Exercise and Weight Loss in Obese Older Adults with Knee Osteoarthritis: A Preliminary Study

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OBJECTIVE: The purposes of this pilot study were to determine if a combined dietary and exercise intervention would result in significant weight loss in older obese adults with knee osteoarthritis, and to compare the effects of exercise plus dietary therapy with exercise alone on gait, strength, knee pain, biomarkers of cartilage degradation, and physical function.

DESIGN: Single-blind, two-arm, randomized clinical trial conducted for 24 weeks.

SETTING: A university health and exercise science center.

PARTICIPANTS: Twenty-four community-dwelling obese older adults aged ≥ 60 years, body mass index ≥ 28, knee pain, radiographic evidence of knee osteoarthritis, and self-reported physical disability.

INTERVENTION: Randomization into two groups: exercise and diet (E&D) and exercise alone (E). Exercise consisted of a combined weight training and walking program for 1 hour three times per week. The dietary intervention included weekly sessions with a nutritionist utilizing cognitive-behavior modification to change dietary habits to reach a group goal of an average weight loss of 15 lb (6.8 kg) over 6 months.

MEASUREMENTS: All measurements were conducted at baseline and 3 and 6 months, except for synovial fluid analysis, which was obtained only at baseline and 6 months. In addition, weight was measured weekly in the E&D group. Physical disability and knee pain were measured by self-report and physical performance was measured using the 6-minute walk and stair climb tasks. Biomechanical testing included kinetic and kinematic analysis of gait and isokinetic strength testing. Synovial fluid was analyzed for levels of total proteoglycan, keratan sulfate, and interleukin-1 β.

RESULTS: Twenty-one of the 24 participants completed the study, with one dropout in the E&D group and two in the E group. The E&D group lost a mean of 18.8 lb (8.5 kg) at 6 months compared with 4.0 lb (1.8 kg) in the E group ($P = .01$). Significant improvements were noted in both groups in self-reported disability and knee pain intensity and frequency as well as in physical performance measures. However, no statistical differences were found between the two groups at 6 months in knee pain scores or self-reported performance measures of physical function. There was no difference in knee strength between the groups, with both groups showing modest improvements from baseline to 6 months. At 6 months, the E&D group had a significantly greater loading rate ($P = .03$) and maximum braking force ($P = .01$) during gait. There were no significant between-group differences in the other biomechanical measures. Synovial fluid samples were obtainable at both baseline and 6 months in eight participants (four per group). The level of keratan sulfate decreased similarly in both groups from an average baseline of 96.8 ± 37.1 to 71.5 ± 23 ng/μg total proteoglycan. The level of IL-1 decreased from 25.3 ± 9.8 at baseline to 8.3 ± 6.1 pg/mL. The decrease in IL-1 correlated with the change in pain frequency ($r = -0.77$, $P = .043$).

CONCLUSIONS: Weight loss can be achieved and sustained over a 6-month period in a cohort of older obese persons with osteoarthritis of the knee through a dietary and exercise intervention. Both exercise and combined weight loss and exercise regimens lead to improvements in pain, disability, and performance. Moreover, the trends in the biomechanical data suggest that exercise combined with diet may have an additional benefit in improved gait compared with exercise alone. A larger study is indicated to determine if weight loss provides additional benefits to exercise alone in this patient population. **J Am Geriatr Soc 48:1062–1072, 2000.**

Key words: disability, physical function, diet

Osteoarthritis is the most common rheumatic disease and currently affects over 20 million Americans, mostly older adults.[1,2] Joints affected by osteoarthritis are characterized by degradation and loss of articular cartilage.[2,3] Cartilage loss is accompanied by hypertrophic changes in neighboring bone, appearing as sclerosis and osteophytes. The major symptoms of osteoarthritis, which occur in 25 to 50% of persons with radiographic evidence of the disease, are joint pain and stiffness.[4,5] The joint damage and chronic pain from osteoarthritis lead to muscle atrophy, decreased joint range of motion, instability, and, ultimately, to physical disabili-

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ry.[6,7] Indeed, the high prevalence, long duration, pain, and limited efficacy of therapeutic drugs make osteoarthritis one of the most frequent causes of physical disability in older adults.[8]

The knee is the most often affected weight-bearing joint and is second only to the hand as the most common site of osteoarthritis.[4] In certain populations, the incidence of symptomatic knee osteoarthritis is higher than hand or hip osteoarthritis.[9] In addition to age,[5,9–12] obesity is strongly associated with the development of knee osteoarthritis.[13–15] Moreover, obesity exacerbates pain and disability once the disease is clinically manifest.[16] The first National Health and Nutrition Examination Survey (NHANES I) epidemiologic follow-up study found that greater body mass index (BMI) at age 40 years was a major factor contributing to disability 10 years later.[17]

Obesity is a preventable and modifiable risk factor. In the Framingham Knee Osteoarthritis Study, weight loss significantly decreased the risk of subsequent development of symptomatic knee osteoarthritis.[18] Weight loss is often recommended for obese patients with knee osteoarthritis and is included in recent American College of Rheumatology guidelines for the medical management of hip and knee osteoarthritis.[19] The feasibility and potential benefit of a weight loss program for patients with knee osteoarthritis, however, has not been established.

Aerobic exercise is a safe and effective noninvasive therapy for osteoarthritis that improves physical function and relieves symptoms, with effects comparable to those associated with drug therapy.[20,21] Indeed, exercise maintains or increases joint range of motion, enhances stability, and improves functional mobility and muscular strength.[6,22,23] More specifically, a program of supervised fitness walking and education improved functional status without exacerbation of arthritis-related symptoms in a cohort of persons aged 40 years and older with knee osteoarthritis.[20] Furthermore, physical conditioning exercises have helped improve aerobic capacity, walking time, and even depression in persons with rheumatoid arthritis and osteoarthritis.[24] Recent work from our laboratory has shown, however, that exercise without dietary intervention in an older osteoarthritic cohort improves physical function but does not result in significant weight loss.[25] The purposes of this pilot study were to determine if a combined dietary and exercise intervention would result in significant weight loss in older, obese adults with knee osteoarthritis, and to compare the effects of exercise plus dietary therapy with exercise alone on gait, strength, knee pain, biomarkers of cartilage degradation, and physical function.

