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A RANDOMIZED TRIAL OF EXERCISE TRAINING AFTER RENAL TRANSPLANTATION

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Background. **Significant health benefits result from regular physical activity, many which are important for transplant recipients. Although exercise capacity improves initially after transplant, it is not normalized, and only two studies have reported the effects of exercise training in this population. We report a randomized clinical trial of exercise after renal transplantation (RTX).**

Methods. **One hundred sixty-seven patients were randomized at 1 month after RTX into two groups: exercise intervention (EX) and usual care (UC), with repeat testing at 6 and 12 months. Ninety-five patients completed the following testing at both testing times: symptom-limited treadmill testing with measurement of peak oxygen uptake (peak V_{O_2}); isokinetic muscle testing for muscle strength; and dual-energy X-ray absorptiometry scans for body composition. The SF-36 Health Status Questionnaire assessed self-reported functioning. The exercise intervention consisted of individually prescribed programs to be conducted at home with regular phone follow-up to enhance adherence. Repeated measures analysis of variance was performed to determine differences between the groups for the three testing times.**

Results. **At 1 year 67% of the EX group were exercising regularly compared with 36% of the UC group (P=0.01). Compared with the UC group, the EX group had significantly greater gains in peak V_{O_2} (P=0.016), percent age-predicted V_{O_2} (P=0.03), and muscle strength (P=0.05), and a trend toward higher self-reported physical functioning (P=0.06). There were no differences between the groups in changes in body composition. At 1 year, peak V_{O_2} was significantly correlated with age, percent fat, muscle strength, hematocrit, and self-reported physical functioning.**

Conclusions. **Exercise training after RTX results in higher levels of measured and self-reported physical functioning; however, exercise alone does not affect body composition.**

The health benefits of regular physical activity are clearly known. The Surgeon General's Report on Physical Activity and Health (*1*) presents scientific evidence supporting the beneficial effects of regular physical activity, many which are relevant to the overall health of transplant recipients. Specifically, regular physical activity (1) decreases the risk of cardiovascular disease mortality; (2) prevents or delays the development of high blood pressure and reduces blood pressure in people with hypertension; (3) is necessary for maintaining normal muscle strength, joint structure, and joint function; (4) is essential for normal skeletal development and maintaining peak bone mass in adults; (5) relieves symptoms of depression and anxiety and improves mood; and (6) improves quality of life through enhanced psychological well-being and by improved physical functioning in persons compromised by poor health (*1*).

Patients presenting for renal transplantation are physically inactive and have low levels of exercise capacity (*2–14*) related to uremia and the dialysis treatment. Although exercise capacity significantly improves soon after successful transplant with removal of the uremia (*8*, *10*, *15*), it is not clear whether these levels are optimal. In a cross-sectional sample of highly motivated transplant recipients, we reported that those who exercise regularly have significantly higher levels of health-related fitness and quality of life than those who are inactive (*16*). In this cross-sectional study active kidney transplant recipients achieved exercise capacity of 101.7% of age-predicted normal values compared with only 72.7% in those who were inactive. This study was cross-sectional and involved participants in the 1996 U.S. Transplant Games, thus may not reflect the general transplant population.

Two exercise training studies have been reported in renal transplant recipients, both with small numbers of subjects and without randomized controls. Miller et al. (*17*) studied patients who started participation in a cardiac rehabilitation program 2 weeks after kidney transplant for 3 months, then participated in home exercise for the next 2 years. Exercise capacity increased significantly during the follow-up time with training; however, the lack of a control group prevents determination of how much of this improvement was the result of training versus the transplant alone. Kempeneers et al. (*18*) reported the effects of a 6-month program of exercise training in 16 patients who were an average of 62 months after kidney transplant. Exercise capacity as measured by maximal oxygen uptake (V_{O_2}) increased significantly with training by 29%. They also reported improved muscle strength, improved blood pressure control, and evidence of bone remodeling.

The present study is a randomized clinical trial to study the effects of an exercise intervention after renal transplant recipients on health-related fitness (exercise capacity, muscle strength, body composition) and quality of life.

