Effect of resistance training on self-reported physical functioning in HIV infection

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ABSTRACT

ROUBENOFF, R., and I. B. WILSON. Effect of resistance training on self-reported physical functioning in HIV infection. *Med. Sci. Sports Exerc.*, Vol. 33, No. 11, 2001, pp. 1811–1817. **Purpose:** To assess whether progressive resistance training (PRT) improves functional status, measured using a validated Physical Function Scale, in both wasted and nonwasted patients with HIV infection, and to compare the relative contributions of increased lean body mass (LBM) and increased strength with the change in physical function. **Methods:** Six patients with AIDS wasting and 19 patients with HIV but without wasting trained three times per week for 8 wk, followed by 8 wk of usual activity. Physical function, strength, and LBM were measured at 0, 8, and 16 wk. Self-reported physical functioning was measured using the physical functioning subscale of the Medical Outcomes Study (MOS) Short Form-36 (SF-36) questionnaire. **Results:** Significant improvements occurred in strength (1-RM averaged for four machines increased 44% in the nonwasted and 60% in the wasted patients, each $P < 0.0001$) and LBM (2.3% increase in the nonwasted and 5.3% in the wasted patients, each $P < 0.05$) with resistance training. Physical function increased significantly in the wasted subjects (6 points, $P < 0.02$) but not in the nonwasted subjects, so that at 16 wk the wasted subjects functioned at a higher level than the nonwasted patients ($P < 0.05$). Both increase in LBM ($P < 0.001$) and increase in strength ($P < 0.001$) were significantly and independently associated with increase in physical function. **Conclusion:** PRT increases functional status in patients with HIV wasting, both by increasing strength and by increasing LBM. **Key Words:** AIDS WASTING, STRENGTH, BODY COMPOSITION, LEAN BODY MASS

Weight loss in persons with HIV infection is an important predictor of mortality (12,14,16,21,33). Wasting, defined as unintentional loss of 10% or more of usual body weight (4), occurred in 10–20% of patients with AIDS in the United States before the advent of highly active antiretroviral therapy (HAART) and remains almost universal in patients with AIDS in the developing world. Wasting is one of only three serious sequelae of HIV infection that have not rapidly declined since the HAART became widely available (19). Recently, recognition of wasting has been broadened as data have accumulated showing that even 5% weight loss or a body mass index (BMI) < 20 kg·m^{-2} is associated with worse prognosis and increased mortality in HIV infection (21,22). Based on a definition of 10% weight loss at any time, 5% weight loss over 6 months, or BMI < 20 kg·m^{-2}, Wanke et al. (30) found a prevalence of 32% for wasting in a Boston cohort of men and women with HIV infection even during the HAART era (1995–1999). Thus, wasting remains a serious problem in HIV infection.

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Short of death, wasting is also associated with poor physical functioning in observational studies (34,35). It is presumed that the association between physical function and weight loss is driven by the decline in lean body mass (LBM), and specifically muscle mass, that occurs with wasting. A recent report shows that cross-sectional muscle area is associated with function (Karnovsky scores) and muscle strength in men with wasting (5). Although some clinical trials of pharmacological agents used to treat wasting have demonstrated small gains in lean body mass (LBM) (5,9,10,18,27,29,32), these gains have not been consistently associated with improved functioning. However, to date, no trials of the effect of exercise on physical function have been reported in patients with HIV infection.

We have recently shown that progressive resistance training (PRT) can substantially increase strength and LBM in adults with HIV infection, with a greater effect in wasted subjects than in those without wasting (24). We also showed that one bout of acute exercise was safe and did not increase circulating HIV RNA levels (26). We now examine the effect of PRT on functional status in patients with and without wasting who completed an 8-wk supervised strength training program followed by an additional 8 wk of observation during usual activity. Results of the study intervention in terms of change in body composition and strength have been reported elsewhere (24), but to our knowledge this is the first report of the effect of increasing strength and LBM on functional status in patients with HIV infection, with and without wasting.