METHODS

Design

This study was a single-blind, randomized clinical trial designed to determine the effects of 6 months of exercise, and exercise and dietary interventions on weight loss, knee pain, gait mechanics, knee strength, physical performance, and synovial fluid biomarkers of cartilage degradation in older, obese adults with knee osteoarthritis. The study was approved by the university institutional review board.

Participants

The eligibility criteria for participation in the study were: (1) age ≥60 years; (2) calculated BMI ≥ 28 (BMI = weight/height (kg/m^2)); (3) knee pain on most days of the month; (4) self-reported difficulty in at least one of the following activities ascribed to knee pain: walking one quarter mile (three to four city blocks); climbing stairs, bending, stooping, or kneeling (e.g., to pick up clothes); shopping, housecleaning, or other self-care activities; getting in and out of bed; standing up from a chair; lifting and carrying groceries; or getting in and out of the bathtub; (5) radiographic evidence of tibiofemoral osteoarthritis as determined by a single observer and based on weight-bearing anteroposterior X-rays[19]; and (6) willingness to undergo testing and intervention procedures.

Potential participants were excluded if they: (1) had a serious medical condition that prevented safe participation in an exercise program; (2) planned to leave the area or be admitted to a nursing home within the next 6 months; (3) were unable to walk at least 420 ft in 6 minutes without a cane or other assistive device; (4) were unable to walk on a treadmill without a cane or other assistive device; (5) were participating in a regular exercise program more than one time per week for 20 minutes per session; (6) were participating in another research study; (7) were unable to participate in most of the facility-based intervention; or (8) would not be able to complete the protocol, in the opinion of the clinical staff, because of frailty, illness, or other reasons.

Participants who met the inclusion criteria had a physical examination and an exercise stress test to exclude for cardiovascular disease. Upon meeting all eligibility requirements they completed baseline testing then were randomized into two groups: exercise and diet (E&D) (n = 13), and exercise (E) only (n = 11). All participants were encouraged to continue medications and other treatments as prescribed by their physicians. No attempts were made to alter medication regimens or to manage the participants' medical problems, including osteoarthritis. First aid and emergency care were available for the participants, if necessary. The use of acetaminophen and cold or heat packs was recommended if needed. Descriptive characteristics of the two groups are shown in Table 1.

Interventions

Exercise

Both groups exercised 3 days per week, 1 hour per day, for 6 months. The exercise program consisted of a combination of aerobic walking and strength training exercises. Exercise sessions began and ended with 5-minute warm-up and cool-down periods. The exercise phase included two 10-minute walking sessions separated by 20 to 30 minutes of

Table 1. Descriptive Characteristics (Mean ± SE) of the Exercise and Exercise and Diet Groups

	Exercise (n = 11)	Exercise and Diet (n = 13)
Age (years)	69 ± 5	67 ± 4
Weight (lbs)	239 ± 37	201 ± 28
BMI (kg/m^2)	38 ± 6	35 ± 5
Gender		
Male	4	3
Female	7	10

strength training. Participants were provided with an aerobic exercise prescription that included walking within a heart rate range of 50–75% of heart rate reserve. Each strength training session consisted of 10 to 12 repetitions of the following exercises: leg extension, toe raise, leg curl, military press, upright row, chest fly, and pelvic tilt. Upper body exercises were performed with dumbbells and lower body exercises with cuff weights. A 1- to 1.5-minute rest interval separated each exercise. All exercise sessions were supervised by American College of Sports Medicine certified exercise leaders. Exercise and attendance logs were used to gather data and monitor progress.

Dietary therapy

The primary objective of the dietary therapy was a group mean weight loss of at least 15 lb (6.8 kg) over the 6-month intervention period. The E&D group participated in a 1-hour nutrition class each week. Participants were instructed on how to modify caloric intake in the context of a well-balanced, nutritious diet to lose body weight. Cognitive-behavioral modification strategies were used to promote behavior change.[26] After an introductory session, three group sessions and one individual session were held monthly. Each group session was used to review a topic, followed by food-tasting of several well-balanced, low-fat, nutritious meals, prepared with widely available food products. The individual sessions were used to answer questions, solve problems, and set goals. Weight for those in the E&D group was measured weekly and recorded to the nearest 0.1 lb. Participants were provided a packet containing 4-day food records along with the necessary instructions for proper completion, and a calendar marked with the days in which the record was to be kept. Food records were completed at baseline and 3 and 6 months by all participants. In addition, the E&D group kept food records 4 days per week for the duration of the trial.

Measurements

Data collection visits occurred at baseline and 3 and 6 months, and included the recording of body weight, completion of self-report questionnaires, physical performance tests, and analysis of gait. Synovial fluid aspiration was performed at baseline and 6 months. Age, race, educational attainment, income, and comorbid condition data were obtained by self-report at baseline. The data collection staff was blinded to the group assignment of the participants.

The frequency and intensity of knee pain during ambulation and transfer were assessed using a scale specifically developed for patients with knee osteoarthritis.[27] Briefly, subjects rated the frequency of knee pain during the past week on six activities of daily living using Likert scales from 1 (never) to 5 (always). In addition, the subjects were asked to rate the intensity of knee pain during the past week on Likert scales from 1 (no pain) to 6 (excruciating pain) during the same six activities. Ambulation activities included walking a short distance and up and down a flight of stairs, while transfer activities included getting in and out of a bed, car, and chair. Scores for each activity were averaged to give frequency and intensity pain scores for ambulation and transfer activities.[27]

Disability was measured by self-report of physical function using the Fitness Arthritis and Seniors Trial (FAST) Functional Performance Inventory.[28] This measure uses 23 questions to assess perceived difficulty with a number of activities, including activities of daily living (ADLs), complex or instrumental ADLs, ambulation, transferring, and upper extremity strength. For each activity, the participants were asked, "How much difficulty, if any, do you have doing (name of activity), over the past month, because of your health?" The scale for each question ranged from 1 (no difficulty) to 5 (unable to do). Totals were added and averaged to generate a summary score. Ambulation, transfer, and summary scores are presented here.