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MATERIALS AND METHODS

Subjects

Patients were recruited within 2 months after kidney transplantation at the University of California at San Francisco. Recruitment took place from January 1994 through November 1995. Patients were excluded from entry into the study if they had transplant rejection or psychiatric or neurologic disorder that would preclude participation; had orthopedic limitations that precluded exercise testing or training; were unavailable for regular follow-up; had any absolute contraindications to exercise testing as established be the American Heart Association or the American College of Sports Medicine (*19*); or had any medical complications that would prevent regular participation. All subjects were recruited by study staff, and consent was obtained according to procedures approved by the Committee on Human Research at the University of California at San Francisco.

Study Design

This study was a prospective design in which patients were tested at 1 (baseline), 6, and 12 months after transplant. After baseline testing patients were randomized into two groups: exercise intervention (EX) and usual care (UC). Randomization was performed using a restricted randomization procedure, which was managed using prepared sealed envelopes containing a card indicating the allocated treatment group. After the baseline testing, the next envelope was opened. It was expected that randomization would assure equal distribution between the groups of demographics, comorbidities, transplant function, and so forth. There was no attempt to direct healthier patients into the exercise training group.

Outcome Measures and Procedures

Cardiorespiratory fitness. Symptom-limited exercise testing was performed on a treadmill. VO_2 was determined using an open-circuit spirometry system (Vacu-Med, Ventura, CA), which was calibrated against known gasses before each test. Respiratory gases were analyzed for volume and fractions of oxygen and carbon dioxide, and VO_2 was calculated. Peak VO_2 is expressed in terms relative to body weight (milliliters of VO_2 per kilogram of body weight per minute). Age-predicted peak VO_2 was determined using formulas reported for sedentary normal individuals by Bruce et al. (*20*): peak VO_2 for males$=57.8-0.445\times$age, and peak VO_2 for females$=42.3-0.356\times$age.

The branching protocol (*21*) was used for testing, which established a comfortable walking speed, after which the work intensity was increased by increasing grade to achieve approximately 1 metabolic equivalent (MET) increment between stages. The work rate increased every 2 min until the subject was unable to continue (volitional fatigue) or until there was indication to discontinue the test (i.e., electrocardiographic changes, inappropriate blood pressure response) (*22*). A 12- lead electrocardiogram was monitored continuously throughout the test, and blood pressure was auscultated at every stage. Ratings of perceived exertion (subjective rating of effort) were measured at each stage on a 6–20 scale (*23*).

Muscle strength. Quadriceps muscle strength was measured using a computerized isokinetic muscle function testing system (Biodex II). The right leg was attached to a dynamometer allowing for isolation of the quadriceps muscle group. The patient kicked at a controlled speed of 180° per second for 20 repetitions. Variables measured for analysis were peak torque (the highest torque developed during the set of repetitions) and peak torque per body weight. Normal values for peak torque per body weight are presented in data from Biodex.

Body composition. Body composition was determined using dual-energy X-ray absorptiometry (Norland X-R 26). The machine was calibrated daily using known phantoms. The software from a full body scan determined bone mineral density (grams per square centimeter), lean body mass (grams), and fat mass (grams). Percent body fat was calculated from the fat mass and total body weight.

Health-related quality of life. The Medical Outcomes Short Form (SF-36) questionnaire (*24*) was used to evaluate self-reported domains of health status (*24*). The SF-36 is a 36-item questionnaire that includes eight components of health-related quality of life: physical functioning (PF), role limitations owing to physical health (RP), body pain (BP), general health (GH), vitality (VT), social functioning (SF), role limitations owing to emotional health (RE), and mental health (MH). These scales are scored from 0 to 100, with higher scores being more positive (i.e., less pain, less limitation). Normalized scores representing overall physical functioning and mental functioning are calculated from the individual scales and are presented as the physical composite scale (PCS) and the mental composite scale (MCS). The PCS includes the dimensions of PF, RP, BP, GH, VT, and SF. The MCS is composed of the RE and MH and includes elements of the GH, VT, and SF scales as well (*25*). The scaling of these component scores are approximately 50 for normal population values. Questionnaires were given to patients after each testing session to be completed independently and returned by mail.

