

Effects of Testosterone and Progressive Resistance Training in Eugonadal Men with AIDS Wasting

A Randomized, Controlled Trial

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Background: Substantial loss of muscle mass occurs among men with AIDS wasting.

Objective: To investigate the independent effects of testosterone therapy and progressive resistance training in eugonadal men with AIDS wasting.

Design: Randomized, controlled trial.

Setting: University hospital.

Patients: 54 eugonadal men with AIDS wasting (weight < 90% ideal body weight or weight loss > 10%).

Intervention: In a 2 × 2 factorial design, patients were assigned to receive testosterone enanthate (200 mg/wk) or placebo injections and progressive resistance training (three times weekly) or no training for 12 weeks.

Measurements: Cross-sectional muscle area and other indices of muscle mass.

Results: Cross-sectional muscle area increased in response to training compared with nontraining (change in arm muscle mass,

499 ± 349 mm² vs. 206 ± 264 mm² [*P* = 0.004]; change in leg muscle mass, 1106 ± 854 mm² vs. 523 ± 872 mm² [*P* = 0.045]) and in response to testosterone therapy compared with placebo (change in arm muscle mass, 512 ± 371 mm² vs. 194 ± 215 mm² [*P* < 0.001]; change in leg muscle mass, 1236 ± 881 mm² vs. 399 ± 729 mm² [*P* = 0.002]). Levels of high-density lipoprotein cholesterol decreased in response to testosterone therapy compared with placebo (−0.03 ± 0.13 mmol/L vs. 0.05 ± 0.13 mmol/L [−1 ± 5 mg/dL vs. 2 ± 5 mg/dL]; *P* = 0.011) and increased in response to training compared with nontraining (0.05 ± 0.13 mmol/L vs. 0.00 ± 0.16 mmol/L [2 ± 5 mg/dL vs. 0 ± 6 mg/dL]; *P* = 0.052).

Conclusions: In contrast to anabolic therapies that may have adverse effects on metabolic variables, supervised exercise effectively increases muscle mass and is associated with significant positive health benefits in eugonadal men with AIDS wasting.

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Substantial loss of lean body and muscle mass occur among HIV-infected patients with relatively preserved body weight (1); these changes are associated with reduced functional status and strength (2). Protease inhibitor therapy has not been shown to increase muscle mass in patients with AIDS wasting (3), suggesting the need for successful anabolic strategies in these patients. Testosterone therapy and progressive resistance training increase lean body mass in hypogonadal men with AIDS wasting (4–6). However, most men with AIDS wasting have normal testosterone levels (7). We assessed the independent effects of progressive resistance training and testosterone in eugonadal men with AIDS wasting. Baseline (2) and screening data (7) from a subset of participants were previously reported.

Methods

Patients

From 1997 to 1999, 54 HIV-infected men with AIDS-related wasting (weight < 90% ideal body weight or

self-reported weight loss > 10%) and a normal serum level of free testosterone (>42 pmol/L) were recruited through community advertisements and contact with physicians in the multidisciplinary HIV practice at the Massachusetts General Hospital, Boston, Massachusetts, and other community clinics. Exclusion criteria were new opportunistic infection diagnosed within 6 weeks of the study; other contraindication to exercise; use of a new antiretroviral agent within 8 weeks of the study; abnormal prostate-specific antigen level; symptomatic prostatism; prostate malignancy; bipolar disorder; use of parenteral nutrition, megestrol acetate, glucocorticoids, androgen, estrogen, growth hormone or other anabolic agent within 3 months of the study; hemoglobin value less than 90 g/L or greater than 170 g/L; platelet count less than 50 000 cells/mm³; or serum creatinine concentration greater than 177 μmol/L (2.0 mg/dL). All patients gave written consent, and the study was approved by the Human Studies Committee of the Massachusetts General Hospital.

Protocol

Eligible patients were stratified for weight less than 90% of ideal body weight or 90% or greater than ideal body weight. Using a 2×2 factorial design, we randomly assigned patients to receive intramuscular injections of testosterone enanthate (200 mg/wk; Bio-Technology General Corp., Iselin, New Jersey) or placebo and to progressive resistance training (three times per week) or no training for 12 weeks. The study statistician used a permuted-block algorithm with blocks of 8 to perform randomization; the code was available only to the hospital pharmacy that bottled the study drug. Placebo contained sesame oil with chlorobutanol as a preservative and matched testosterone enanthate in color and consistency. Compliance with drug therapy was confirmed by history, outpatient injection records, and vial counts.