Two physical performance tasks, with high test-retest reliability (>0.85) for patients with knee osteoarthritis, were administered.[28] These included the distance walked in 6 minutes and a timed stair climbing task.[28] General instructions, a demonstration, including a question-and-answer period, and a habituation period preceded the testing. Participants were asked to perform both tasks as quickly as possible without wearing a watch. No cues or encouragement were given during the testing.

Biomechanical measures of function included kinematic and kinetic analyses of gait and isokinetic strength testing. Two days before each test interval (baseline and 3 and 6 months), subjects' freely chosen walking speeds were assessed using a Lafayette Model 63501 photoelectric control system interfaced with a digital timer. The photocells were positioned 7.3 m apart on an elevated walkway. After three practice trials, subjects traversed the 7.3-m course six times. Freely chosen walking speed was calculated as the mean of the six trials. This speed (±3.5%) was used in all subsequent gait evaluations for the particular test period. To control for the effects of footwear on gait, each subject wore a pair of Etonic Stable Air Base athletic shoes during testing. Clothing consisted of a close fitting sleeveless shirt and nylon gym shorts.

Kinematic analysis was performed using high-speed video analysis (60 Hz) with a Motion Analysis Corporation 60/200 Hz monochrome video camera interfaced to a VP 320 dynamic image processor, a Panasonic 60-Hz VHS video recorder, and a microcomputer. The camera was positioned 5.28 m from and perpendicular to the subjects' lateral side. Reflective markers, used to aid computer digitization, were placed on each side of the subject in the following locations: acromium process, iliac crest, greater trochanter, joint line of the knee, lower third of the tibia, calcaneus, and fifth metatarsal.

Using the photoelectric timers mentioned above, the subjects were instructed to walk along a 22.5-m walkway at their freely chosen walking speed (±3.5%). The raw data were smoothed using a Butterworth low-pass digital filter with a cutoff frequency of 6 Hz. The kinematic variables calculated included knee and ankle ROM (i.e., total range of motion in one gait cycle) and mean absolute angular velocities (i.e., velocity averaged across the stance and swing phase); knee and ankle maximum flexion and extension angular velocities; walking velocity (centimeters per second); stride length; cadence (steps per minute); and stance time. Selection of the knee and ankle joints for analysis was based on previous work that showed that long-term exercise influenced knee and ankle kinematics but had no positive effect on hip kinematics.[29] Three videotaped trials for the most affected and least affected sides were analyzed and averaged to yield representative values for each subject. All joint angles were positive in flexion (dorsiflexion) and negative in extension (plantar flexion).

Kinetic analysis was performed after completion of the kinematic analysis and a subsequent rest period. Ground reaction force data were collected as subjects walked along the same walkway. The walkway was equipped with an AMTI force platform interfaced with a six-channel amplifier and a microcomputer. The force platform was mounted in concrete within the walkway and was set to sample data at 500 Hz. Walking speed was monitored as noted above.

Each subject was instructed to walk along the walkway at their freely chosen walking speed (±3.5%) and contact the force platform in normal stride with either the right or left foot. Sufficient practice time was allowed to habituate the subjects to the testing environment. The order of trials (i.e., right vs left foot) was randomized to limit any practice effect. An acceptable trial constituted walking within the designated range of velocities and contacting the force platform with the correct foot while maintaining normal gait mechanics. Three acceptable trials were obtained for each foot and averaged to yield representative values. The force variables selected for analysis included the vertical and anteroposterior (braking and propulsive) components of the ground reaction force.

Knee concentric strength was assessed using a Kin-Com 125E isokinetic dynamometer. Before testing, a warm-up period was provided to habituate the subjects to the testing equipment. Each subject was secured with the torso and tested leg strapped to the testing chair, hands across the chest, the axis of the dynamometer aligned with the knee, and the resistance pad attached to the lower leg proximal to the ankle joint. Gravity effect torque was calculated based on the subject's leg weight at a 45° angle. An angular velocity of 30° per second was used for all tests. The activation force for each muscle group was set at 50% of maximal voluntary isometric contraction. Setting of a relatively high activation force was based on reports that the amount of activation force significantly influences the magnitude of the average force recorded.[30,31]

Knee extensors and knee flexors were tested through a joint arc from 90° to 30° (0° = full extension). The first and last 10° were subsequently deleted to account for the acceleration and deceleration of the dynamometer at the ends of the range of motion, and also to account for possible inconsistent effort.[32] Hence, average force was calculated as the average force between joint angles of 40° and 80°. A rest period of 30 to 60 seconds was used between each trial. Subjects were instructed to give a maximal effort. Two maximal reproducible trials were averaged and the maximum number of trials for each test condition did not exceed six.[32] The most affected leg was tested for each test.

Synovial fluid biomarker measurements were performed using fluid obtained from the most symptomatic knee joint. A minimum of 0.5 mL of fluid was required for the biomarker assays. Immediately after aspiration, the fluid was centrifuged to remove cell debris and then frozen at −70°C until completion of the study when the samples were assayed for total sulfated proteoglycan (PG), keratan sulfate (KS) PG, and interleukin-1β (IL-1). Total sulfated PG was measured by its ability to bind to the dye dimethymethylene blue (DMMB assay) as previously described.[33,34] KS was measured using the monoclonal antibody 5D4 in an inhibition ELISA.[35,36] The 5D4 antibody and purified PG standard were kindly provided by Dr. Bruce Caterson, University of Wales at Cardiff. Enzyme-linked immunosorbent assay (ELISA) plates (Dynatech Immulon 2 plates; obtained from Dynatech Laboratories, Chantilly, VA) were coated overnight with chondroitinase ABC-digested bovine nasal cartilage A1D1 purified PG (25 ng/mL of post-chondroitinase digestion product in 20 mM sodium carbonate, pH 9.6). After washing and blocking with 1% bovine serum albumin, samples predigested with