Activity participation. Activity levels were determined by self-report, and subjects were classified as active or inactive using the following sequence of questions: Do you exercise regularly? If yes, what type(s) of exercise do you do? How many times per week do you exercise? How long do you exercise per session? How hard do you exert yourself during your exercise (rating of 1–5). This allowed us to classify patients into active or inactive according to the Surgeon General's report guidelines. The classification of active required cardiovascular exercise three or more times per week for at least 30 or more minutes per session at an intensity described as "somewhat hard" or greater. All others were classified as inactive. In the EX group, this self-report was confirmed with activity logs and phone follow-up questionnaires (see below).

Exercise intervention. Individualized prescriptions were developed for each subject randomized into the EX on the basis of their treadmill test results. The prescription was for independent home-based exercise and included cardiovascular exercise (primarily walking or cycling); frequency of at least four times per week; duration that worked up to at least 30 min per session; and an intensity that was initially 60–65% of maximal heart rate, which was gradually (approximately every 2 weeks) increased to 75–80% of maximal heart rate. Patients kept exercise logs, which were returned to the study staff every 2 weeks. Exercise patients were initially contacted weekly, then every other week, by phone by the exercise study staff to assess progress and adherence to the program. During these phone contacts, participation rate was assessed, the program was adjusted as needed, any problems (e.g., muscle soreness) were discussed and suggestions made, and encouragement for continued participation was given.

Data Analysis

Descriptive statistics (means, standard deviations) were calculated for all continuous variables, and frequencies were generated for other variables. Repeated measures analysis of variance with one within subjects factor (time: baseline, 6 and 12 months) and one between subjects factor (group: EX, UC) was used to determine differences between the EX and UC groups as a function of time. This analysis allows for testing of the main effects of group and the main effects of time as well as the interaction of group by time. The group by time interaction indicates whether the change with time differs between the groups. All analysis was performed using an intent-to-treat design. An analysis conducted by intent-to-treat compares outcomes between the study groups with every participant analyzed according to the randomized group assignment, regardless of whether they received the assigned intervention. Only those who completed all three tests are included in the analysis. Pearson correlations were used to determine associations between variables of interest at the 12-month testing time. Statistical significance was set at $P<0.05$.

RESULTS

Subjects. A total of 167 patients were recruited, which represents 54% of the eligible patients who received transplants at our institution during that time. Seventy patients (42%) did not complete all three testing sessions (29 in EX, 41 in UC). Seventy-three percent of the dropout patients did so between baseline and 6 months, with 29% discontinuing between 6 months and 12 months. The reasons for dropping out were disinterest (9 in EX, 10 in UC), lost to follow-up (14 in EX, 16 in UC), medical concerns (5 in EX, 14 in UC), and death (1 in each group). The medical reasons for dropping out were transplant rejection (2 in UC), cardiovascular concerns (1 in UC), orthopedic limitations (4 in EX, 10 in UC), and other (1 in each group). Although a greater percentage of the UC patients dropped out than EX patients (49% vs. 35%) the difference was not statistically significant (Fisher's exact test, P=0.08).

Baseline demographic characteristics of the patients who completed the study are shown in Table 1. There were no significant differences between the EX and UC groups on any demographic characteristics The doses of immunosuppression decreased significantly with time in both groups (Table 2). There were no differences between the groups in creatinine or blood urea nitrogen; however, a significant time by group interaction was found in hematocrit and hemoglobin with the EX group showing a greater increase during the 12 months (Table 2).

Exercise participation. Figure 1 shows the percent of patients who were classified as active and inactive at each testing time. At baseline there was no difference between groups. The EX group increased participation at both 6 and 12 months, with higher percentages of the EX group being classified as active at both follow-up testing times.

