Resistance Training to Reduce the Malnutrition-Inflammation Complex Syndrome of Chronic Kidney Disease

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• ***Background:*** **Systemic inflammation and protein-energy malnutrition may be associated with poor outcomes in kidney disease.** ***Methods:*** **We studied 26 adults (age, 65 ± 10 [SD] years) with chronic kidney disease, not on dialysis therapy. Subjects were randomly assigned to resistance training (n = 14) or a control group (n = 12) for 12 weeks, while counseled to consume a low-protein diet (protein, ~0.6 g/kg/d). We determined whether resistance training reduces levels of inflammatory mediators (serum C-reactive protein [CRP] and interleukin-6 [IL-6]), in addition to previously reported improvements in nutritional and functional status in this same subject population.** ***Results:*** **Serum CRP levels were reduced in subjects undergoing resistance training (−1.7 mg/L) compared with controls (1.5 mg/L;** $P = 0.05$**). Similarly, IL-6 levels were reduced in the resistance-exercise group versus controls (−4.2 versus 2.3 pg/mL;** $P = 0.01$**). Resistance training lead to skeletal muscle hypertrophy, shown by increases in type I (24% ± 31%) and type II (22% ± 41%) muscle fiber cross-sectional areas, compared with control subjects (−14% ± 34% and −13% ± 18%, respectively;** $P < 0.05$**). Muscle strength also improved with resistance training (28% ± 14%) compared with controls (−13% ± 22%;** $P = 0.001$**).** ***Conclusion:*** **Resistance training reduced inflammation and improved nutritional status in individuals with moderate chronic kidney disease consuming a low-protein diet. These results need to be investigated further in larger cohorts of patients with varying stages of kidney disease to determine whether resistance training can improve disease outcomes long term.** ***Am J Kidney Dis*** **43:607-616.**

INDEX WORDS: Inflammation; malnutrition; resistance training; chronic kidney disease (CKD).

PROTEIN-ENERGY malnutrition starts in the early stage of chronic kidney disease and increases steadily as kidney function declines.[1] Recent evidence from The National Institutes of Health–sponsored Hemodialysis (HEMO) Study indicates worrisome trends in baseline nutritional status for maintenance dialysis patients.[2] The HEMO Study is the largest study to date to assess the nutritional status of long-term hemodialysis patients. The proportion of patients with values less than HEMO Study nutritional standards included 29% for serum albumin levels less than 3.5 g/dL (<35 g/L), 76% for dietary energy intake less than 28 kcal/kg/d, and 61% for dietary protein intake less than 1.0 g/kg/d.[2] These results show that a majority of maintenance dialysis patients have protein and energy intakes less than those recommended by the National Kidney Foundation-Kidney Disease Outcomes Quality Initiative.[3]

Low-grade chronic inflammation characterized by increased levels of serum C-reactive protein (CRP) and interleukin-6 (IL-6), a proinflammatory cytokine, may be a mediator of protein-energy malnutrition[4] and survival[5,6] in patients with kidney failure. Inflammatory cytokine–mediated catabolism is associated with hypoalbuminemia,[7] hypermetabolism,[8] and loss of body cell mass.[9] Additionally, severity of carotid atherosclerosis in hemodialysis patients has been associated with elevated serum IL-6 levels.[10,11]

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The combined occurrence of protein-energy malnutrition and inflammation in kidney failure, referred to as malnutrition-inflammation complex syndrome,[12] may be associated with such poor outcomes as cardiovascular atherosclerotic disease, decreased quality of life, increased mortality, and hospitalization.

We previously showed in a randomized controlled trial of subjects with moderate chronic kidney disease asked to consume a low-protein diet (the same trial used for the present study) that 12 weeks of resistance-exercise training resulted in significant improvements in protein utilization, nutritional status, and functional capacity.[13] The purpose of the present study is to further characterize whether the anabolic stimulus of resistance training would lead to a reduction in systemic inflammation, measured by serum CRP and IL-6 levels. In addition, we are interested in determining the association between inflammatory markers and nutritional and functional parameters.

METHODS

Study Population

Twenty-six subjects older than 50 years with moderately severe chronic kidney disease (median glomerular filtration rate [GFR], 27.5 mL/min/1.73 m^2), not on dialysis therapy, participated in this study, as previously described.[13] Briefly, subjects were recruited from the greater Boston, MA, area. Screening procedures included sociodemographic and health history questionnaires, physical examination, electrocardiogram, blood hematologic and chemistry tests, urine analyses, and a treadmill stress test. Eligibility criteria included serum creatinine concentrations from 1.5 to 5.0 mg/dL (133 to 442 μmol/L), confirmation of the diagnosis of renal disease, and physician approval for prescription of a low-protein diet. Reasons for early termination of the study included loss of greater than 25% of initial body weight, need for dialysis therapy or transplantation, development of a serious condition requiring hospitalization or precluding exercise, and signs of malnutrition (ie, decrease in serum transferrin levels to < 150 mg/dL (< 1.5 g/L) or a 15% decrease in hemoglobin level or white blood cell count less than baseline). Eligible subjects gave written informed consent approved by the Institutional Review Board at Tufts-New England Medical Center (Boston, MA). On enrollment, subjects were randomly assigned to a low-protein diet plus resistance training or a low-protein diet alone (control) for 12 weeks.