Table 2. Knee Pain Intensity and Frequency Scores During Ambulation and Transfer Activities Across the 6-month Intervention Period

Variable	Group	Adjusted Baseline	3 Months	6 Months	%Δ	*P*-value (Within Group)
Ambulation intensity	E	2.60	1.68 (0.53)	1.57 (0.41)	40	.032*
	E&D		1.74 (0.29)	2.21 (0.36)	15	.307
Ambulation frequency	E	3.60	2.88 (0.80)	2.21 (0.66)	39	.067
	E&D		2.59 (0.45)	2.10 (0.59)	42	.029*
Transfer intensity	E	2.34	2.15 (0.13)	1.60 (0.14)	32	.151
	E&D		1.66 (0.33)	1.57 (0.41)	33	.089
Transfer frequency	E	3.21	3.11 (0.60)	1.99 (0.33)	38	.022*
	E&D		2.37 (0.33)	1.72 (0.42)	46	.004*

Adjusted baseline and 3- and 6-month mean values (±SE) plus the % change from adjusted baseline values to 6 months are presented.
Scales: intensity (1 = no pain to 6 = excruciating pain) and frequency (1 = never to 5 = always).
Note: a positive value for %Δ denotes an improvement from baseline.
*Within group difference: 6 months < baseline.
E = exercise; E&D = exercise and diet.

Table 3. Physical Performance Measures Across the 6-Month Intervention Period

Variable	Group	Adjusted Baseline	3 Months	6 Months	%Δ	*P*-value (Within Group)
6 minute walk (ft)	E	1408	1649 (58)	1718 (41)	22	<.001*
	E&D		1700 (55)	1821 (36)	29	<.001*
Stair climb (seconds)	E	9.81	8.19 (0.40)	8.67 (0.36)	12	.005*
	E&D		8.08 (0.39)	7.39† (0.32)	25	<.001*

Adjusted baseline and 3- and 6-month mean values (±SE) plus the % change from adjusted baseline values to 6 months are presented.
Note: a positive value for %Δ denotes an improvement from baseline.
*Within-group difference: 6 months different from baseline.
†Between-group difference: E&D < E, $P = 0.02$.
E = exercise; E&D = exercise and diet.

Table 4. Self-reported Physical Function Measures Across the 6-Month Intervention Period

Variable	Group	Adjusted Baseline	3 Months	6 Months	%Δ	*P*-value (Within Group)
Ambulation	E	2.65	1.97 (0.18)	2.00 (0.18)	25	.002*
	E&D		2.12 (0.17)	1.64 (0.16)	38	<.001*
Transfer	E	1.88	1.52 (0.11)	1.50 (0.11)	20	.003*
	E&D		1.52 (0.11)	1.44 (0.10)	23	<.001*
Summary score	E	1.77	1.51 (0.09)	1.48 (0.10)	17	.008*
	E&D		1.58 (0.09)	1.42 (0.09)	20	<.001*

Adjusted baseline and 3- and 6-month mean values (±SE) plus the % change from adjusted baseline values to 6 months are presented.
Scales: 1 = no difficulty to 5 = unable to do.
Note: a positive value for %Δ denotes an improvement from baseline.
E = exercise; E&D = exercise and diet.
*Within-group difference: 6 months < baseline.

hyaluronidase were serially diluted and added to the coated wells along with serially diluted standards of the coating PG. A 1:100,000 dilution of 3D4 was then added to the wells and the plates were incubated for 2 hours at 37°C followed by a second antibody (rabbit anti-mouse IgG at 1:5000) and colorometric detection. Results for the samples were calculated from the linear portion of the standard inhibition plot. Intra- and interassay coefficients of variation were less than 5%. The quantification of IL-1β was by sandwich ELISA with amplification using an enzyme-linked coagulation assay (ELCA) to increase the sensitivity of the assay.[34] Microtiter plates (NUNC) were coated with a monoclonal antibody against human IL-1β (R&D Systems, Minneapolis, MN) at 1 μg/mL and blocked with 1% bovine serum albumin. Synovial fluid samples and IL-1 standards from 1600–2.2 pg/mL (IL-1β from Cistron Biotechnology, Pine Brook, NJ) were next added to the coated wells followed by a 1:1000 dilution of polyclonal anti-human IL-1β (Sigma, St. Louis, MO) labeled with Russell's viper venom. The plates were incubated overnight at 4°C. Unbound material was washed out and bound antibody was detected with the ELCA system as described.[37]

Statistical Analysis

After eligibility was determined, subjects were randomized to one of the two groups. The effects of the interventions on weight loss, knee pain, gait mechanics, physical performance, and knee strength at 6 months postrandomization were determined by repeated measures analysis of covariance (ANCOVA). Analyses were conducted using SAS PROC MIXED,[38] which analyzes all available follow-up information. Analyses of group differences were adjusted for the prerandomization levels of baseline factors. This comparison adjusts for small random imbalances between the groups and provides for a precise and unbiased estimate of treatment effects. All reported *P*-values are two-sided.

In addition, within group pre-post intervention comparisons were estimated and tested using repeated measures analyses. These results are similar to a paired *t* test.