Table 1. Demographic characteristics[a]

	Exercise (n=54)	Usual Care (n=43)
Age (mean±SD)	39.7±12.6	43.7±10.7
Gender (n) (%)		
Males	30 (55.5)	30 (69.1)
Females	24 (44.4)	13 (30.2)
Ethnicity (n) (%)		
Caucasian	27 (50)	20 (46.5)
Hispanic	12 (22)	10 (23.3)
African American	6 (11)	6 (13.9)
Asian	5 (9)	4 (9.3)
Other	4 (7)	3 (6.9)
Cause of renal failure (n) (%)		
Glomerulonephritis	10 (18.5)	2 (4.6)
Hypertension	9 (17)	8 (18.6)
Diabetes mellitus	3 (5)	8 (18.6)
Lupus	6 (11)	3 (6.9)
PCKD	1 (1.8)	5 (11.6)
IGA nephropathy	4 (7.4)	2 (4.6)
Unknown	7 (12.9)	6 (13.9)
Other	14 (25.6)	9 (20.9)
Type of transplant (n) (%)		
Cadaveric	35 (64.8)	25 (58.1)
Living related	15 (27.7)	17 (39.5)
Living unrelated	4 (7.4)	1 (2.3)

[a] Abbreviations used: IGA, immunoglobulin A; PCKD, polycystic kidney disease.

Exercise testing. The physiologic responses at peak exercise and muscle functioning test are presented in Table 3. The values for respiratory exchange ratio and ratings of perceived exertion indicate that the two groups achieved similar levels of exertion at each testing time. All patients increased their peak systolic and diastolic blood pressures with time, and peak ventilation was higher in both groups with time.

The change for the three testing times in both peak Vo_2 and the percent age-predicted peak Vo_2 was significantly different between the two groups (P=0.001). There was a trend for patients in both groups to increase from baseline to 6 months; however, the EX group continued to increase out to 12 months which was not the case with the UC group (Fig. 2).

Muscle testing. Both groups increased in their muscle strength with time; however, the change in quadriceps peak torque during the 12 months was greater in the EX compared with the UC group (P=0.003; Table 3). Likewise the increase in peak torque per body weight was significantly different between the two groups. The peak torque per body weight was low in both groups at 12 months compared with normal values.

Body composition. All patients increased in body weight, body mass index (BMI), fat mass, lean mass, and percent body fat (Table 4). There was no difference between the two groups in body composition changes during the 12 months. The percent of patients with BMI>25 at 12 months was 50% in the EX group and 59% in the control group (not significant).

Health-related quality of life. The only scale on the SF-36 questionnaire that approached significant differences between the two groups during the 12 months was the PF scale (baseline: EX: 68.1±19.5, UC 64.1±19.7; 12 months: EX 84.8±21.6, UC 73.2±29.4; P=0.06). Although both groups improved in the RP during the 12 months (baseline: EX 39.0±37.5, UC 542.9±37.4; 12 months: EX 59.4±40.5, UC 60.6±39.5), it remained low compared with the general population (average for general population is 83) (*24*, *25*). Both groups improved with time in the PCS during the 12 months, (baseline: EX 40.1±8.7, UC 40.8±8.2; 12 months: EX 47.0±11.3, UC 44.8±12.9; P<0.0001), but there were no significant differences between the groups as a function of time. At 12 months, both groups were similar to the general population scores for MH and the MCS; all other scale scores remained lower than the scores reported for the general population

Correlations. At 12 months, peak Vo_2 was significantly correlated with several physiologic measures: age (r=−0.48; P<0.001), hematocrit (r=0.30; P<0.001), BMI (r=−0.23; P=0.02), fat mass and total fat percentage (r=−0.45; P<0.001; r=−0.51; P<0.001, respectively), and physical activity (r=0.24; P=0.01). Significant correlations between peak Vo_2 and several physical scales on the SF-36 were also noted at 12 months: PF (r=0.46; P<0.001), RP (r=0.31, P<0.005); VT (r=0.22; P=0.05), and the PCS (r=0.40; P<0.001).