METHODS

Patient population. Six men with AIDS wasting (defined as body mass index < 20 kg·m^{-2} or an unintentional weight loss of 10% or more of usual weight over the previous year (20), and 19 control men and women with HIV infection but without wasting were recruited for this study. All subjects were also participants in the Tufts Nutrition for Healthy Living cohort, an ongoing study of over 700 men and women with HIV infection (as of January 2000) who are being followed at 6-month intervals for assessment of the effect of nutritional status on HIV disease progression. Inclusion criteria were interest in the study and ability to give informed consent. Written informed consent was obtained from all participants, using a consent form approved by the Human Investigations Review Committee of Tufts University/New England Medical Center. Exclusion criteria included participation in resistance training over the 6 months preceding study entry, a contraindication to progressive resistance exercise (myocardial infarction within 6 months, unstable angina, uncontrolled congestive heart failure, or uncontrolled hypertension), diabetes mellitus (an exclusion from the main cohort), renal insufficiency (serum creatinine > 2.0 mg·dL^{-1}), hepatic disease (AST or ALT > 5 times the upper limit of normal, total bilirubin $>$ 2.0 mg·dL^{-1}), muscle disease (creatine kinase > 500 IU/mL), and arthritis or low back pain limiting activities of daily living. Because PRT has been shown to be useful in some or all of these conditions, we excluded them in order to study patients with HIV infection alone. Patients taking anabolic therapy (growth hormone, androgens, or megestrol acetate) were also excluded.

Body composition and nutritional assessment. Subjects were evaluated in the General Clinical Research Center (GCRC) at New England Medical Center. Lean body mass (fat-free, mineral-free mass), bone mineral content (BMC), and fat mass were estimated by dual energy x-ray absorptiometry of the whole body using a Hologic QDR 2000 instrument (Waltham, MA) operating in the array mode. Scans were performed at baseline, week 8, and week 16 of the study. Body composition data at week 16 were unavailable in four nonwasted subjects because of technical problems with the scanner, but strength changes at 8 and 16 wk, and body composition changes at 8 wk, were not different in these subjects from the rest of the volunteers. We have previously demonstrated that this method gives estimates of fat and fat-free mass that are very close to that obtained with *in vivo* neutron activation analysis, with a correlation of $r = 0.87$ and a mean difference of < 0.5 kg (25). The coefficient of variation for five healthy persons measured twice over 2 d was 0.4% of total lean body mass and 1.4% for fat mass (6). Dietary intake was measured using 3-d food records and averaged 2590 $\pm$ 723 kcal·d^{-1} and 97.3 $\pm$ 34.7 g protein·d^{-1} in the entire group at baseline, as previously reported (25). There were no differences between the wasted and nonwasted patients in dietary energy or protein intake and no significant changes in intake over the 16 wk of the study (25).

Progressive resistance training (PRT) period. Each participant trained three times per week for 8 wk using Keiser pneumatic resistance equipment (Keiser Sports Health Equipment Inc., Fresno, CA). The double leg press, leg (quadriceps) extension, seated chest press, and seated row machines were used in order to focus on large muscle groups that have an effect both on whole-body composition and on function. One subject (without wasting) had moderate chronic low back pain and did not perform the leg press or quadriceps extension exercises in most of his sessions. Baseline strength was assessed using the 1-repetition maximum (1-RM) test, determined for each of the four exercise machines twice at baseline to account for learning effects and repeated every 2 wk. Participants trained at 50% of their 1-RM for the first session, 60% for the second session, and at 75–80% of their 1-RM for the remainder of the sessions. They performed three sets of eight repetitions on each machine, working with an exercise physiologist on a one-to-one basis or in small groups (2–3 volunteers at a time). They were asked to rate the difficulty of each exercise at the end of each set by using a Borg Relative Perceived Effort Scale (3), and if the RPE was less than 16 out of a possible 20, the resistance was increased by 1–2 pounds without waiting for the next scheduled 1-RM test. After each 1-RM test, the level of resistance was reset to 80% of the new (and higher) 1-RM, so that the training remained intensive and progressive during the entire 8-wk program.