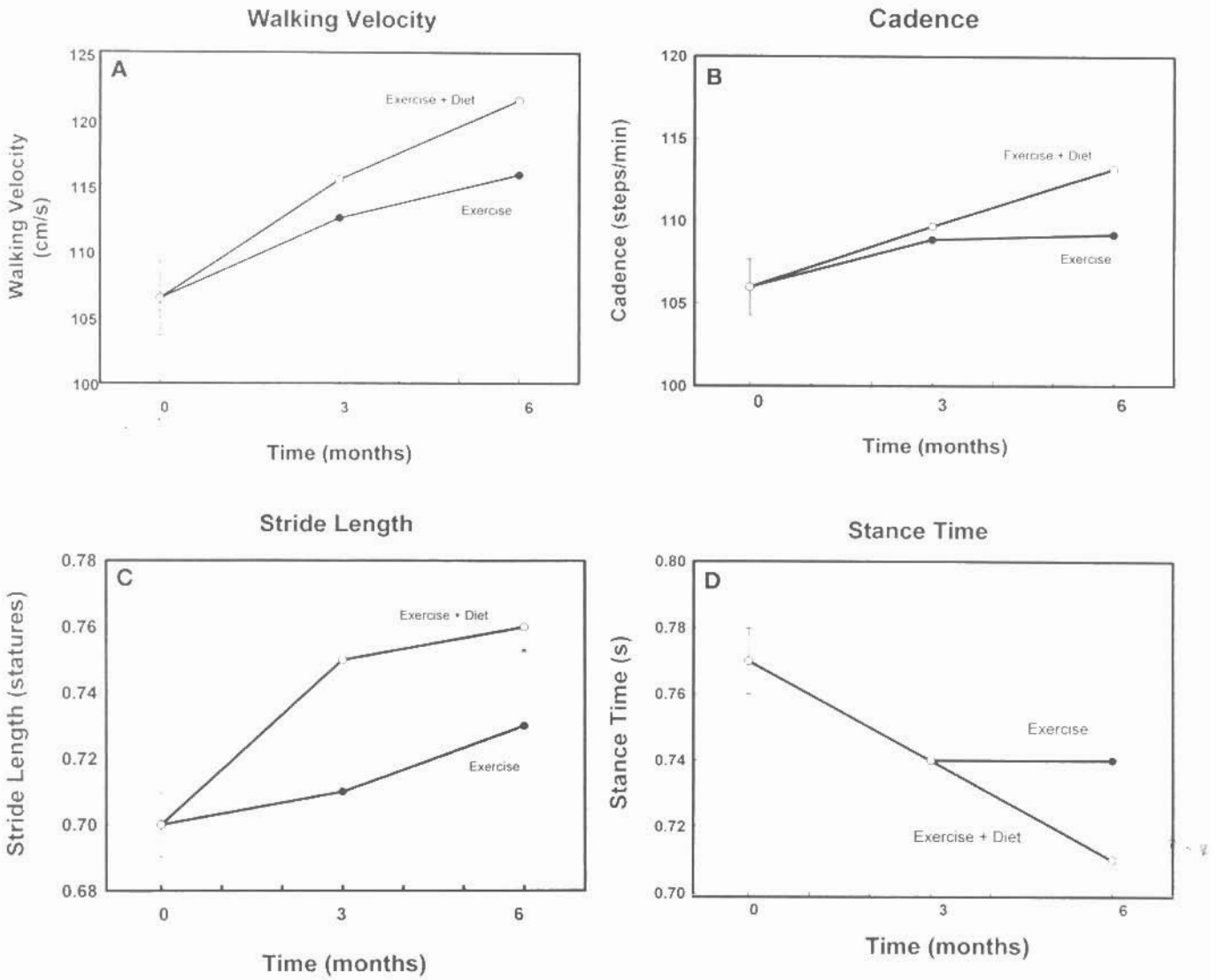

Figure 1. Temporal characteristics of gait across the 6-month intervention period for the exercise and exercise and diet groups. Adjusted baseline (0) and 3- and 6-month data are presented. (A) Walking velocity, (B) cadence, (C) stride length, and (D) stance time. For clarity, the mean SE across the two intervention groups is shown only at baseline. * Denotes significant ($P = .03$) between-group main effect

RESULTS

Retainment and Compliance

Twenty-one (87.5%) of the 24 participants completed the study. One participant from the E&D group and two from the E group dropped out. One did not wish to continue, one left for medical reasons, and the third subject left for family illness. Percent compliance to the exercise program was defined as the ratio of the number of exercise sessions attended to the number of exercise sessions prescribed. Compliance was 82.6% and 94.7% for the E and E&D groups, respectively.

Weight Loss, Knee Pain, and Physical Performance

After adjusting for baseline differences in body weight, the E&D group weighed significantly less ($P = .007$) than the E group after the 6-month intervention. The exercise group lost an average of 4.0 lb (1.8 kg), whereas the E&D group lost an average of 18.8 lb (8.5 kg).

Both groups showed similar and significant improvements in ambulation and transfer pain measures. The range of improvements for the E group was 32 to 40% from adjusted baseline values, whereas the E&D group's improvements ranged from 15 to 46% (Table 2). There were no significant differences in knee pain frequency or intensity between groups after the 6-month intervention.

There was a significant difference in the stair climb physical performance task between the groups (Table 3). The E&D group improved stair climb time by 25%, whereas the E group improved 12%. There was, however, no between-group difference in 6-minute walk distance. Both groups improved walk distance from baseline. More specifically, the distance walked increased by 22% and 29% in the E and the E&D groups, respectively.

There were no significant between-group differences in adjusted 6-month self- reported measures of physical function. The greatest mean percentage change from adjusted baseline values was noted in ambulation, with a 25% im-

provement in the E group and a 38% improvement in the E&D group (Table 4).

Gait Mechanics

Temporal Characteristics

There was a significant group main effect for normalized stride length, with the E&D group exhibiting a longer stride length consequent to the 6-month intervention than the E group ($P = .03$). There were no between-group differences in stance time, walking velocity, or cadence (Figure 1A–D). Finally, there were significant within-group effects, with 6-month values being greater than baseline values for walking velocity, cadence, and stride length ($P \leq .05$). Stance time was significantly shorter ($P \leq .01$) at 6 months relative to baseline in both groups.

Kinematics

Analysis of knee and ankle kinematic variables revealed no significant between-group main effects. Generally, knee and ankle range of motion and angular velocities increased across the 6-month intervention for both groups. Of particular note was the significantly greater knee mean angular velocity within the E&D group at 6 months relative to the baseline value (Table 5).

Kinetics

The E&D group showed significantly greater loading rate ($P = .02$) (most affected leg) and maximum braking force ($P < .01$) values than the E group after the 6-month intervention. In general, the magnitude of all the force variables increased for both groups across the 6-month intervention. These data are presented in Table 6 and Figure 2.