DISCUSSION

We have previously reported that health-related fitness and quality of life are higher in physically active transplant recipients than in those who are sedentary (*16*). These cross-sectional data were from a group of highly motivated trans-

TABLE 2. Laboratory measures and medications at the three testing times in the exercise (n=54) and usual care (n=43) groups[a]

Variable	Group	Baseline	6 months	12 months
Creatinine (mg/dl)	Exercise	1.7±1.6	1.5±.6	1.5±.7
	Usual care	1.6±.6	1.6±.8	1.8±1.5
BUN (mg/dl)	Exercise	28.5±9.2	28.1±19.6	30.5±24.4
	Usual care	29.1±9.1	29.1±14.0	32.2±28.2
Hematocrit (%)	Exercise	34.1±5.0	40.6±6.3	41.1±5.5
	Usual care	35.2±5.0	39.3±5.5	39.4±6.1[b]
Hemoglobin (mg/dl)	Exercise	11.3±1.7	13.4±1.9	13.6±1.7
	Usual care	11.6±1.6	13.1±1.8	13.1±1.9[b]
Prednisone dose (mg/d)	Exercise	25.6±15.6	8.5±2.9	7.8±8.1
	Usual care	21.6±7.4	8.8±4.7	7.4±4.0[c]
Azathioprine dose (mg/d)	Exercise	103±41	94±46	85±49
	Usual care	103±39	96±38	95±37[c]
Cyclosporine dose (mg/d) (n=34 Ex; 30 UC)	Exercise	638±253	401±156	387±145
	Usual care	591±190	476±184	375±131[c]
Neoral dose (mg/d) (n=5 Ex; 3 UC)	Exercise	650±206	400±122	470±238
	Usual care	450±312	333±76	283±28
Prograf dose (n=17 Ex; 13 UC)	Exercise	11.3±7.4	11.1±5.4	9.2±4.7
	Usual care	11.3±5.3	10.2±5.1	8.3±4.6[c]
Mycophenolate mofetil dose (mg/d) (n=11 Ex; 7 UC)	Exercise	1577±745	1500±447	1225±376
	Usual care	929±785	1571±553	1250±458
BP meds[d]	Exercise	1.3±.6	1.5±.6	1.5±.7
	Usual care	1.5±.6	1.8±.9	1.8±.9

[a] Values are mean±SD. Abbreviations used: BP, blood pressure; BUN, blood urea nitrogen.
[b] Time by group interaction $P<0.04$.
[c] Effects of time: $P<0.001$.
[d] Sum of angiotensin-converting enzyme inhibitors, α-adrenergic blocking agents, β-adrenergic blocking agents, calcium-channel blockers, clonidine, and diuretics.

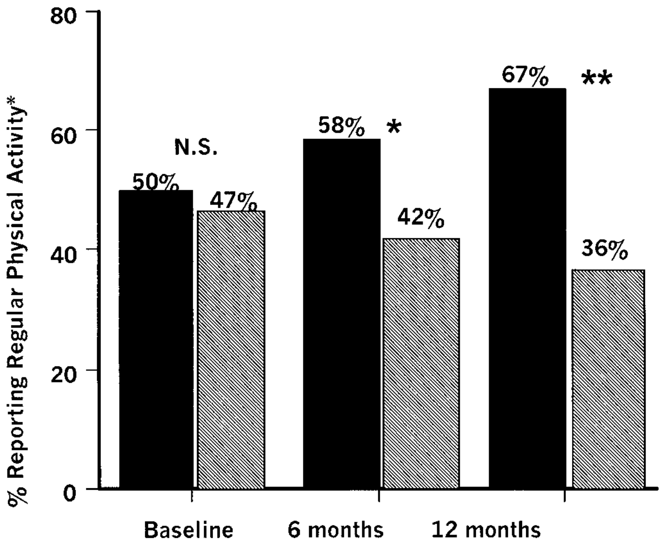

FIGURE 1. Percent of patients participating in regular exercise at each time point. * X^2=2.9; P=0.06; ** X^2=5.2; P=0.02.**

plant recipients (participants in the U.S. Transplant Games) and are probably not reflective of the general population of transplant recipients. Nor do they provide information on the effects of exercise training after transplant.

The two published studies of exercise training in renal transplant recipients had small numbers and no control subjects. In one study, patients initiated exercise within 2 weeks of renal transplant in a cardiac rehabilitation setting for 3 months, then patients were instructed to continue exercise independently and were retested at 2 years after transplant (*17*). The second study involved patients who were 3 years after transplant and who were interested in training for the transplant games (*18*). This study involved a high level of training in a group of very motivated patients. Both studies reported significant improvements in exercise capacity. Kempeneers et al. (*18*) also reported significant increases in muscle strength, improved blood pressure control, and evidence suggesting bone remodeling.