Usual activity phase. After the initial 8-wk period, subjects were again evaluated in the GCRC as described above. Upon completing this evaluation, they were asked to return to their usual activity pattern. Because we did not think it ethical to discourage subjects who wished to continue to exercise from doing so, we did not discourage this but asked all subjects to keep logs of their activity as a tool to improve compliance and retention within the study. The goal of this phase was to examine the change in strength and body composition during a period of time without investigator-initiated intervention. Therefore, during this phase subjects were not trained at our center, nor were they in contact with their trainers from the first phase. At the end of 8 wk, they were again invited to the GCRC for evaluation.

Self-reported functional status assessment. Physical functioning was assessed at baseline, week 8, and week 16, using the physical functioning subscale of the Medical Outcomes Study (MOS) Short Form-36 (SF-36) questionnaire (31). The SF-36 has undergone extensive psychometric testing. This includes assessment of reliability, including test-retest, alternative form, and internal consistency reliability of the physical functioning subscale. These reliabilities range from 0.81 to 0.94 (17,31). A study coordinator administered all questionnaires to the subjects. Subjects were asked whether their health limited their ability to perform vigorous and moderate activities (with examples);

lift and carry groceries; climb stairs (one flight and several flights); bend, kneel, or stoop; walk more than a mile and more than a block; and bathe and dress. In these items, available answers were "yes, limited a lot"; "yes, limited a little"; or "no, not limited at all." The four-item role-physical subscale from the MOS-36 was used to assess role limitation due to physical problems. Role functioning refers to the degree to which an individual performs or has the capacity to perform activities typical for a specified age and social responsibility. Respondents are asked to attribute the limitations in role function either physical or mental problems. Items asked whether over the previous 4 wk patients' health had caused them to cut down on the amount of time spent on work or other activities; to accomplish less than they would like; to limit the kind of work or other activities they performed; and to have difficulty performing work or other activity. For each of these four items, the possible answers were "yes" or "no."

Statistical analysis. The primary outcome of the study was change in LBM $\geq 2\%$, as previously reported (25), and the study was powered for this outcome at an $\alpha = 0.05$ and $= 0.2$. Prestudy power calculations indicated that a sample size of 20 persons would be adequate to detect such a change; 25 patients were recruited to allow for dropouts. The outcome of the present secondary analysis was change in physical function score at the end of 16 wk of the study, based on the expectation that there may be a lag time between the end of the thrice-weekly exercise intervention (8 wk) and the time of significant functional benefit, as has been noted by others (28). All data were examined for normality graphically and statistically. The physical function results were checked, scored as described in the SF-36 user's manual (31) to give a number between 0 and 100, and the data were entered into a computer file for analysis. This analysis was performed using a *t*-test on the change in score, first using the whole study group compared with no change, and then comparing wasted and nonwasted subjects. Secondary analyses of the change at 8 wk and the change in role-physical score were performed using *t*-tests or Wilcoxon tests, as appropriate. The relationship between change in lean mass or strength and change in physical function score was examined using linear regression. In the model, the changes in lean mass and strength were expressed as % to keep them on a similar scale; additional analyses using the raw data showed similar results. One subject was an outlier (change in functional score > 4 SD below the mean in an obese patient who lost >5 kg during the study period and was later found to be dieting as well as exercising) and was excluded. Differences between groups were considered statistically significant if the two-tailed *P*-value was less than 0.05.