Patients assigned to training participated in supervised progressive strength training and aerobic conditioning three times per week for 12 weeks. During each session, patients began by performing 20 minutes of aerobic exercise on a stationary bicycle at a target heart rate of 60% to 70% of their age-predicted maximum, in accordance with American College of Sports Medicine recommendations (8). A cool-down period of 15 minutes and normalization of heart rate preceded resistance training. Training was performed isotonicly on the following computerized equipment (Life Fitness, Franklin Park, Illinois): leg extension, leg curl, leg press, latissimus dorsi pull-down, arm curl, and triceps extension. A one-repetition maximum weight was established at baseline for each patient on each machine in the best of three efforts. Patients increased resistance as follows: weeks 1 and 2, 2 sets, 8 repetitions/set, 60% one-repetition maximum; weeks 3 through 6, 2 sets, 8 repetitions/set, 70% one-repetition maximum; weeks 7 through 12, 3 sets, 8 repetitions/set, 80% one-repetition maximum. Patients were asked to refrain from exercise for 2 weeks before the baseline visit and to refrain from any exercise or activity beyond normal daily activity during the study. Food intake was ad libitum; caloric intake was determined by using a 4-day food record (Nutrition Data System for Research, version 12A/2.91, Nutrition Coordinating Center, University of Minnesota, Minneapolis, Minnesota). Resting and predicted energy expenditure were calculated (VMAX 29N, SensorMedics, Inc., Loma Linda, California).

Clinical End Points

Clinical end points were assessed at baseline and 12 weeks. Lean body mass and fat mass were measured by

using dual-energy x-ray absorptiometry (QDR-4500 Densitometer, Hologic, Inc., Waltham, Massachusetts) with a precision error of 1.5% for fat-free mass (9). Cross-sectional muscle areas of the leg and arm were assessed by performing computed tomography of the midfemur and humerus (General Electric High Speed Helical CAT Scanner, Milwaukee, Wisconsin; SE $\pm 3\%$ for arm muscle area and $\pm 1\%$ for leg muscle area). The location of the midfemur and humerus were determined from the scout image. Upper- and lower-extremity muscle strength were measured by using the quantitative muscle function test (10, 11). Peak isometric force of shoulder flexion, shoulder extension, elbow flexion, elbow extension, knee flexion, knee extension, dorsiflexion, and grip were measured on the best of two repetitions (10, 12). *Z* scores were calculated for upper- and lower-extremity strength (MVCT Computer Analysis Software, Boston, Massachusetts) by standardizing to a group of healthy male controls (11, 12). Serum levels of total and free testosterone were measured by using a radioimmunoassay kit (Diagnostics Products Corp., Los Angeles, California) (4). CD4 cell counts were measured by using flow cytometry (Becton-Dickinson Immunocytometry Systems, San Jose, California); viral load was measured by using the Amplicor HIV-1 Monitor (Roche Molecular Systems, Branchburg, New Jersey). Other tests were done according to published methods (13). A digital prostate examination was performed at each visit.

Statistical Analysis

The effects of training and testosterone were simultaneously assessed in the same factorial model. In the primary analysis, we used analysis of covariance to assess change from baseline at 3 months simultaneously in the testosterone arm (testosterone recipients vs. placebo recipients) and the training arm (trained patients vs. nontrained patients), controlling for baseline values. To test for an interaction between testosterone and training, we used analysis of covariance with an interaction term. Change in lean body mass was the primary clinical end point for the effect of testosterone, and change in cross-sectional muscle area was the primary end point for the effect of resistance training. Change from baseline was also determined within each individual treatment group and was compared with zero change by using analysis of covariance. The *t*-test was used to compare treatment groups at baseline. All available data are included in the analysis. Results are reported as the mean \pm SD.