Our study supports the above findings in a randomized controlled design, which was prospective in nature, designed to follow patients for the first 12 months after transplant. The significant time by group interaction in peak VO_2 is impressive, as we performed an intent-to-treat analysis, which included the 33% of the EX group that remained inactive throughout the study. The levels of peak VO_2 achieved at 12 months remained lower than sedentary normals in the EX group, which is similar to the results of Kempeneers et al.(*18*), who reported lower peak VO_2 in the exercise-trained transplant recipients compared with age-matched sedentary control subjects. The peak VO_2 at 12 months in the UC group was strikingly low, not only compared with age-predicted values, but it was similar to that reported in several studies of hemodialysis patients. This low level was similar to that observed in the inactive transplant games patients (*16*).

The improvement in muscle strength in the EX group was encouraging because the exercise that was prescribed was cardiovascular exercise. Similar improvements were reported in Kempeneers et al. (*18*) with cardiovascular training. The muscle strength measured at 12 months remained lower than normal values, however, suggesting that resistance training may be needed to normalize muscle strength.

TABLE 3. Physiologic variables at peak exercise and muscle function data in exercise (n=52) and usual care (n=43) groups[a]

Variable	Group	Baseline	6 months	12 months
Peak $\dot{V}O_2$ (ml/kg/min)	Exercise	24.0±7.5	27.8±11.0	30.1±10.3
	Usual care	24.7±6.7	28.3±9.2	26.5±8.7[b]
Peak $\dot{V}O_2$ (L/min)	Exercise	1.67±.62	2.05±.83	2.2±.78
	Usual care	1.78±.63	2.15±.78	2.07±.80[b]
% Age-predicted $\dot{V}O_2$	Exercise	70.9±19.7	81.3±27.8	85.4±29.1
	Usual care	71.6±19.9	81.8±26.1	77.4±21.8[b]
Peak respiratory exchange ratio	Exercise	1.32±.17	1.3±.17	1.35±.16
	Usual care	1.38±.14	1.31±.13	1.37±.16
Peak rating of perceived exertion	Exercise	16.7±1.7	16.4±2.1	16.5±2.0
	Usual care	16.3±2.3	16.2±2.5	16.7±2.1
Peak torque (ft · lbs)	Exercise	53.6±20.7	65.5±27.1	70.9±28.3
	Usual care	51.4±17.7	61.2±22.6	61.2±23.0[b]
Peak torque per body wt (ft · lbs/kg)[c]	Exercise	34.5±11.8	39.5±15.0	42.5±15.1
	Usual care	33.7±9.5	37.2±11.2	37.2±11.6[b]

[a] Values are mean±SD.
[b] Time by group interaction: $P<0.03$.
[c] Age group norms for peak torque/body weight: male (58–75), female (50–65).

Horber et al. (*26*) reported normalization of quadriceps muscle strength with resistance exercise training. Severe muscle weakness is prevalent in dialysis patients, and the administration of prednisone may prevent normalization of muscle function after transplantation without exercise intervention.

The lack of differences in body composition between the groups during the 12 months after transplant was disappointing, although not unexpected. Exercise alone has never been effective in weight management (*27*). Successful weight management requires careful dietary management to balance caloric intake to energy expenditure. Because a major benefit of renal transplant is the lack of restrictions in diet, it is expected that dietary intake is high after transplant. A few studies have reported dietary interventions as an intervention for dyslipidemia after kidney transplant (*28–31*); however, none of these studies reported body composition data. A subset of 42 patients in our study completed food frequency questionnaires, and there was no difference in caloric intake between the EX and UC groups.