Low-Protein Diet

Subjects were asked to follow a low-protein diet (protein, 0.6 g/kg body weight/d) for 2 to 8 weeks (run-in period) before randomization. They continued on the low-protein diet for an additional 12 weeks after randomization (intervention period). Subjects were counseled to reduce their habitual protein intake by eating food sources with less protein or reducing portion sizes of higher protein foods. Behavior modification strategies were adapted from the Modification of Diet in Renal Disease Study.[14] The study dietitian monitored dietary protein adherence and energy intake regularly by using 3-day diet diary–assisted recalls. Dietary data were coded and analyzed using Nutritionist-IV Software (N-Squared Computing, San Bruno, CA). Subjects were asked to provide one 24-hour urine sample for every 3-day dietary diary collected during the study. Protein intake was estimated from urinary urea nitrogen appearance[15] and used to assess adherence.[13]

Intervention

Resistance-exercise training group. Subjects exercised 3 times/wk under supervision at the Jean Mayer USDA Human Nutrition Research Center on Aging. Each session lasted approximately 45 minutes and included a 5-minute warm-up, 35-minute resistance training (using 5 pneumatic resistance training machines; Keiser Sports Health Equipment Inc, Fresno, CA: chest and leg press, latissimus pull down, knee extension and flexion), and a 5-minute cooldown. Subjects performed 3 sets of 8 repetitions on each machine per training session. Each repetition consisted of a 2-count concentric (lifting) phase, a slight pause, and a 4-count eccentric (lowering) phase. There was a 1- to 2-count pause between repetitions and a 1- to 2-minute rest period between sets. Proper breathing technique was emphasized at all times to avoid an increase in thoracic pressure. Training intensity was targeted at 80% of 1 repetition maximum (1RM). Training intensity was increased progressively as needed to ensure that target intensity was maintained as subjects got stronger and set workloads became easier, assessed by subjects' self-perceived levels of exertion using a Rating of Perceived Exertion Scale.[16] Cool-down exercises included 5 to 8 stretching and flexibility exercises for the upper and lower body.

Control group. Subjects performed the same stretching and flexibility exercises as those used during cool-down in the exercise group. These exercises were used to ensure there would not be a physiological impact, but rather provide contact time and socialization similar to those of the resistance-training group.

Outcome Measures

All measures were obtained before (week 0) and 12 weeks after randomization. The study dietitian and exercise trainer were not blinded to group assignment. However, baseline muscle strength was assessed before randomization. Observers blinded to group assignment performed all other study measurements.

Systemic inflammation. Serum CRP levels were measured by means of an immunoturbidimetric method[17] in a Cobas Fara II automated centrifugal analyzer (Rankin Biomedical Corp, Clarkson, MI) using a commercially available kit (CRP SPQ Test System; DiaSorin Inc, Stillwater, MN).

IL-6 levels were determined using a commercially available quantitative sandwich enzyme immunoassay kit (R&D Systems Quantikine High Sensitivity Enzyme-Linked Immunosorbent Assay kit for human IL-6, Minneapolis, MN). Intra-assay and interassay coefficients of variation were less than 5% and less than 10%, respectively. Serum albumin concentrations were estimated by means of dye-binding end-point reaction using the Cobas Fara II automated centrifugal analyzer.[18] Transferrin was analyzed by means of immunoturbidimetric analysis using antiserum and standard (Behring Diagnostics, La Jolla, CA). Coefficients of variation for albumin and transferrin were less than 6%.

Nutritional and functional measures. The size of skeletal muscle mass was determined by estimating the cross-sectional area of types I and II muscle fibers at baseline and 48 hours after strength testing at 12 weeks. For this, vastus lateralis muscle samples were obtained by percutaneous needle biopsy, as previously reported.[13] Samples were stained for myofibrillar adenosine triphosphatase and analyzed under light microscopy (original magnification ×280) using optical densities determined using NIA Image Software, version 1.39, modified for our laboratory (SyLoc Consulting LLP, Lexington, MA) with a coefficient of variation of 3%.[19] Seventy to 100 fibers per subject per time point were analyzed.

Body weight was measured to the nearest 0.1 kg on a Toledo Weight-Plate (Bay State Scale & Systems Inc, Burlington, MA). Height was measured once to the nearest 0.25 cm without shoes using a wall-mounted stadiometer. Body mass index was determined from body weight and height as kg/m^2.