RESULTS

Study population. Six men with wasting and 19 men and women without wasting completed the 8 wk of PRT. Their mean age was 39 (range 25–56 yr) and a mean BMI was 21.5 kg·m^{-2} in the wasted group and 27.0 kg·m^{-2} in the nonwasted group ($P < 0.01$, see Table 1). The wasted patients had significantly less fat mass than the nonwasted subjects (13.0 kg vs 24.7 kg, $P < 0.05$) and showed a trend toward lower lean body mass index (16.7 vs 18.1 kg LBM·m^{-2}, $P < 0.2$). The wasted patients also had lower CD4 cell counts than the nonwasted patients, but there was no significant difference in their circulating HIV RNA levels. Among the patients with wasting, all six completed the entire 16-wk study. Among the 19 nonwasted patients, 18 (95%) completed the first 8-wk phase, and 15 (79%) completed the second 8-wk phase. Adherence with the exercise regimen was excellent, with all 24 participants who completed phase one having a 90% or better attendance rate. The response to exercise in the dropouts was not significantly different from those who continued the study in terms of strength change or change in body composition. Two of the wasted patients and seven of the nonwasted patients reported going to a health club at least once a week during weeks 8–16 of the study (25). Results of the study in terms of improvement in strength and body composition have been published elsewhere and are recapitulated in Table 2 (24). For all 24 participants, the mean increase in strength over 16 wk, averaged over the four exercises, was 48.6 ± 8.7% (mean ± SE). The increase in LBM over this period was 2.5 ± 0.8%. The wasting group increased their LBM more than the nonwasted patients (2.8 vs 1.4 kg, $P < 0.05$) and gained more weight (+3.9 vs −0.2 kg, $P < 0.002$) and fat mass (+ 0.95 kg vs −1.5 kg, $P < 0.002$) at 8 wk, which persisted at 16 wk (weight: + 4.0 vs −1.6 kg, $P < 0.0002$; fat: +1.6 vs −1.9 kg, $P < 0.01$; LBM: 2.4 vs 1.1 kg, $P < 0.09$).

TABLE 1. Demographic and clinical characteristics of the study population at baseline.

Parameter	Wasting	Nonwasting
Male:female	6:0	14:5
Age	39.1 (6.2)	38.8 (7.8)
Ethnicity—white:African-American	4:2	12:7
HIV risk factor		
Intravenous drug use	3	6
Homosexual	3	12
Transfusion	0	1
Antiretroviral therapy		
None	2	0
Monotherapy/dual therapy	1	9
HAART	3	10
CD4 count·mL^{-1}	181 (143)	368 (132)**
Circulating HIV RNA (copies·mL^{-1})	16999 (13962)	10191 (21810)
Dietary intake		
Energy (kcal·d^{-1})	2804 (664)	2517 (747)
Protein (g·d^{-1})	111.5 (32.6)	92.3 (34.6)
Body composition		
BMI (kg·m^{-2})	21.5 (3.1)	27.0 (4.2)**
Weight (kg)	69.4 (8.2)	79.2 (15.7)*
Lean body mass index (kg·m^{-2})	16.7 (1.4)	18.1 (2.2)
Fat mass (kg)	13.0 (6.8)	24.7 (12.5)*
Bone mineral content (kg)	2.5 (0.7)	2.7 (0.4)

Data are mean (SD) unless otherwise indicated; HAART, highly active antiretroviral therapy; compartment weights may not add up to total weight because of rounding.
* $P < 0.05$; ** $P < 0.01$.

Effect of wasting and PRT on functional status. In all subjects taken together, self-reported baseline physical function was quite good, with a mean score of 92 (on a 0–100 scale, where 100 represents excellent function) at

TABLE 2. Physical functional status at baseline, 8 wk, and 16 wk of subjects with and without wasting.

	Baseline	Week 8	Change Baseline to Week 8	Week 16	Change Baseline to Week 16
Lean body mass					
No wasting	53.0 (8.7)	54.4 (9.7)	1.4 (2.0)	54.0 (10.0)	1.1 (1.9)
Wasting	53.4 (35.4)	56.2 (38.6)	2.8 (1.3)*	56.0 (4.0)	2.6 (1.2)*
Strength (1-RM)					
No wasting					
Chest press	113 (37)	141 (46)	28 (18)	138 (56)	25 (27)
Leg press	813 (319)	1102 (461)	289 (220)	1111 (431)	298 (249)
Leg extension	60 (26)	74 (30)	14 (19)	73 (32)	13 (16)
Upper back	150 (49)	195 (51)	45 (18)	183 (57)	33 (16)
Wasting					
Chest press	87 (33)	121 (39)	34 (29)	122 (15)	35 (28)
Leg press	533 (238)	761 (355)	228 (149)	753 (97)	220 (163)
Leg extension	45 (12)	62 (16)	17 (19)	56 (14)	11 (10)
Upper back	121 (28)	190 (29)	69 (29)	177 (26)	56 (27)
Physical function scale					
No wasting	92.4 (8.9)	92.9 (10.0)	0.4 (10.4)	89.1 (13.0)	−3.3 (10.2)
Wasting	90.9 (9.2)	95.7 (7.5)	4.7 (5.1)	96.9 (5.9)*	5.9 (6.0)**
Role—physical scale					
No wasting	70.0 (11.7)	60.0 (13.5)	−10.0 (19.1)	47.5 (15.1)	−22.5 (19.5)
Wasting	87.5 (12.5)	93.8 (6.3)	6.3 (6.3)	87.5 (7.2)	0.0 (6.25)