Physical activity may be important in weight management in posttransplant patients longer term. Van Den Han et al. (*32*) reported body composition in a group of 77 renal transplant recipients taking varying doses of prednisone (0, 5, and 10 mg/day). Although they found no difference in body fat, percent fat, lean body mass, or BMI among groups, they did report significant negative correlations between leisure time activity and fat mass, lean mass, percent fat, and BMI. This association with leisure time activity remained significant in a multiple regression analysis that included age, time after transplant, and daily and cumulative doses of prednisone. We also saw significant correlations between peak $\dot{V}O_2$ and fat mass and percent body fat at 1 year, suggesting some relationship between exercise and body composition, which was not reflected in significant differences between groups within the first year after transplant. It is highly probable that for posttransplant weight management, a combination program of diet and exercise is required. The impact of such programs may not be as effective in weight management during the first year after transplant when medications are fluctuating and dietary liberalization is being experienced to its fullest.

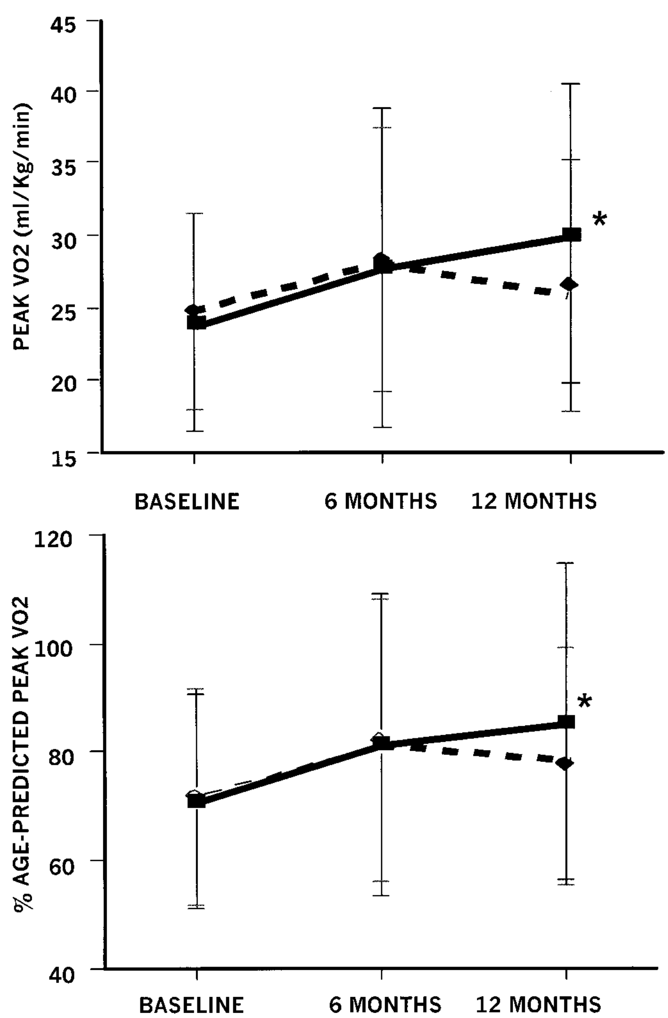

FIGURE 2. Peak O_2 and percent age-predicted peak O_2 as a function of time. *Time by group interaction, P=0.001. **Time by group interaction, P=0.03. —■— exercise; – –◆– – usual care.

TABLE 4. Body composition variables in exercise and usual care groups[a]

Variable	Group	Baseline	6 months	12 months
Stature (cm)	Exercise	167.3±0.9		
	Usual care	167.6±10.7		
Weight (kg)	Exercise	70.0±14.5	74.1±14.7	78.1±22.0
	Usual care	71.5±16.6	76.5±18.4	77.0±20.4[b]
BMI	Exercise	24.8±4.6	26.3±4.9	27.7±7.4
	Usual care	25.1±4.8	26.9±5.5	27.1±6.1[b]
% patients with BMI>25	Exercise	41.0%	51.8%	50.0%
	Usual care	44.0%	53.6%	59.0%
Lean body mass (kg)	Exercise	49.2±11.3	49.7±11.6	49.7±11.8
	Usual care	50.1±11.1	51.8±11.2	51.8±11.6[b]
Fat mass (kg)	Exercise	20.78±7.1	25.1±9.5	25.8±10.8
	Usual care	21.2±9.2	26.2±10.4	27.6±10.5[b]
% Body fat	Exercise	28.7±8.6	32.0±9.9	32.3±11.2
	Usual care	27.8±7.1	31.7±7.9	32.9±8.4[b]
Bone mineral density (g/cm^2)	Exercise	0.970±0.114	0.983±0.104	0.995±0.108
	Usual care	1.012±0.147	1.018±0.157	1.024±0.144

[a] Values are mean±SD.
[b] Effects of time: $P<0.03$.