Whole-body muscle strength, a determinant of functional status, was assessed from 1RM testing twice before randomization and once after 12 weeks. The greater of 2 baseline 1RM values was used to set initial training loads and for analyses. Baseline and final muscle strength were calculated as the sum of 1RM measures for all machines used for testing.

Biochemical measures. These measures included serum creatinine and urea nitrogen concentrations measured using a Cobas Fara II automated centrifugal analyzer and GFR determined from iodine 125–iothalamate clearance (Glofil; Cypros Pharmaceutical Corp, Carlsbad, CA). Hematocrit and hemoglobin were measured using a Serono-Baker 9000 cell counter (Serono Laboratories, Norwell, MA). Coefficients of variation of these measures were less than 6.5%. Plasma volume shifts were determined from pre-exercise and postexercise hematocrit and hemoglobin measurements using the equation developed by Costill and Fink.[20]

Statistical Analysis

Statistical analysis was performed using SPSS 10.0 for Windows (SPSS Inc, Evanston, IL). Results are considered statistically significant if 2-tailed P is less than 0.05. Variables were checked for normality. Data are shown as mean ± SD, except for non–normally distributed variables, for which geometric mean and median are shown.

Baseline comparisons between groups were assessed by means of 2-independent-sample tests using t-test for normally distributed continuous variables, Mann-Whitney test for non–normally distributed continuous variables, and chi-square for categorical variables. Treatment group effect (resistance training versus control) on change in each study outcome (inflammation, negative acute-phase proteins, nutritional, functional, and biochemical) was determined by linear regression analysis for normally distributed variables and median regression analysis for non–normally distributed variables and adjusted for sex and baseline body weight (the only variable significantly different between groups despite randomization). Additionally, analysis of CRP and IL-6 also was adjusted for each respective baseline value because of observed trends for these markers to be different between groups. Finally, Spearman's correlation analyses of both groups combined was performed to determine the association between absolute changes (delta) in each inflammatory marker and those observed for nutritional (skeletal muscle fiber areas) and functional (muscle strength) variables controlled for sex and baseline body weight. For purposes of the figures, non–normally distributed inflammatory markers were plotted as log-transformed variables.

RESULTS

There were no differences between groups at baseline in physiological, biochemical, or health parameters, except for body weight (Table 1).

Systemic Inflammation

Table 2 lists markers of inflammation (acute and negative acute-phase proteins). Twelve weeks of resistance training resulted in a significant reduction in circulating CRP and IL-6 levels compared with the control group. Conversely, serum transferrin concentrations improved significantly with resistance exercise training, whereas there was no change in control subjects. These results remained statistically significant after adjusting for sex, baseline body weight, and each respective baseline inflammatory marker, as appropriate. There was a trend for an improvement in serum albumin concentrations, shown by a modest 3% increase with exercise compared with a −2% reduction in the low-protein diet alone or control group. Plasma volume changes before and after the intervention showed small nonsignificant shifts equivalent to −1.5% ± 2.5% in the resistance-training group and 0.6% ± 3.2% in the control group, respectively ($P = 0.289$).

Nutritional and Functional Status

Nutritional and functional variables are listed in Table 3. Body weight was significantly different between groups at baseline despite randomization. However, body weight was maintained

Table 1. Baseline Subject Characteristics

Variables	Low-Protein Diet + Resistance Training (n = 14)	Low-Protein Diet Alone (control) (n = 12)	*P** Baseline Comparisons
Age (y)	65 ± 9	64 ± 12	0.835
Sex (F/M)	6/8	3/9	0.340
Body weight (kg)	84.6 ± 15.8	76.1 ± 13.5	0.034
Body mass index (kg/m^2)	29.3 ± 6.6	26.8 ± 2.7	0.108
Hematocrit (%)*	33.7 (31.6)	33.2 (33.1)	0.938
Hemoglobin (g/dL)	11.6 ± 1.7	11.3 ± 1.3	0.523
GFR (mL/min/1.73 m^2)	29.3 (24.8)	29.7 (30.0)	0.859
Serum creatinine (mg/dL)	2.29 (2.12)	2.76 (2.29)	0.425
Serum urea nitrogen (mg/dL)	26.4 (24.1)	23.5 (29.1)	0.350
Serum albumin (g/dL)	3.7 ± 0.3	3.8 ± 0.4	0.873
CRP (mg/L)	7.8 (6.0)	6.2 (6.0)	0.106
Serum IL-6 (pg/mL)	11.3 (10.5)	7.7 (6.9)	0.089
No. of chronic conditions	5.5 ± 1.5	6.4 ± 1.7	0.159
No. of medications†	5.6 ± 2.4	6.4 ± 1.6	0.341
Current smoker % (n)	7.1 (1)	8.3 (1)	0.910

NOTE. Values expressed as mean ± SD and geometric mean (median), unless noted otherwise. To convert serum creatinine in mg/dL to μmol/L, multiply by 88.4; urea nitrogen in mg/dL to mmol/L, multiply by 0.357; and hemoglobin and albumin in g/dL to g/L, multiply by 10.