Muscular Strength

Analysis of the strength data using an ANCOVA revealed no significant differences in mean concentric flexion and concentric extension between the groups (Figure 3). Strength values tended to increase more from baseline to 6 months in the E group compared with the E&D group.

Synovial Fluid Biomarkers

Synovial fluid samples (average of 1.4 mL; range, 0.5–4 mL) were obtained at both baseline and at 6-month follow-up in only 8 of the 24 subjects. At baseline the required minimum of 0.5 mL of fluid was aspirated from 14 of the 24 subjects, with the other 10 subjects having insufficient amounts of fluid aspirated. At the 6-month follow-up, reaspiration of the same joint was attempted in the 14 subjects who had sufficient fluid obtained at baseline and at least 0.5 mL of fluid was obtained in 8 of the 14. Levels of KS did not change

Table 5. Knee and Ankle Joint Range of Motion and Angular Velocities Across the 6-Month Intervention Period

Variable	Group	Adjusted Baseline	3 Months	6 Months	%Δ	*P*-value (Within Group)
Knee ROM (degrees)	E	55.27	55.42 (0.62)	56.73 (1.02)	3	.170
	E&D		57.05 (0.59)	56.47 (0.91)	2	.209
Knee mean velocity (degrees/second)	E	110.05	115.72 (2.87)	117.44 (3.28)	7	.036*
	E&D		117.03 (2.75)	122.70 (3.00)	12	<.001*
Knee maximum extension velocity (degrees/second)	E	−356.36	−368.84 (8.64)	−367.38 (11.71)	3	.359
	E&D		−374.10 (8.27)	−385.94 (10.42)	8	.011*
Ankle ROM (degrees)	E	29.64	29.77 (0.77)	31.56 (0.86)	7	.037*
	E&D		31.74 (0.74)	31.66 (0.75)	7	.014*
Ankle mean velocity (degrees/second)	E	72.00	77.23 (1.94)	79.75 (2.11)	11	.002*
	E&D		81.33 (1.87)	83.25 (1.87)	16	<.001*
Ankle maximum plantarflex velocity (degrees/second)	E	−267.25	−282.25 (6.08)	−289.89 (9.81)	9	.032*
	E&D		−296.44 (5.85)	−301.19 (8.68)	13	<.001*

Adjusted baseline and 3- and 6-month mean values (±SE) plus the % change from adjusted baseline values to 6 months are presented.
Note: a positive value for %Δ denotes an improvement from baseline.
Negative velocity values denote extension and plantarflexion movement.
E = exercise; E&D = exercise and diet.
*Within-group difference: 6 months > baseline.

Table 6. Vertical and Anteroposterior Ground Reaction Forces Across the 6-Month Intervention Period

Variable	Group	Adjusted Baseline	3 Months	6 Months	%Δ	*P*-value (Within Group)
Vertical impact peak (% BW)	E	1.03	1.05 (.01)	1.06 (.01)	3	.049*
	E&D		1.06 (0.01)	1.08 (0.01)	5	<.001*
Vertical propulsive peak (% BW)	E	1.00	1.00 (0.01)	1.01 (0.01)	1	.096
	E&D		1.00 (0.01)	1.01 (0.01)	1	.059
Maximum braking (% BW)	E	0.145	0.158 (0.01)	0.164† (0.01)	13	.003*
	E&D		0.172 (0.01)	0.185 (0.01)	28	<.001*
Maximum propulsive (% BW)	E	−0.165	−0.179 (0.01)	−0.179 (0.01)	9	<.010*
	E&D		−0.182 (0.01)	−0.186 (0.01)	13	<.001*

Adjusted baseline and 3- and 6-month mean values (±SE) plus the percentage change from adjusted baseline values to 6 months are presented.
Note: a positive value for %Δ denotes an improvement from baseline.
E = exercise; E&D = exercise and diet.
*Within-group difference: 6 months > baseline.
†Between-group difference: E&D > E, $P = 0.01$.
BW = Body weight.

significantly during the study. The baseline level of KS was 2.81 ± 1.15 μg/mL and the final level was 2.20 ± .62 μg/mL. The proportion of KS to total PG, measured using the DMMB assay, decreased from 96.83 ± 37.11 ng KS/μg total PG at baseline to 71.50 ± 23.01 ng KS/μg PG at the end of the study, but this also did not reach statistical significance. Levels of IL-1β, an inflammatory cytokine that may play an important role in mediating cartilage degradation in osteoarthritis,[39,40] decreased significantly ($P < .04$) from 25.325 ± 9.75 pg/mL at baseline to 8.306 ± 6.112 pg/mL at study completion (Figure 4). A correlation analysis was performed with change in IL-1 level and change in the pain scores. The decrease in IL-1 was found to correlate with the decrease in total pain frequency ($r = -0.77$, $P = .04$) but not intensity ($r = -0.04$, $P = .922$).

DISCUSSION

Using a dietary intervention combined with exercise, we achieved a significant weight loss in a cohort of community-dwelling, older, obese adults with disabling knee osteoarthritis. Weight loss is frequently recommended to overweight patients with knee osteoarthritis; however, to our knowledge this is the first study to demonstrate that significant weight loss can be realized in this population. Although the amount of weight loss necessary to be of clinical benefit for patients with knee osteoarthritis is unknown, the average weight loss of 18.8 lb (8.5 kg) noted in our E&D group exceeded the 11-lb (5-kg) average that Felson and colleagues[24] showed can result in a 50% decrease in the odds of developing knee osteoarthritis 10 years later. Parenthetically, exercise without specific dietary intervention resulted in only a 4.0-lb (1.8 kg) weight loss.

The E&D group showed greater between-group improvements in measures where weight may have a greater effect. Specifically, relative to the E group the E&D group significantly improved stair climb time and stride length and had nonsignificant improvements in walking velocity, cadence, and 6-minute walk. These data suggest that the subjects in the E&D group may have had better mobility during activities of daily living than their E group counterparts.