Table 1. Results of Factorial Analysis*

Variable	Testosterone Comparison				P Value†
	Placebo-Treated Patients		Testosterone-Treated Patients		
	Baseline (n = 26)‡	Change (n = 22)§	Baseline (n = 24)‡	Change (n = 21)§	
Body composition					
Weight, kg	69.5 ± 9.3	0.4 ± 3.0	66.8 ± 8.4	2.6 ± 2.5	0.024
Lean body mass, kg	53.0 ± 6.5	1.0 ± 2.7	51.6 ± 6.9	4.4 ± 2.2	<0.001
Fat mass, kg	12.7 ± 4.8	-0.8 ± 2.6	11.8 ± 3.6	-2.4 ± 2.3	0.005
Arm muscle area, mm ²	4289 ± 890	194 ± 215	4018 ± 756	512 ± 371	<0.001
Leg muscle area, mm ²	13 464 ± 2062	399 ± 729	13 438 ± 2170	1236 ± 881	0.002
Muscle strength					
Shoulder extension, kg	24.9 ± 6.9	1.8 ± 3.5	23.7 ± 6.4	5.3 ± 5.9	0.033
Elbow flexion, kg	19.1 ± 4.0	0.8 ± 3.3	18.2 ± 3.5	3.9 ± 4.1	0.014
Knee flexion, kg	18.4 ± 4.3	0.2 ± 4.4	17.0 ± 5.2	2.6 ± 4.7	0.121
Knee extension, kg	35.0 ± 8.5	0.3 ± 8.1	31.1 ± 8.4	3.6 ± 7.6	>0.2
Dorsiflexion, kg	19.7 ± 4.0	0.8 ± 4.6	20.5 ± 4.4	2.9 ± 4.7	0.1
Upper-extremity Z score	-1.1 ± 0.8	0.3 ± 0.5	-1.3 ± 0.9	0.8 ± 0.7	0.031
Lower-extremity Z score	-1.2 ± 0.6	0.1 ± 0.6	-1.3 ± 0.7	0.4 ± 0.7	0.183
Hormone and lipid levels					
Total testosterone, nmol/L (ng/dL)	23.0 ± 7.3 (662 ± 210)	1.6 ± 7.1 (46 ± 206)	22.5 ± 5.7 (648 ± 163)	14.7 ± 12.0 (424 ± 345)	<0.001
Free testosterone, pmol/L (pg/mL)	76 ± 21 (21.8 ± 6.1)	0 ± 23 (0.0 ± 6.6)	81 ± 26 (23.3 ± 7.6)	66 ± 53 (19.1 ± 15.2)	<0.001
Luteinizing hormone, IU/L	6.5 ± 4.8	0.3 ± 2.2	9.0 ± 8.0	-6.5 ± 3.0	<0.001
Follicle-stimulating hormone, IU/L	7.4 ± 5.3	0.0 ± 1.7	7.6 ± 6.0	-6.5 ± 5.3	<0.001
Sex hormone-binding globulin, nmol/L	40.0 ± 18.6	0.0 ± 9.3	40.4 ± 20.2	-11.8 ± 9.6	<0.001
Total cholesterol, mmol/L (mg/dL)	4.53 ± 1.32 (175 ± 51)	0.10 ± 0.78 (4 ± 30)	4.65 ± 1.50 (180 ± 58)	-0.34 ± 0.80 (-13 ± 31)	0.051
LDL cholesterol, mmol/L (mg/dL)	2.79 ± 1.01 (108 ± 39)	-0.10 ± 0.54 (-4 ± 21)	2.64 ± 1.29 (102 ± 50)	-0.26 ± 0.57 (-10 ± 22)	>0.2
Triglycerides, mmol/L (mg/dL)	2.16 ± 1.93 (191 ± 171)	0.56 ± 1.74 (50 ± 154)	2.60 ± 2.22 (230 ± 197)	-0.06 ± 1.59 (-5 ± 141)	0.178
HDL cholesterol, mmol/L (mg/dL)	0.93 ± 0.36 (36 ± 14)	0.05 ± 0.13 (2 ± 5)	0.88 ± 0.28 (34 ± 11)	-0.03 ± 0.13 (-1 ± 5)	0.011
Safety					
AST level, μ kat/L	1.15 ± 1.78	-0.33 ± 1.35	0.88 ± 0.88	0.05 ± 0.58	0.193
Hematocrit, %	39.8 ± 3.7	1.1 ± 2.9	40.1 ± 4.7	2.4 ± 3.4	0.088
Prostate-specific antigen level, pmol/L	23.5 ± 11.8	2.9 ± 14.7	23.5 ± 11.8	5.9 ± 8.8	>0.2
Immune function					
CD4 count, cells/mm ³	313 ± 242	32 ± 90	430 ± 296	-10 ± 142	>0.2
Viral load, log ₁₀ copies	4.7 ± 5.0	3.7 ± 4.8	4.6 ± 5.0	-4.0 ± 4.8	0.041

* Values are the mean ± SD. AST = aspartate aminotransferase; HDL = high-density lipoprotein; LDL = low-density lipoprotein.