*Baseline comparisons between groups were assessed by means of 2-independent-sample tests using *t*-test for normally distributed continuous variables, Mann-Whitney test for non–normally distributed continuous variables, and chi-square for categorical variables.

†Frequency of use per medication prescribed in all study participants (N = 26) was as follows: angiotensin-converting enzyme inhibitors, β-blockers, and nephrovitamins (16 of 26 patients); calcium-channel blocker (14 of 26 patients); diuretics (12 of 26 patients); aspirin (11 of 26 patients); cholesterol-lowering agents (8 of 26 patients); insulin, oral hypoglycemics, and allopurinol (5 of 26 patients); antiacid, hormone replacement therapy, and antidepressants (4 of 26 patients); epoetin, prednisone, thyroid replacement, albuterol, bronchodilator, and colchicine (2 of 26 patients); and warfarin and digoxin (1 of 26 patients). Proportion of use of each of these medications was not different between groups.

with resistance training, whereas there was a significant loss in the low-protein diet alone (control) group. Body mass index did not change within or between groups. Resistance-exercise training significantly increased types I and II skeletal muscle fiber size compared with mean reductions observed in the control group. In addition to the gains observed in muscle mass, subjects randomly assigned to resistance training also showed significant gains in whole-body muscle strength compared with those randomly assigned to the control group. The latter showed significant mean losses in muscle mass and muscle function. Differences in nutritional and functional measures between groups remained statistically significantly after adjusting for sex and baseline body weight.

Dietary Compliance

Dietary counseling from screening to week 12 of the intervention resulted in a 24% reduction in protein intake in each group.[13] Adherence to the low-protein diet indicated that subjects in the resistance-training group consumed an average of 108% ± 8% of the target protein, whereas subjects in the low-protein diet alone group consumed approximately 112% ± 12%. These estimates were not different between groups. Mean energy intake was similarly low in both groups. Mean energy intake in exercisers was 67.7 ± 26.9 and 76.4 ± 32.2 j/kg/d at 0 and 12 weeks, respectively. For control subjects, energy intake was 87.1 ± 28.4 j/kg/d at week 0 and 98.3 ± 24.9 j/kg/d at 12 weeks.

Secondary Analyses

We observed a direct correlation between changes in CRP and IL-6 levels ($r = 0.46$; $P = 0.04$). More importantly, we found significant inverse associations between changes in serum IL-6 levels and type I ($r = -0.58$; $P = 0.02$; Fig 1) and type II muscle fiber size ($r = -0.68$; $P =$

Table 2. Systemic Inflammation

Dependent Variables	Low-Protein Diet + Resistance Training (n = 14)	Low-Protein Diet Alone (control) (n = 12)	*P** Group Effect
CRP (mg/L)			
Week 0	7.8 (6.0)	6.2 (6.0)	
Week 12	6.1 (6.0)	7.7 (6.0)	
Change	−1.7 (0.0)	1.5 (0.0)	0.049
Serum IL-6 (pg/mL)			
Week 0	11.3 (10.5)	7.7 (6.9)	
Week 12	6.9 (6.5)	10.0 (9.8)	
Change	−4.2 (−3.6)	2.3 (3.0)	0.012
Serum transferrin (mg/dL)			
Week 0	178 ± 32	175 ± 34	
Week 12	258 ± 52	177 ± 37	
Change	80 ± 25	2 ± 34	0.042
Serum albumin (g/dL)			
Week 0	3.7 ± 0.3	3.8 ± 0.4	
Week 12	3.8 ± 0.2	3.6 ± 0.4	
Change	0.1 ± 0.2	−0.2 ± 0.2	0.091

NOTE. Data expressed as mean ± SD and geometric mean (median). To convert transferrin in mg/dL to g/L, multiply by 0.01; albumin in g/dL to g/L, multiply by 10.

*Treatment group effect on change in each main outcome was determined by means of linear regression analysis for normally distributed variables and median regression analysis for non–normally distributed variables, adjusted for sex, baseline body weight, and each respective baseline inflammation marker (ie, CRP or IL-6 level), as appropriate.