Data shown are means (standard deviation).
* $P < 0.05$, wasting vs nonwasting, Wilcoxon test; ** $P < 0.02$, wasting vs nonwasting, *t*-test.
All strength changes are significant at 8 and 16 wk in both wasted and nonwasted subject ($0.01 > P > 0.0001$). There were no differences between wasted and nonwasted patients in the strength changes.

baseline, 93.5 after 8 wk, and 91 after 16 wk. Wasted ($N = 6$) and nonwasted ($N = 18$) subjects did not differ in their baseline self-reported functional status, with a mean score of 91 in the wasted group and 92 in the nonwasted subjects ($P < 0.75$). However, the response to exercise training was different between the two groups (Table 2). At 8 wk, the wasted subjects had a 4.7-point improvement in function compared with a 0.4-point improvement in the nonwasted subjects ($P < 0.2$). This result was similar when only the subjects who completed all 16 wk of the study were analyzed at week 8 (0.5 vs 4.3 points, $P < 0.2$). At 16 wk, the wasted subjects had improved by 5.9 points, whereas the nonwasted subjects' self-reported physical function declined by a nonsignificant 3.3 points ($P < 0.017$ between groups, see Table 2). At 16 wk, the wasted subjects reported a significantly higher functional status than the nonwasted subjects ($P < 0.05$, Wilcoxon test). The role-physical scale did not change significantly over the study period (Table 2, $P < 0.25$).

Correlation of change in physical function with change in lean mass and in strength. Both percentage and total kg change in LBM and the percentage and total pound change in strength, calculated as the average of the four machines used for training, were significantly correlated with change in the physical function scale (Fig. 1, a and b). Although a large amount of collinearity between these two measures was expected, it was in fact relatively small ($r = 0.21$, $P < 0.4$). Therefore, both change in strength and change in LBM were entered into a multiple regression model with the outcome of change in physical function score (Table 3). Both change in LBM ($P < 0.001$) and change in strength ($P < 0.001$) were significantly associated with change in physical function, and no significant interaction term was found ($P < 0.29$).

DISCUSSION

This is the first study to examine the effect of PRT on functional status in HIV infection. We found a significant improvement in function in the wasted subjects but not in the nonwasted subjects. In contrast, in the entire Nutrition for Healthy Living cohort ($N = 1407$ observations), the mean change over 6 months in physical functioning was an increase of 1.3 points (I. Wilson, unpublished observations). Thus, the changes seen with the intervention in both groups were substantially larger than those seen in a cohort of free-living patients with HIV infection, supporting the conclusion that PRT can substantially affect functional status. We chose the MOS SF-36 physical function scale as our primary outcome because it has been widely used in many different patient populations (31). In addition, this is the first study, to our knowledge, that examines the relative roles of change in strength and change in lean mass in predicting change in self-reported function. Although we expected strength to be more important than change in lean mass in this regard, we were surprised to find that the two acted independently in predicting change in self-reported functional status.

We found resistance training to have a greater effect in wasted subjects than in nonwasted ones. This is consistent with previous observations that the amount of strength gain, expressed as a percentage of baseline strength, is greater in frailer elderly subjects and patients with rheumatoid arthritis than in controls (7,23). Better strength gains would be expected to lead to greater functional gains, and indeed that is what was found in the present study. Thus, the finding of better response in the wasted subjects is consistent with previous studies, although this is the first demonstration of it of which we are aware.