Walking velocity is the product of stride length and cadence. At cadences less than 120 steps/minute, an increase in walking velocity is accomplished by increasing stride length and cadence equally.[41] Indeed, this was the case in our cohort. More specifically, cadence and stride length increased 3% and 4%, respectively, from adjusted baseline values in the E group, while 7% and 9% increases in these variables were found in the E&D group. The significantly greater stride length and, to a lesser extent, the 4% higher cadence in the E&D group accounted for this group's marginally greater walking velocity.

In a recent study from our laboratory, we found that long-term exercise in an older, osteoarthritic population improved walking velocity relative to an attention control group.[29] Furthermore, the evaluation of lower extremity function showed that greater knee and ankle angular velocities were distinguishing characteristics of the exercise groups relative to the control group. In the present study, there were significant increases in knee and ankle joint velocities over the 6-month intervention in both groups with the E&D group consistently demonstrating higher values (*Note:* there were no between-group differences). Although these data do not provide evidence that weight loss provided an added benefit to exercise in improving knee and ankle function, the trends suggest that further study using a larger sample size is warranted.

Previous work has shown that subjects with knee osteoarthritis have a limping gait.[42] This abnormal gait pattern is

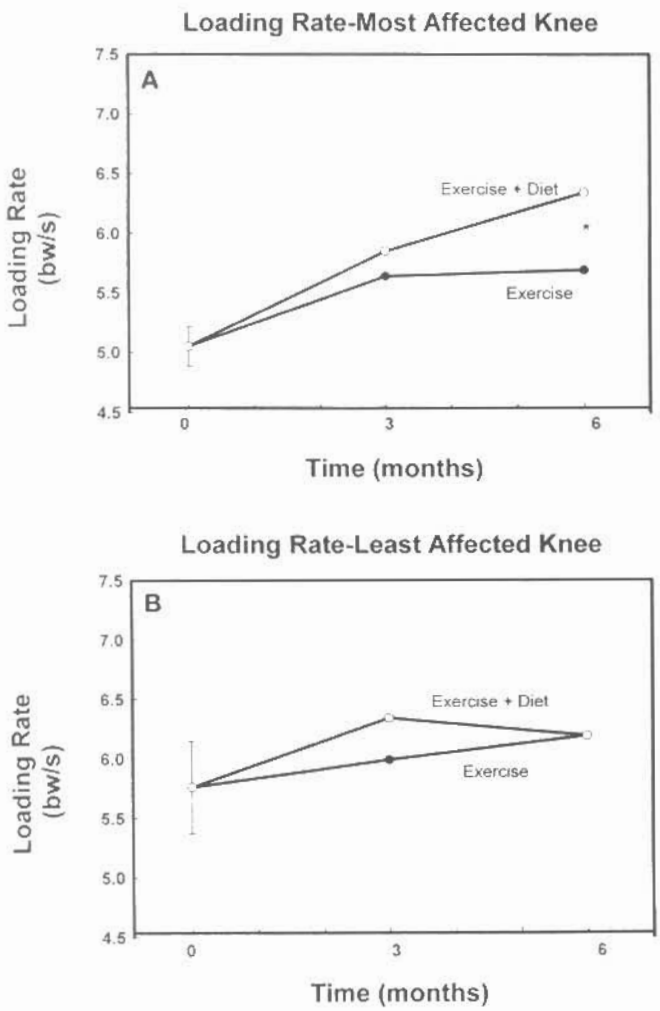

Figure 2. Loading rates for the most affected (A) and least affected (B) legs across the 6-month intervention period for the exercise and exercise and diet groups. Adjusted baseline (0) and 3- and 6-month data are presented. For clarity, the mean SE across the two intervention groups is shown only at baseline. *Denotes significant (P = .02) between-group main effect

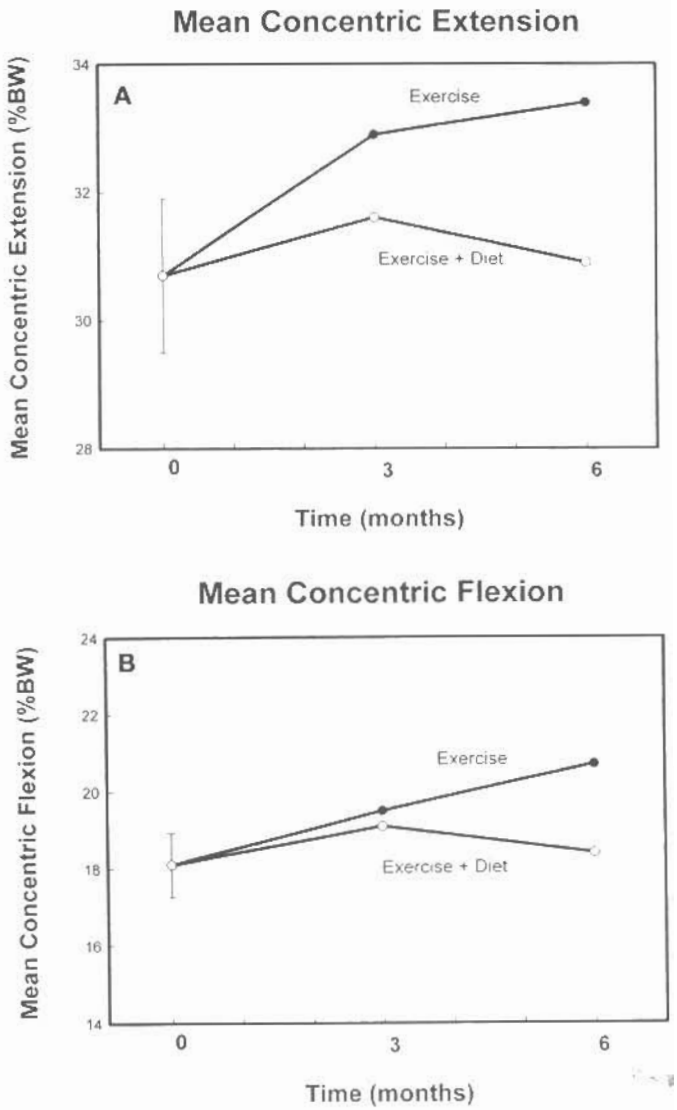

Figure 3. Mean concentric extension (A) and flexion (B) isokinetic strength across the 6- month intervention period for the exercise and exercise and diet groups. Adjusted baseline (0) and 3- and 6-month data are presented. For clarity, the mean SE across the two intervention groups is shown only at baseline.