Table 3. Nutritional and Functional Parameters

Dependent Variables	Low-Protein Diet + Resistance Training (n = 14)	Low-Protein Diet Alone (control) (n = 12)	*P** Baseline Comparisons	*P*† Group Effect
Body weight (kg)				
Week 0	84.6 ± 15.8	76.1 ± 13.5	0.034	
Week 12	84.8 ± 16.2	72.5 ± 9.0		
Change	0.2 ± 2.6	−3.6 ± 1.5		0.049
Body mass index (kg/m^2)				
Week 0	29.3 ± 6.6	26.8 ± 2.7	0.108	
Week 12	29.3 ± 6.6	25.7 ± 2.1		
Change	0.0 ± 0.8	−1.1 ± 0.7		0.232
Type I muscle fiber area (μm^2)				
Week 0	3,887 ± 1,566	4,578 ± 1,524	0.334	
Week 12	4,821 ± 1,411	3,960 ± 998		
Change	934 ± 1,486	−618 ± 967		0.031
Type II muscle fiber area (μm^2)				
Week 0	3,626 ± 1,216	3,957 ± 988	0.504	
Week 12	4,437 ± 1,393	3,399 ± 814		
Change	811 ± 1,479	−558 ± 1,126		0.045
Muscle strength (kg)				
Week 0	298 ± 106	265 ± 86	0.453	
Week 12	384 ± 123	230 ± 94		
Change	86 ± 45	−35 ± 62		0.001

NOTE. Data expressed as mean ± SD.

*Baseline comparisons between groups were assessed using *t*-test for 2 independent samples.

†Treatment group effect on the change in each main outcome was determined by means of linear regression analysis adjusted for sex and baseline body weight.

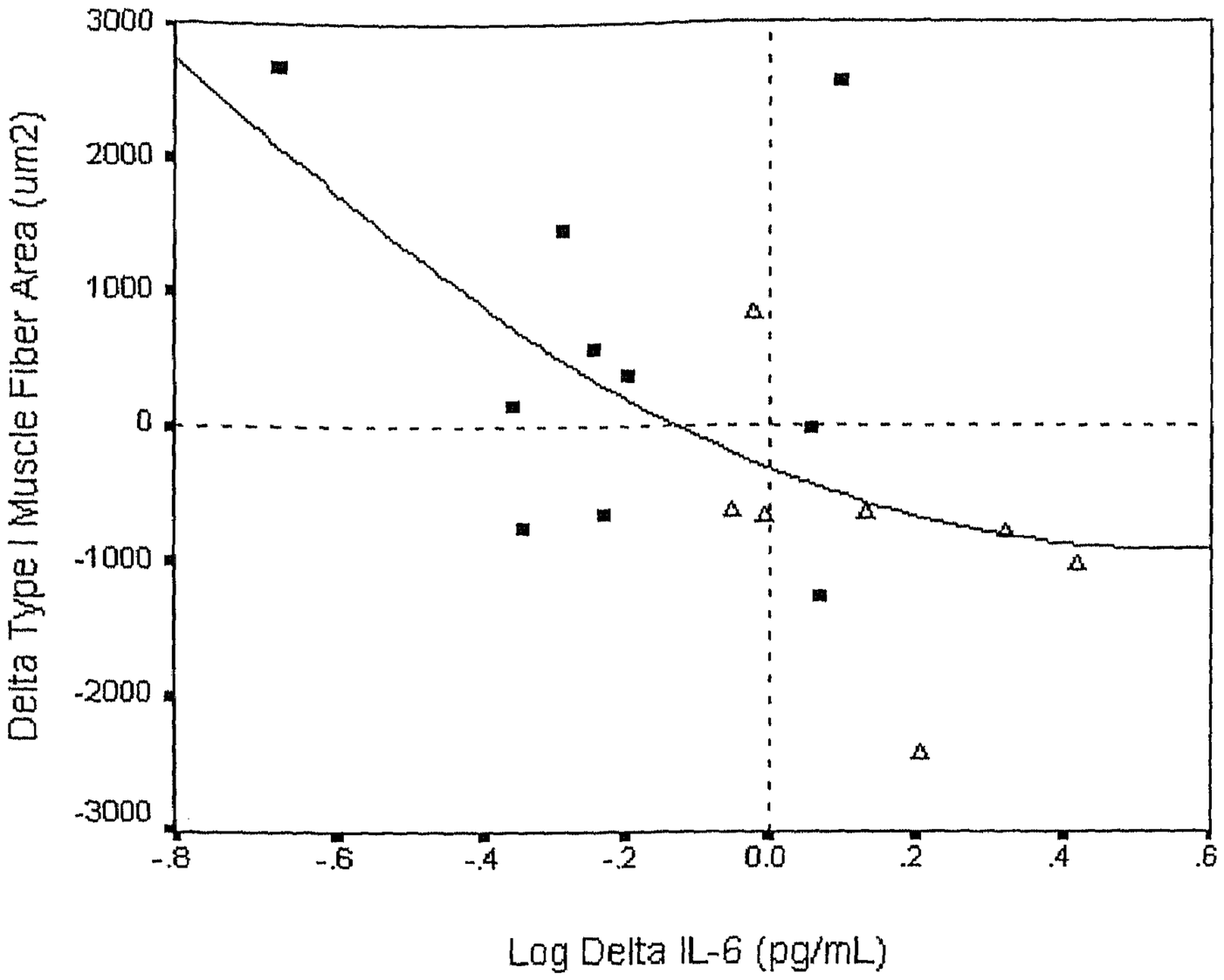

Fig 1. Spearman's correlation analyses between absolute change (delta) in serum IL-6 levels and delta in type I muscle fiber cross-sectional area, controlled for sex and baseline body weight, are shown for each subject in the resistance-training (squares) and control (triangles) groups ($r = -0.58$; $P = 0.02$). This figure shows log-transformed IL-6 levels.