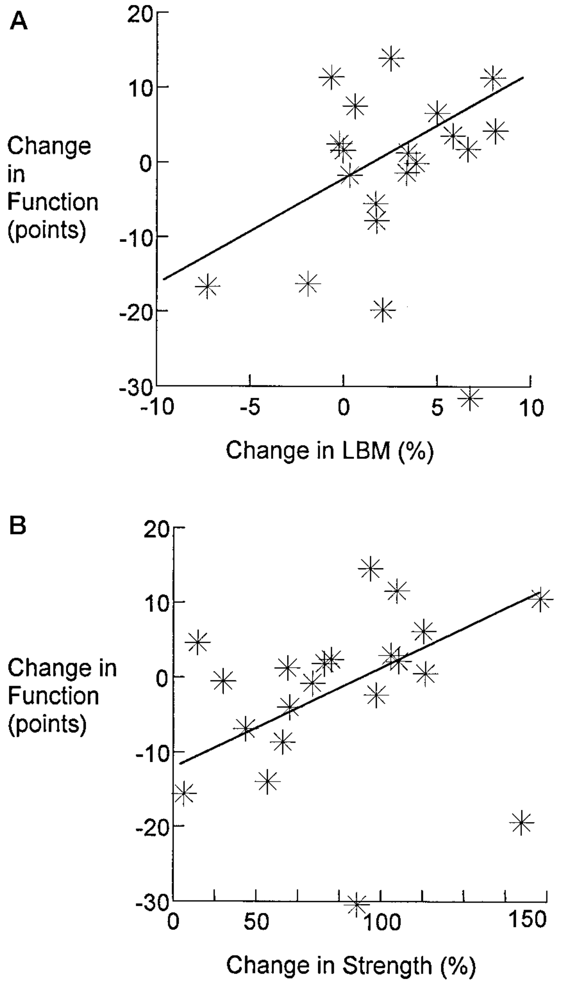

FIGURE 1—a) Correlation between percent change in LBM and change in physical function score. The equation for the line is Δ Function = −2.6 + 1.26 × (Δ LBM [%]); b) correlation between percent change in strength averaged over four exercises (leg press, chest press, back extension, and leg extension) and change in physical function score. The equation for the line is Δ Function = −5.7 + 0.15 × (Δ Strength [%]), $P < 0.004$.

In reviewing the recent literature, studies of exercise and anabolic therapy such as testosterone or growth hormone either did not report on physical functioning with testosterone and exercise (10,11), showed an improvement of approximately 10% with growth hormone (32), showed an 8% decline in self-reported physical function with growth hormone (27), a 10% improvement with nandrolone (9), a "significant" improvement of comparable magnitude with resistance exercise and with androgen therapy (29), or no effect of either resistance training or testosterone (2). Thus, our finding of a 6-point (approximately 7%) increase in self-reported physical functioning is consistent with the literature, but this is the first paper to show such an effect from resistance training without pharmacological therapy and to examine differential responses between people with HIV infection with and without wasting. It is likely that the lack of statistical significance to the change in role-physical despite the large point estimate is due to the larger standard deviation for this scale than for the physical function scale, which has more items and is more robust.

TABLE 3. Multivariate linear regression analysis of the association between change in strength, change in LBM, and change in physical function score (in points) over 16 wk; R^2 for the model = 0.732; SEE = 4.48.

Variable		SE	Partial R^2	P
Constant	−7.754	1.851	—	0.001
% Change in LBM	1.190	0.301	0.249	0.001
% Change in strength	0.133	0.032	0.433	0.001

Even a large improvement in strength may not translate into a large change in function, for several reasons. On one hand, function may be normal, causing a "ceiling effect" so that even if strength is increased significantly, function cannot improve. Alternatively, strength and function may both be below their optimal levels, but the functional limitation may not be driven by weakness. Rather, it may be due to comorbid conditions such as retinopathy, depression, pulmonary disease, or other factors that are not affected by strength training. Furthermore, the notion that there is a direct and linear connection from strength to physical performance to functional status may well be an oversimplification, and the impact of strength training on function may occur through changes in neural input to muscle, muscle quality, or other factors beyond simply increased muscle mass. Nevertheless, it is functional status that reflects, however imperfectly, the impact of an intervention on the day-to-day life of the patient. Thus, functional status is an important goal of any intervention in wasting, and, in fact, it may be argued that it is the most important outcome to assess with any nutritional, exercise, or pharmacological intervention that purports to provide a benefit to patients.