† For comparison of treatment groups (testosterone-treated vs. placebo-treated and training vs. no training) by analysis of covariance.

‡ All patients for whom baseline data were available.

§ All patients for whom paired baseline and end-of-study data were available.

Results

No patient withdrew from the study because of an adverse event or side effect; dropout rates did not differ by group (Appendix Figure). Patients had lost significant weight but were not severely ill or low weight at study entry (Table 1). Seventy-six percent of patients were receiving antiretroviral therapy and 72% were receiving highly active antiretroviral therapy. Seventy-six percent of patients had previously had an opportunistic infection.

Changes in response to testosterone therapy and training are shown in Table 1. Lean body mass and muscle area increased significantly in response to training and testosterone therapy. Muscle strength on elbow flexion and shoulder extension and overall upper-extremity Z score increased in response to testosterone therapy. The change in muscle

area correlated with the change in muscle strength ($R = 0.48$; $P = 0.001$ for mid-thigh muscle area and strength on knee extension). No interaction was found between testosterone therapy and training.

Levels of high-density lipoprotein (HDL) cholesterol increased in response to training but decreased in response to testosterone therapy. Levels of total and free testosterone increased in response to testosterone therapy, and levels of gonadotropin and sex hormone-binding globulin decreased. Caloric intake did not change significantly between the groups. The CD4 count did not change significantly in response to training or testosterone therapy ($P > 0.2$). Viral load decreased in testosterone-treated patients. Use of antiretroviral therapy did not change in any study group.

Table 1—Continued

Training Comparison				
Patients Who Had No Training		Patients Who Had Training		P Value†
Baseline (n = 24)‡	Change (n = 22)§	Baseline (n = 26)‡	Change (n = 21)§	
68.2 ± 8.3	0.9 ± 3.0	68.2 ± 9.5	2.1 ± 2.8	>0.2
52.3 ± 6.6	1.9 ± 3.3	52.4 ± 6.9	3.5 ± 2.4	0.052
12.2 ± 3.8	-1.1 ± 2.6	12.3 ± 4.7	-2.1 ± 2.6	>0.2
4017 ± 802	206 ± 264	4290 ± 852	499 ± 349	0.004
13 085 ± 2043	523 ± 872	13 790 ± 2121	1106 ± 854	0.045
23.3 ± 6.5	3.0 ± 5.5	25.2 ± 6.8	4.0 ± 4.6	>0.2
18.5 ± 4.0	1.7 ± 3.9	18.9 ± 3.6	2.9 ± 4.0	>0.2
17.5 ± 5.1	0.74 ± 4.6	17.9 ± 4.5	2.0 ± 4.8	>0.2
31.3 ± 8.4	1.7 ± 8.4	34.7 ± 8.6	2.2 ± 7.6	>0.2
20.4 ± 3.6	1.1 ± 4.1	19.7 ± 4.8	2.6 ± 5.2	>0.2
-1.3 ± 0.9	0.5 ± 0.7	-1.1 ± 0.8	0.6 ± 0.6	>0.2
-1.3 ± 0.6	0.2 ± 0.6	-1.2 ± 0.7	0.4 ± 0.7	>0.2
22.7 ± 7.4 (655 ± 213)	5.6 ± 9.7 (161 ± 280)	22.7 ± 5.7 (656 ± 165)	10.5 ± 13.3 (303 ± 384)	0.16
75 ± 21 (21.5 ± 6.2)	26 ± 40 (7.4 ± 11.4)	81 ± 25 (23.4 ± 7.3)	40 ± 63 (11.4 ± 18.1)	0.132
8.3 ± 8.1	-2.2 ± 4.1	7.2 ± 4.7	-3.9 ± 4.3	0.088
6.6 ± 4.7	-2.2 ± 3.5	8.3 ± 6.3	-4.2 ± 6.2	>0.2
43.6 ± 21.0	-7.8 ± 11.2	37.2 ± 17.3	-3.6 ± 10.9	0.134
4.40 ± 1.50 (170 ± 58)	-0.16 ± 0.91 (-6 ± 35)	4.78 ± 1.29 (185 ± 50)	-0.05 ± 0.72 (-2 ± 28)	>0.2
2.51 ± 1.22 (97 ± 47)	-0.08 ± 0.57 (-3 ± 22)	2.90 ± 1.06 (112 ± 41)	-0.26 ± 0.52 (-10 ± 20)	>0.2
2.70 ± 1.99 (239 ± 176)	0.24 ± 1.84 (21 ± 163)	2.07 ± 2.13 (183 ± 189)	0.29 ± 1.54 (26 ± 136)	>0.2
0.83 ± 0.26 (32 ± 10)	0.00 ± 0.16 (0 ± 6)	0.98 ± 0.36 (38 ± 14)	0.05 ± 0.13 (2 ± 5)	0.052
0.93 ± 0.90	-0.10 ± 0.38	1.08 ± 1.78	-0.22 ± 1.47	>0.2
38.3 ± 4.6	2.4 ± 2.2	41.5 ± 3.1	1.0 ± 3.9	>0.2
23.5 ± 11.8	2.9 ± 14.7	23.5 ± 11.8	5.9 ± 8.8	>0.2
366 ± 287	21 ± 53	372 ± 264	1 ± 162	>0.2
4.6 ± 5.0	2.8 ± 4.7	4.7 ± 5.0	-3.7 ± 4.8	>0.2