0.005; Fig 2), as well as for muscle strength ($r = -0.49$; $P = 0.05$; Fig 3), after adjusting for sex and baseline body weight. We did not observe significant associations between changes in CRP levels and skeletal muscle areas for either fiber type. However, there was a similar inverse association between changes in CRP levels and muscle strength ($r = -0.45$; $P = 0.03$). In

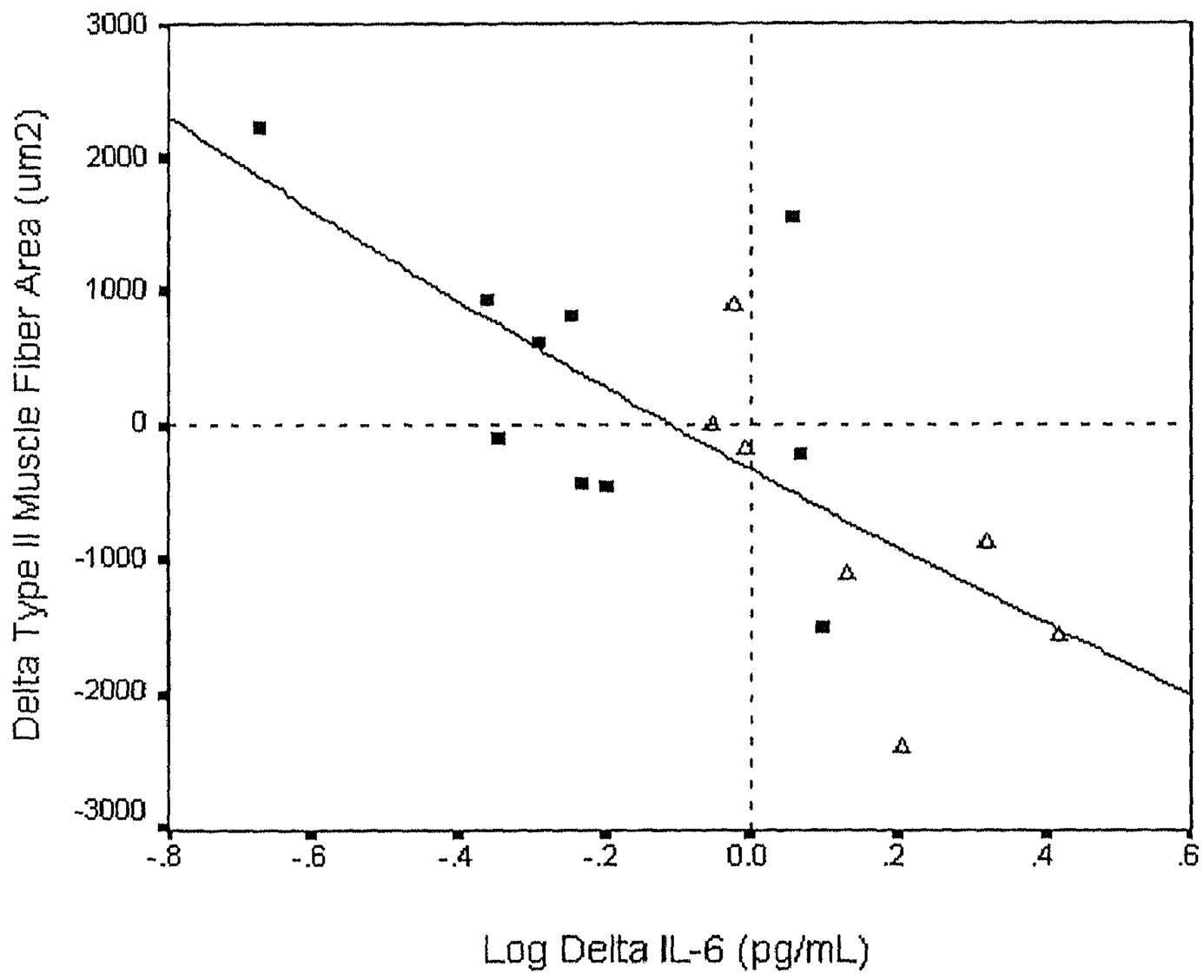

Fig 2. Spearman's correlation analyses between absolute change (delta) in serum IL-6 levels and delta in type II muscle fiber cross-sectional area, controlled for sex and baseline body weight, are shown for each subject in the resistance-training (squares) and control (triangles) groups ($r = -0.68$; $P = 0.005$). This figure shows log-transformed IL-6 levels.