The goal of treatment in wasting has traditionally been to normalize lean body mass, with the assumption that normalization of structure will lead to normalization of function. In fact, this concept is not proven, and experience with strength training as a means to increase LBM has shown that strength gains are far greater than increases in lean tissue (7,8,23). Nonexercise interventions, such as recombinant human growth hormone, produce very small changes in strength or aerobic fitness, despite changes in LBM that are the same or larger than those produced by strength training (27). On the other hand, pharmacological doses of testosterone have been shown to increase strength comparably to resistance training, with the strengthening effect of both far exceeding the change in LBM they cause (1,10).

Several years ago, Jeejeebhoy (13) asked whether the goal of anabolic interventions should be to increase mass ("bulk") or muscle function ("bounce"). To address this issue, we sought to compare the effects of gain in LBM and gain in strength on the change in self-reported physical performance by using multiple regression analysis. Both changes in LBM and in strength were predictors of change in function, and the two variables were remarkably independent of each other and without an interaction. The effect size due to change in strength was approximately double that attributable to change in LBM. This is calculated from the mean change in strength (48%) multiplied by the beta for strength (0.133), compared with the mean change in LBM (2.5%) multiplied by the beta for LBM (1.19). The independence of these two covariates suggests that increase in LBM affects self-reported function through other mechanisms in addition to the increase in strength that it confers. These additional mechanisms remain unknown. Furthermore, this analysis suggests that interventions that increase strength may have a larger effect on function than interventions that only increase LBM with little or no effect on strength.

We examined the effect of 8 wk of PRT on self-reported function at 8 wk and again at 16 wk, after 8 wk without supervised training. This study design was chosen because when the study was originally proposed for funding in 1992, it was unlikely that patients could stay on a stable medication regimen for longer than 16 wk. The confounding effect of changes in medication is so large that avoiding it was a high priority. As we previously reported (25), nine of the subjects (3 with wasting) continued to train on their own during this phase. We could not ethically discourage them from doing this. At week 16 of the evaluation, subjects who continued to train showed a trend toward higher strength in the leg press and chest press but not on leg extension or upper back exercises (25). They did not differ significantly from the more sedentary subjects in LBM ($+1.1 \pm 1.6$ kg vs $+0.2 \pm 1.4$ kg LBM gain over the second 8 wk, $P = 0.2$). There was no difference in physical function scale change between the subjects who exercised in the second phase and those who did not. Because in the first 8 wk training was performed using Keiser pneumatic resistance machines, and because we did not instruct subjects on how to train on their own until after the completion of the 16 wk study, it was difficult for the patients to continue an effective training program on their own in the second phase of the study. Thus, it is unlikely that the level of activity in the second 8 wk of the study greatly affected the results, although we recognize that this is a potentially important limitation of the present study.

Several other limitations of the study should also be considered. First, the sample size is small, with only 6 patients with wasting and 18 without. Second, the baseline functional status was relatively good, at 92 points, so some ceiling effect may have occurred in the physical function scale despite the significant results obtained. For comparison, national norms for healthy 35–44 yr old adults are 94.9 on the physical functioning scale and 91.86 on the role-physical scale (31). However, any ceiling effect would tend to bias the results toward the null, so it is not likely to be a cause of spuriously positive results. Furthermore, the applicability of these results to more disabled populations is not clear. Third, the patients in this study were predominantly men, so its generalizability to women may be limited. However, current evidence suggests that wasting is more common in men than women (15). Fourth, self-reported physical function and physical performance measured under observation may not show the same results, and such direct measurements of physical performance (other than 1-RM) were not included in this study. Fifth, the study is essentially an "open-label" design, without a direct control group, and thus some of the effect attributed to exercise may in fact have been due to the attention and social contact inherent in participating in an exercise program. However, these subjects were recruited from our large ongoing cohort study, and the lack of change in physical functioning in the overall cohort is in striking contrast to the results of our trained subjects. This point will be addressed directly in new and larger studies now under way. However, the present results indicate that PRT is capable of improving not only muscle mass in adults with HIV infection but physical function as well. Further study of the mechanisms by which change in strength and LBM alter function may offer important insight into the optimal training methods for these patients.

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