Levels of aspartate aminotransferase or prostate-specific antigen did not change significantly ($P > 0.2$). No patient developed new prostate nodules. Three patients developed breast tenderness or gynecomastia (two were receiving testosterone and one was receiving placebo). Compliance with the training program was 78% among patients who completed the study; compliance with testosterone therapy was 98%.

Discussion

Previous studies suggest that testosterone therapy, alone (4, 5) and in combination with resistance training, increases lean body mass in hypogonadal men with AIDS wasting (6). However, recent data indicate that androgen levels are normal in most HIV-infected men (7), and the independent effects of testosterone and supervised exercise

in eugonadal men with AIDS wasting are not known. The patients in our study generally had normal body weight and a normal Karnofsky score but had lost substantial weight. Most patients had a history of opportunistic infection, and although they were not cachectic or malnourished, they had reduced muscle mass (2).

Previous studies have shown that resistance training in combination with testosterone or anabolic steroid therapy increases lean body mass (6, 14, 15). In contrast, we found that training had a significant effect (increase of 2.3 kg) on lean body mass ($P = 0.05$) and muscle area ($P < 0.05$), independent of testosterone administration. The increase in lean body mass in response to exercise alone is equivalent to the effects of lower doses of testosterone (4, 6) and those of anabolic steroids (16, 17). We used a reproduc-