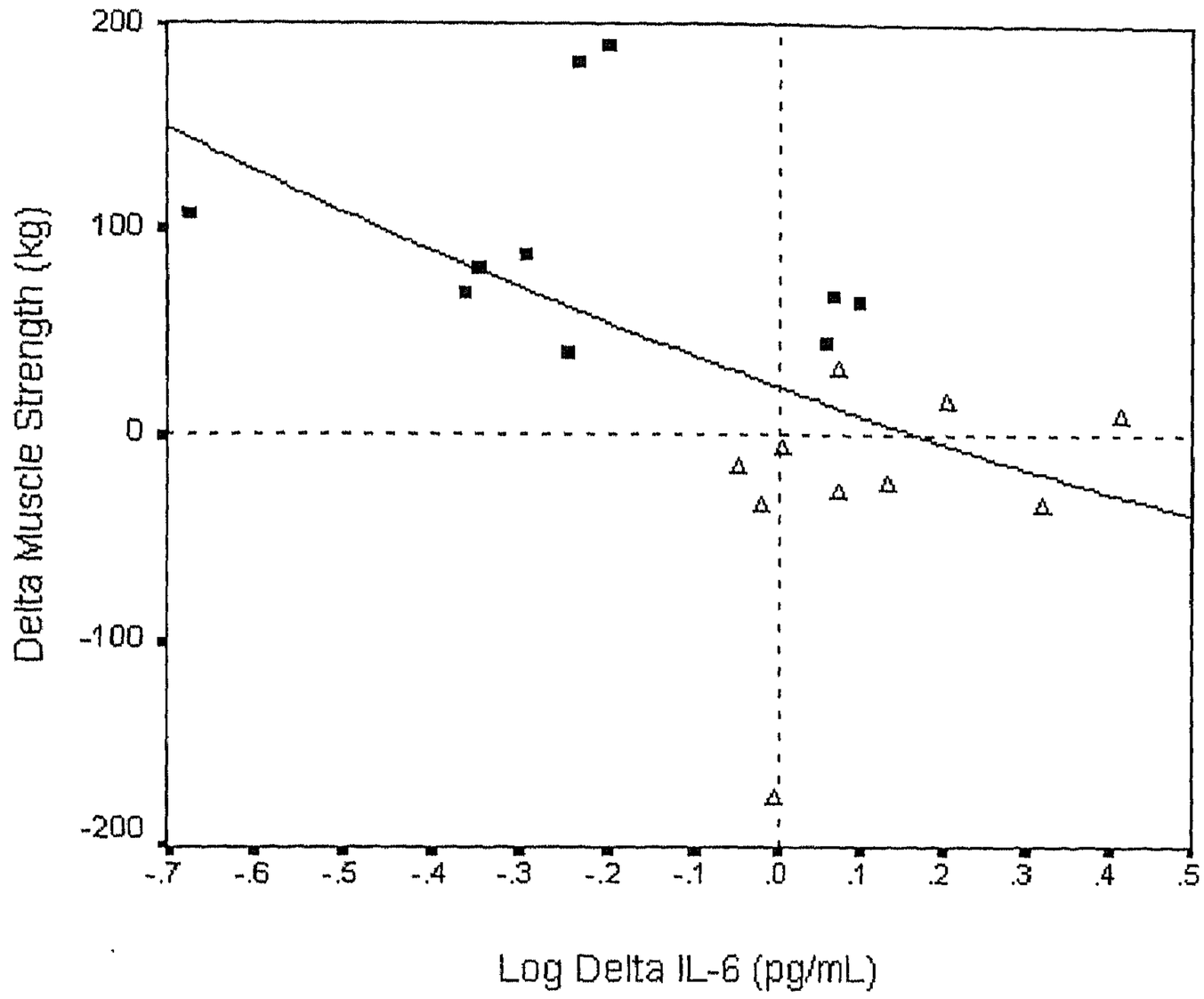

Fig 3. Spearman's correlation analyses between absolute change (delta) in serum IL-6 levels and delta in whole-body muscle strength, controlled for sex and baseline body weight, are shown for each subject in the resistance training (squares) and control (triangles) groups ($r = -0.49$; $P = 0.05$). This figure shows log-transformed IL-6 levels.

addition, we found an inverse association between changes in CRP levels and those for serum albumin levels ($r = -0.47$; $P = 0.05$).

DISCUSSION

This study shows that individuals with moderately severe chronic kidney disease, consuming a low-protein diet and undergoing resistance training for 12 weeks, showed a reduction in systemic inflammation characterized by declines in serum CRP and IL-6 levels. A concomitant increase in serum albumin and transferrin concentrations was observed. Muscle hypertrophy and strength also improved significantly with resistance training. The observed reduction in inflammatory mediators was significantly associated with improved nutritional status and functional capacity.