Health-related quality of life improved in most domains; however, the EX group showed greater improvements in the PF scale than did the UC group. The other scale scores were similar after transplant to those of the general population, with the exception of RP. Both groups started very low in this health-related quality-of-life domain, and both increased significantly during the year. In longer-term transplant recipients, we have reported significantly lower scale scores for all the physical scales for patients who are physically inactive (*16*, *33*). In both of these studies, the GH score was also lower, which made it difficult to determine whether the inactive patients had poorer overall health that lowered their physical functioning reports. However, in this study the GH scores were not different between groups; thus the difference in the PF score is most likely a direct effect of the exercise intervention.

The significance of self-reported functioning has not been established in transplant recipients. In dialysis patients, the physical functioning and the overall physical component scores have been shown to be predictive of outcomes, specifically hospitalizations and death—even when controlled for case mix (*34*, *35*). In the gerontology population, self-reported functioning is also highly predictive of outcomes such as hospitalization, need for institutionalization, and death (*36–39*). The high scores similar to those of the general population on most scales in our subjects may reflect the honeymoon of the first year after transplant, as longer term after transplant, the scores are lower (unpublished data, Painter). Thus differences between the two groups at a time when most patients self-report high was not expected.

Limitations of this study were that the exercise prescribed was not supervised and that the control group did not receive any sham training or attention. Home-based exercise has been well documented to result in low dropout and significant improvements in exercise capacity in patients after myocardial infarction ((*40*, *41*). We are confident that the regular phone interviews of patients about their exercise and their exercise logs provided accurate information about participation. It is also clear that patients in the EX group who did not participate regularly were honest in their reporting of participation. The two groups of patients had no formal opportunity for contamination of the control group. All patients received information about exercise during their inpatient stay. Recruitment into the study and randomization into the two groups did not occur until 2 months after transplant.

Despite these limitations, we were impressed by the percent participation in the EX group, who continued regular participation during the study time. The high participation rates in both groups at baseline may be a reflection of the University of California San Francisco transplant rehabilitation program in which all transplant recipients participated in an inpatient program of flexibility and strengthening and were given a program of cardiovascular exercise to follow at home on discharge. This education may have also resulted in a greater percent of exercise participation in the UC group that may not be seen elsewhere without an inpatient rehabilitation program. This program did not include routine follow-up after discharge. Clinically we have noted that with time, many patients discontinue exercise at critical times such as return to work, hospitalizations, or other medical events. The regular follow-up in the EX group provided guidance and encouragement during these critical times to restart or maintain their participation.

The regular exercise participation of 67% of patients in the EX group was surprisingly high, and well above that reported in the general population (approximately 24%) (*1*). Patients have compelling reasons to optimize physical functioning after transplant, as they typically experience severe deconditioning before surgery. Although exercise capacity increases soon after transplant (*10*), it is clear that transplantation alone does not optimize functioning. Encouragement for participation in regular physical activity as a part of the routine posttransplant recommendations with regular follow-up to maintain adherence will result in regular participation by most patients, thus increasing physical functioning.

Although the Surgeon General's report on physical activity and health does not specifically mention the transplant population, the generally debilitated state of those in need of transplant makes them highly likely to derive benefits from regular physical activity. Our data support this, showing that exercise training after transplant results in higher cardiorespiratory fitness, increased muscle strength, and less limitation in physical functioning compared with usual post-transplant care. Although we did not report cardiovascular risk factors, the high prevalence of hypertension, diabetes, and cardiovascular disease in transplant recipients also suggests that exercise recommendations and encouragement should be a part of the routine medical treatment plan for patients after transplant. This will not only optimize physical functioning, but may positively impact overall health, thus assuring the very best possible outcomes of transplant surgery.

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