-C levels by altering the activity of lipoprotein lipase, although this remains speculative. Taken together, these findings suggest that aerobic and anaerobic exercise modalities are associated with high HDL-C levels in middle-aged men.

Blood pressure is lower in borderline hypertensive and normotensive men after aerobic exercise training.[42,43] However, the effect of resistance training on blood pressure has yielded conflicting results, with some investigators finding a decrease in blood pressure[44] and others finding no change[12] after short-term training. In the present study, diastolic blood pressure was lower in RT men as compared with AT and UT men. Furthermore, variation in diastolic blood pressure among groups was attributable to differences in percent fat mass. Thus, it appears that resistance training is associated with lower blood pressure values in middle-aged men. However, it should be noted that the effect of small differences ($\sim$5 mm Hg) in diastolic blood pressure within the normative range ($<$80 mm Hg) on the risk for cardiovascular disease remains unknown.

The insulin to glucose ratio is significantly correlated to estimates of insulin sensitivity obtained by use of the euglycemic clamp.[45] Furthermore, the insulin to glucose ratio has been shown to be an independent predictor of cardiovascular disease.[46] In the present study, AT and RT men showed a similar insulin to glucose ratio that was lower than that in UT men. After controlling for differences in the sum of nine skinfolds, no differences in the insulin to glucose ratio were found among groups. Our results suggest that even in a healthy, middle-aged, cross-sectional population, an exercise training life-style of either aerobic or resistance training is associated with a more favorable insulin to glucose ratio. These results agree with those of a recent investigation by Smutok et al,[12] who found a marked increase in insulin sensitivity in response to an oral glucose challenge in middle-aged men after 20 weeks of aerobic or resistance training.

In the present study, an index of total body adiposity (ie, percent fat mass, fat mass, and sum of nine skinfolds) was the strongest independent predictor of each cardiovascular risk factor variable examined. This finding suggests that the favorable cardiovascular risk factor profiles observed in the training groups are primarily related to their lower body fat reserves. Thus, it is possible that resistance training, although often not recommended as a therapeutic intervention in cardiovascular risk modification/prevention because it lacks an effect on $\dot{V}O_2$max, may reduce cardiovascular risk through effects on body fat reserves. It is becoming apparent that aerobic exercise may partially influence cardiovascular risk by reducing body fat reserves. Recent evidence[41] has shown that alterations in cardiovascular risk factors (ie, lipoprotein-lipid profile) after aerobic exercise training were more strongly correlated with changes in fat mass than with changes in $\dot{V}O_2$max. However, it is important to note that exercise that induces an increase in $\dot{V}O_2$max may have additional benefits on certain cardiovascular risk factor variables such as plasma triglyceride levels. Collectively, these findings imply that both training regimens are associated with a favorable cardiovascular risk factor profile in non-obese men when accompanied by low body fat reserves.

There are several lines of evidence to suggest that the observed differences in cardiovascular risk factor variables among groups are clinically meaningful. First, evidence from the Framingham population[47] suggests that RT and AT groups have a twofold and eightfold lower incidence rate, respectively, for myocardial infarction as compared with UT individuals, given their lower plasma cholesterol and higher HDL-C levels. Second, both trained groups had a cholesterol level in the range 160 to 199 mg/dL, whereas UT subjects had a cholesterol level greater than 200 mg/dL. A recent review of studies has shown that men with cholesterol levels between 160 and 199 mg/dL showed the lowest total mortality.[48] Third, clinical trials have shown a 2% reduction in risk for coronary heart disease for each 1% reduction in serum cholesterol, and a 2% to 3% increase in risk for coronary heart disease for each 1-mg/dL reduction in HDL-C.[49]

Several caveats should be taken into account when interpreting the results of the present study. First, because of the cross-sectional nature of the study, a causal relationship between aerobic and resistance training and a decreased cardiovascular risk profile cannot be determined. Second, although lower body fat in the trained groups was identified as the major determinant of the more favorable cardiovascular risk profile exhibited in these groups, training-induced fat loss may not be a prerequisite for beneficial changes in risk factors, as several studies have noted.[12,43,44]

Finally, biological variability attributable to genetic influences cannot be ruled out as a factor contributing to variation in RMR and cardiovascular disease risk among the groups, especially in those variables such as plasma cholesterol, LDL-C, and HDL-C, which have been shown to be genotype-dependent.[50] Thus, it is likely that persisting differences among the groups for cardiovascular risk factor variables are attributable to genetic effects.

In conclusion, AT men showed a higher RMR as compared with UT men and a tendency for a higher RMR as compared with RT men. Furthermore, RT and AT middle-aged men have a comparable and favorable cardiovascular risk profile relative to UT men. Our findings suggest that prolonged aerobic or resistance training is associated with a reduction in the clustering of metabolic and cardiovascular risk factors observed in middle-aged UT men.

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