Causes of protein-energy malnutrition in patients with chronic kidney disease are not well understood. However, contributing factors may include inadequate dietary intake, metabolic acidosis, insulin resistance, comorbid conditions, and inflammation.[12,21,22] IL-6 stimulates the production of CRP, a positive acute-phase protein.[23] Serum CRP concentrations reflect the activity of cytokine-mediated inflammatory processes and are approximately proportional to the extent of tissue injury.[23] Cytokine-mediated inflammation is associated with muscle wasting and hypoalbuminemia,[7,23-25] hospitalization,[7] cardiovascular atherosclerotic disease,[4,10,11] and survival[5,25,26] in patients with chronic kidney disease. Therefore, maintenance of nutritional status and reduction of inflammation to the levels observed in this study of resistance-exercise training are provocative and need to be investigated further in this patient population.

Circulating IL-6 levels greater that 1.8 pg/mL were significantly associated with reduced muscle mass and muscle strength in a cohort of well-functioning older men and women from the Health, Aging, and Body Composition Study.[27] Chronic disease conditions characterized by activation of the innate immune system and persistent acute-phase response (ie, rheumatoid arthritis,[28] cardiac heart failure,[29] and diabetes[30]) also have elevated serum IL-6 levels associated with muscle wasting and cachexia. Additionally, Johansen et al[31] found a significant association between the proinflammatory cytokine IL-1β and loss of body cell mass, estimated from the bioelectrical impedance–derived variable referred to as phase angle.[32]

We observed significant inverse associations

between longitudinal changes in serum IL-6 levels and changes in skeletal muscle fiber size and muscle strength. These findings suggest that a potent anabolic stimulus like resistance training may reverse the catabolic state of chronic kidney disease by its beneficial effects on inflammation and nutrition. This study is not designed to examine potential mechanisms for such effects. However, our finding of reductions in IL-6 and CRP levels with resistance training independent of other cofactors suggests that the anabolic influence of resistance training may have shifted the available, although limited, amino-acid pool toward protein synthesis (ie, muscle hypertrophy and visceral proteins). This may be caused in part by downregulation of proinflammatory cytokines, while increasing the action of anabolic mediators such as insulin-like growth factor, as others have shown.[33,34] In the absence of this anabolic stimulus, as in the case of control subjects, the effect of the low-protein diet leads to worsening of nutritional status and systemic inflammation.

Albumin and transferrin are considered negative acute-phase proteins for which circulating concentrations decrease with inflammation. Modest hypoalbuminemia (albumin <4.0 g/dL [<40 g/L]) has been associated with increased mortality risk in the general population[35] and individuals with chronic kidney disease.[36] In the presence of an inflammatory state, albumin synthesis is reduced, whereas that of acute-phase reactant proteins such as CRP is increased.[37]

The inverse relationship between serum albumin and CRP concentrations that we found is suggestive of the inflammatory process and consistent with the same observations by others.[31,36] Resistance training increased transferrin levels and maintained serum albumin levels during the study period.

Findings by Kaysen et al[38] from a large cohort of patients with kidney failure on hemodialysis therapy provide a rational for protein and energy supplementation for optimal nutrition management. Our data provide yet another promising therapeutic modality, resistance training, with the potential to improve malnutrition-inflammation complex syndrome of chronic kidney disease. The efficacy of resistance training has been tested in a few studies of patients with earlier stages of chronic kidney disease,[13] as well as in patients with kidney failure treated by hemodialysis.[39-42] These studies consistently showed that resistance training increases muscle mass, muscle function, and quality of life in individuals with kidney failure.

Some limitations of the present study should be considered. First, unlike CRP levels, circulating IL-6 levels are not clinically available. However, the significant association between these 2 markers suggests that measuring only 1 of them may be sufficient to accurately assess the inflammatory process. Of note is that findings of the present study are based on single CRP and IL-6 measurements at each time point. Second, the resistance training intervention prescribed in the present study required rigorous screening and supervision. Therefore, these findings may not be applicable to individuals with different stages of kidney disease. Third, these preliminary findings may not apply to individuals with chronic renal insufficiency not consuming a low-protein diet. Fourth, sample size was small. However, the outcomes measured showed statistical significance in agreement with the expected direction of hypothesized change after adjusting for variables found to have a confounding effect, such as sex, body weight, and baseline levels of inflammatory markers.

In conclusion, findings of this study suggest that resistance training may reverse malnutrition-inflammation complex syndrome of chronic kidney disease implicated in the poor prognosis of individuals with kidney disease. Although maintenance dialysis therapy and kidney transplantation promote extended survival in kidney failure, these therapies may be less effective in improving nutritional status and quality of life. Therefore, long-term interventions of resistance training should be investigated further as novel therapeutic approaches for this patient population are being considered.

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