Table 2. Baseline and Change from Baseline in Individual Treatment Groups*

Variable	Placebo and No Training		Placebo and Training	
	Baseline (n = 13)†	Change (n = 12)‡	Baseline (n = 13)†	Change (n = 10)‡
Body composition				
Weight, kg	70.1 ± 8.7	−0.6 ± 2.5	69.0 ± 10.2	1.7 ± 3.2
Lean body mass, kg	53.7 ± 6.2	0.0 ± 2.7	52.3 ± 7.0	2.3 ± 2.2§
Fat mass, kg	12.6 ± 4.1	−0.5 ± 2.5	12.8 ± 5.7	−1.3 ± 2.8
Arm muscle area, mm ²	4152 ± 807	66 ± 179	4427 ± 979	346 ± 147
Leg muscle area, mm ²	13 366 ± 2158	68 ± 634	13 562 ± 2046	797 ± 654§
Muscle strength				
Shoulder extension, kg	25.1 ± 6.9	0.6 ± 2.8	24.7 ± 7.2	3.3 ± 3.9
Elbow flexion, kg	18.6 ± 4.2	0.7 ± 3.6	19.6 ± 3.8	0.9 ± 3.1
Knee flexion, kg	18.1 ± 5.3	−0.4 ± 4.8	18.6 ± 3.3	0.8 ± 4.1
Knee extension, kg	33.7 ± 8.7	0.7 ± 9.2	36.1 ± 8.5	0.0 ± 7.0
Dorsiflexion, kg	20.3 ± 4.2	0.5 ± 4.8	19.2 ± 4.0	1.3 ± 4.5
Upper-extremity Z score	−1.2 ± 0.9	0.3 ± 0.6	−0.9 ± 0.8	0.3 ± 0.5
Lower-extremity Z score	−1.2 ± 0.6	0.0 ± 0.6	−1.2 ± 0.5	0.2 ± 0.5
Hormone and lipid levels				
Total testosterone, nmol/L (mg/dL)	22.8 ± 8.2 (658 ± 237)	1.7 ± 6.3 (49 ± 183)	23.1 ± 6.6 (665 ± 189)	1.5 ± 8.3 (42 ± 240)
Free testosterone, pmol/L (pg/mL)	73 ± 19 (21.0 ± 5.6)	6 ± 18 (1.6 ± 5.1)	78 ± 23 (22.5 ± 6.7)	−7 ± 27 (−1.9 ± 7.9)
Luteinizing hormone, IU/L	5.7 ± 2.9	0.9 ± 1.9	7.3 ± 6.1	−0.5 ± 2.4
Follicle-stimulating hormone, IU/L	6.1 ± 3.4	0.1 ± 1.7	8.8 ± 6.6	−0.1 ± 1.8
Sex hormone-binding globulin, nmol/L	40.9 ± 18.4	−2.7 ± 10.3	39.2 ± 19.5	3.3 ± 7.2
Total cholesterol, mmol/L (mg/dL)	4.47 ± 1.40 (173 ± 54)	0.13 ± 0.78 (5 ± 30)	4.55 ± 1.29 (176 ± 50)	0.08 ± 0.83 (3 ± 32)
LDL cholesterol, mmol/L (mg/dL)	2.97 ± 1.24 (115 ± 48)	−0.08 ± 0.62 (−3 ± 24)	2.64 ± 0.72 (102 ± 28)	−0.10 ± 0.49 (−4 ± 19)
Triglycerides, mmol/L (mg/dL)	2.53 ± 1.67 (224 ± 148)	0.54 ± 1.47 (48 ± 130)	1.77 ± 2.17 (157 ± 192)	0.60 ± 2.09 (53 ± 185)
HDL cholesterol, mmol/L (mg/dL)	0.75 ± 0.28 (29 ± 11)	0.05 ± 0.16 (2 ± 6)	1.09 ± 0.39 (42 ± 15)	0.08 ± 0.16 (3 ± 6)§
Safety				
AST level, μ kat/L	0.90 ± 0.80	−0.12 ± 0.32	1.40 ± 2.40	−0.62 ± 2.00¶
Hematocrit, %	38.2 ± 3.7	2.2 ± 1.8	41.4 ± 3.1	−0.3 ± 3.4
Prostate-specific antigen level, pmol/L	26.5 ± 11.8	2.9 ± 17.6	20.6 ± 5.9	5.9 ± 8.8
Immune function				
CD4 count, cells/mm ³	308 ± 280	33 ± 50	318 ± 207	31 ± 125
Viral load, log ₁₀ copies	4.8 ± 5.1	3.1 ± 4.9	4.6 ± 4.8	4.0 ± 4.6

* Values are the mean ± SD. AST = aspartate aminotransferase; HDL = high-density lipoprotein; LDL = low-density lipoprotein.

† All patients for whom baseline data were available.

‡ All patients for whom paired baseline and end-of-study data were available.

§ $P < 0.01$ compared with baseline value.

|| $P < 0.001$ compared with baseline value.

¶ $P < 0.05$ compared with baseline value.

ible, standardized training program that can be implemented in most community-based gyms.

Strength as assessed by isometric testing did not respond significantly to exercise ($P > 0.2$). However, isometric testing may underestimate changes in strength compared with assessment of serial one-repetition maximum weight in patients undergoing isotonic training (18). Patients undergoing resistance training doubled their training volume in 12 weeks, indicating adaptation to an increasing training regimen and increased strength (19).