characterized by greater loading rates on the least affected leg, which the authors suggested was an attempt to shift the body's weight from the affected leg, thereby easing any pain and discomfort. Similarly, adjusted baseline values in the present study showed a greater loading rate on the least affected leg. Of interest was the ability of the E&D group to distribute the loads more evenly by the end of the 6-month intervention (Figure 2), whereas the E group's loading rates remained unbalanced. This suggests that the E&D group was able to eliminate or reduce the limping gait that is characteristic of this population.

Improvements in walking velocity are closely related to the subject exerting greater forces on the ground and thereby increasing the load placed on the lower extremity. Indeed, both groups increased the vertical and anteroposterior ground reaction forces as walking velocity increased. Although these data suggest that both groups exerted a greater load on the lower extremity consequent to the interventions, they also managed to reduce knee pain and improve measures of physical function. It appears that the greater loads did not adversely affect knee pain or measures of physical function. Of interest to our research group is whether a similar weight loss may result in significant long-term improvements in pain and physical function.

The improvements in measures of physical function and pain noted in both groups are comparable to previous studies that examined the effects of exercise interventions in patients with knee osteoarthritis.[20,21,43] For example, previous studies showed an average improvement of 15% in either 6-minute walk distance or 50-foot walk time in subjects participating in 8- to 12-week walking programs compared with the 29% and 22% improvements in the E&D and E groups, respectively, in our 24-week study. Moreover, improvements of 36% (E group) and 24% (E&D group) in pain intensity, and 39% (E group) and 44% (E&D group) in pain frequency compared favorably with the 27% and 24% improvements in arthritis pain in the Kovar[20] and Minor[21] studies, respectively.

Previous short-term exercise studies using similar cohorts found improvements in strength between 9% and

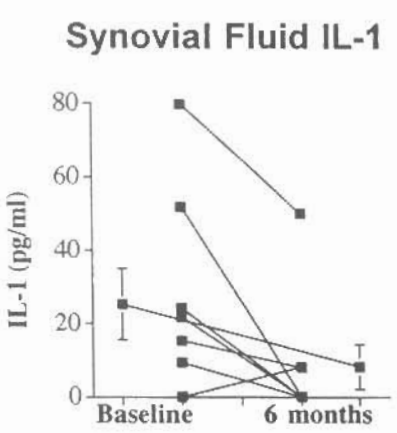

Figure 4. Synovial fluid levels of IL-1 at baseline and 6 months. Combined data for the two intervention groups are presented. A group mean (±SE) is shown along with individual results.

25%.[21,22,44] The E group improved 8.8% and 14.4% in extension and flexion strength, respectively, from adjusted baseline values; however, the E&D group improved less than 3% from the same adjusted baseline means (Figure 3). Closer examination of the means for the E&D group before being adjusted for baseline differences between the groups revealed gains of 9% and 12.4% (extension strength: 0.317 to 0.346 body weight (BW); flexion strength: 0.178 to 0.200 BW). Hence, the improvements in our groups were within the range of previous studies.

In any weight loss program, loss of lean body mass is always a concern. Further scrutiny of our adjusted strength data revealed minimal improvements of less than 5% across both groups when the data were examined in absolute values (N) instead of relative values (%BW). The loss of lean body mass that commonly accompanies weight loss may have contributed to the attenuated gains in absolute strength. Moreover, a large weight loss in an older, predominately female cohort may have an adverse effect on bone mass. Future studies should address these issues when designing their weight loss interventions.

The interventions did not appear to exacerbate osteoarthritis disease activity as measured by levels of synovial fluid biomarkers. Although synovial fluid was only available from 8 of the 24 subjects who entered the study, a significant decrease in the synovial fluid level of IL-1β was noted at 6 months. This inflammatory cytokine has been detected in joint fluids from patients with various forms of arthritis, including osteoarthritis, and is thought to play a role in mediating joint inflammation and cartilage degradation.[39,40,45]

When comparing IL-1β levels in osteoarthritic and rheumatoid arthritic patients, most studies report higher levels in the rheumatoid arthritis cohort. This is consistent with the highly inflammatory nature of this disease. Our study is the first report of which we are aware that has detected a change in IL-1β levels in osteoarthritis. The reduction in IL-1β noted over the course of the study suggests an improvement in disease activity within the joint, specifically a reduction in inflammatory activity. The correlation between the decrease in IL-1β levels and improvement in pain frequency is consistent with a decrease in inflammatory activity and indicates that measurement of IL-1β may be a useful biomarker of disease activity in osteoarthritis. Although it did not reach statistical significance, the reduction in synovial fluid levels of total PG and the proportion of PG measured as KS (mean reduction of 25.33 ng KS/μg PG) are also consistent with a decrease in cartilage degradation over the 6 months of study.

CONCLUSIONS

The results of this study demonstrate that successful weight loss can be achieved in a cohort of older, obese adults with symptomatic osteoarthritis of the knee through a combination of dietary therapy and exercise. The relatively small weight loss in the E group, despite 3 hours per week of exercise and instruction on the importance of weight loss in the management of osteoarthritis, demonstrates the importance of specific dietary therapy and follow-up to achieve significant weight reduction. Moreover, analysis of gait, strength, knee pain, physical function, and biomarkers of disease activity showed positive trends in which both groups improved over the 6-month intervention. Improvements in gait, knee pain, and physical function were generally better in the E&D group. Future work using a larger cohort and a longer intervention period should help clarify the positive impact of combined diet and exercise on older adults with disabling knee osteoarthritis.

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