We also found that administration of testosterone, 200 mg/wk, significantly increased lean body mass, muscle area, and muscle strength. Lean body mass increased 4.2 kg in response to testosterone therapy without resistance training. In contrast, Bhasin and colleagues (6) observed a

2.3-kg increase in lean body mass in hypogonadal men with AIDS wasting who received 100 mg of testosterone per week. Our data suggest that muscle mass and strength may further increase in response to combined testosterone therapy and training (Table 2), but the study was not designed to compare changes in the combined treatment groups with those in the individual treatment groups.

Resistance training was associated with a significant increase in HDL cholesterol level. In contrast, testosterone administration decreased HDL cholesterol level. Concern exists over the development of abnormal lipid profiles in patients recovering from wasting (20); the increased HDL cholesterol level resulting from training may benefit such patients. Progressive resistance training is therefore unique among strategies to increase lean body mass in that it is

Table 2—Continued

Testosterone and No Training		Testosterone and Training	
Baseline (n = 11)†	Change (n = 10)‡	Baseline (n = 13)†	Change (n = 11)‡
66.0 ± 7.6	2.7 ± 2.6§	67.4 ± 9.2	2.5 ± 2.5§
50.6 ± 6.8	4.2 ± 2.3	52.5 ± 7.1	4.6 ± 2.1
11.8 ± 3.7	-2.0 ± 2.5§	11.7 ± 3.7	-2.9 ± 2.1
3858 ± 804	374 ± 258	4154 ± 717	638 ± 424
12 751 ± 1947	1069 ± 821	14 018 ± 2252	1388 ± 945
21.3 ± 5.7	5.9 ± 6.6§	25.8 ± 6.5	4.7 ± 5.3§
18.4 ± 4.0	3.0 ± 4.1¶	18.0 ± 3.3	4.7 ± 4.0
16.8 ± 5.1	2.1 ± 4.2	17.2 ± 5.6	3.1 ± 5.3
28.7 ± 7.6	3.0 ± 7.7	33.3 ± 8.8	4.2 ± 7.8
20.6 ± 3.0	1.8 ± 3.2	20.3 ± 5.6	3.8 ± 5.7¶
-1.4 ± 0.9	0.7 ± 0.9§	-1.2 ± 0.9	0.8 ± 0.6
-1.4 ± 0.5	0.3 ± 0.5	-1.2 ± 0.8	0.5 ± 0.8¶
22.6 ± 6.7 (651 ± 192)	10.2 ± 11.2 (295 ± 324)	22.4 ± 5.0 (646 ± 143)	18.8 ± 11.6 (541 ± 335)
76 ± 25 (22.0 ± 7.2)	50 ± 46 (14.3 ± 13.2)	84 ± 28 (24.3 ± 8.0)	81 ± 56 (23.5 ± 16.1)
11.4 ± 11.1	-5.8 ± 2.8	7.0 ± 3.0	-7.1 ± 3.1
7.2 ± 6.1	-5.0 ± 3.0	7.8 ± 6.2	-7.9 ± 6.6
46.5 ± 24.0	-14.0 ± 9.2	35.2 ± 15.4	-9.8 ± 9.9
4.29 ± 1.68 (166 ± 65)	-0.52 ± 0.96 (-20 ± 37)¶	4.99 ± 1.29 (193 ± 50)	-0.18 ± 0.62 (-7 ± 24)
1.86 ± 0.83 (72 ± 32)	-0.08 ± 0.54 (-3 ± 21)	3.21 ± 1.32 (124 ± 51)	-0.44 ± 0.57 (-17 ± 22)
2.89 ± 2.37 (256 ± 210)	-0.12 ± 2.24 (-11 ± 198)	2.35 ± 2.15 (208 ± 190)	0.01 ± 0.78 (1 ± 69)
0.88 ± 0.21 (34 ± 8)	-0.08 ± 0.16 (-3 ± 6)	0.88 ± 0.34 (34 ± 13)	0.03 ± 0.10 (1 ± 4)
1.00 ± 1.05	-0.07 ± 0.48	0.78 ± 0.75	0.15 ± 0.67
38.4 ± 5.7	2.7 ± 2.7¶	41.5 ± 3.1	2.3 ± 4.1§
20.6 ± 8.8	2.9 ± 8.8	26.5 ± 14.7	5.9 ± 11.8
434 ± 292	8 ± 56	426 ± 310	-27 ± 192
3.0 ± 3.3	1.8 ± 2.6	4.8 ± 5.2	-4.3 ± 4.9

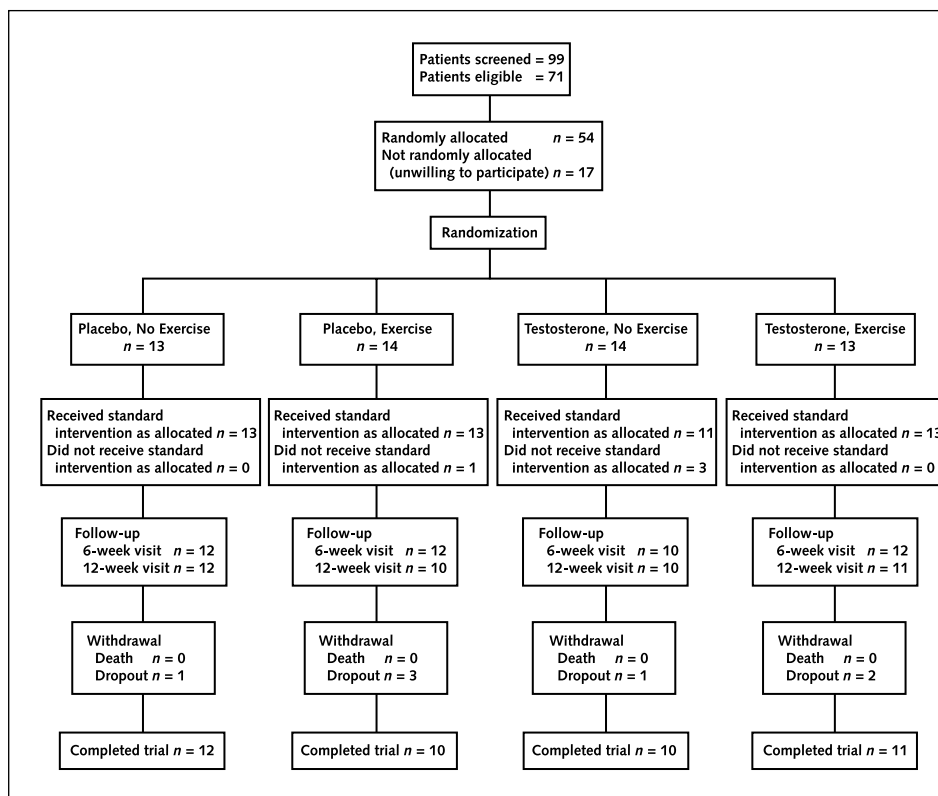
associated with a cardioprotective effect. Conversely, dyslipidemia is commonly seen in HIV-infected patients, particularly in those with the HIV lipodystrophy syndrome; the reduction in HDL cholesterol level produced by testosterone therapy may be detrimental in such patients.

The dose of testosterone used in our study (200 mg/wk) is twice the physiologic replacement dose and was associated with decreased levels of gonadotropin and sex hormone-binding globulin. Breast tenderness and gynecomastia occurred in two testosterone-treated patients. Adverse effects on prostate hypertrophy, acne, mood swings and polycythemia were not observed. However, the study was short, and it is unknown whether similar doses of testosterone would be well tolerated over a longer period. Long-term high-dose testosterone treatment of HIV-in-

fectured men cannot be endorsed until further data on safety become available.

Limited therapies exist for the AIDS wasting syndrome. In the era of highly active antiviral therapy, patients with wasting are most often eugonadal and have substantial muscle loss and muscle dysfunction, but they are generally stable and free of opportunistic infection. Although short-term administration of testosterone increases muscle mass, it may be associated with adverse metabolic effects in these patients. In contrast, our data suggest that supervised exercise training significantly increases muscle mass and offers cardioprotective effects by increasing the HDL cholesterol level in eugonadal men with AIDS wasting. Exercise may therefore be an ideal strategy to reverse muscle loss in these patients.

Appendix Figure. Flow of participants through the study.



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