ORIGINAL ARTICLE

Tai Chi Is Effective in Treating Knee Osteoarthritis: A Randomized Controlled Trial

CHENCHEN WANG,¹ CHRISTOPHER H. SCHMID,¹ PATRICIA L. HIBBERD,² ROBERT KALISH,¹ RONENN ROUBENOFF,³ RAMEL RONES,⁴ AND TIMOTHY MCALINDON¹

Objective. To evaluate the effectiveness of Tai Chi in the treatment of knee osteoarthritis (OA) symptoms.

Methods. We conducted a prospective, single-blind, randomized controlled trial of 40 individuals with symptomatic tibiofemoral OA. Patients were randomly assigned to 60 minutes of Tai Chi (10 modified forms from classic Yang style) or attention control (wellness education and stretching) twice weekly for 12 weeks. The primary outcome was the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain score at 12 weeks. Secondary outcomes included WOMAC function, patient and physician global assessments, timed chair stand, depression index, self-efficacy scale, and quality of life. We repeated these assessments at 24 and 48 weeks. Analyses were compared by intent-to-treat principles. *Results.* The 40 patients had a mean age of 65 years and a mean body mass index of 30.0 kg/m². Compared with the controls, patients assigned to Tai Chi exhibited significantly greater improvement in WOMAC pain (mean difference at 12 weeks –118.80 mm [95% confidence interval (95% CI) –183.66, –53.94; *P* = 0.0005]), WOMAC physical function (-324.60 mm [95% CI –513.98, -135.22; *P* = 0.001]), patient global visual analog scale (VAS; –2.15 cm [95% CI –3.82, -0.49; *P* = 0.01]), physician global VAS (-1.71 cm [95% CI –2.75, -0.66; *P* = 0.002]), chair stand time (-10.88 seconds [95% CI –15.91, -5.84; *P* = 0.00005]), Center for Epidemiologic Studies Depression Scale (-6.70 [95% CI –11.63, -1.77; *P* = 0.009]), self-efficacy score (0.71 [95% CI 0.03, 1.39; *P* = 0.04]), and Short Form 36 physical component summary (7.43 [95% CI 2.50, 12.36; *P* = 0.004]). No severe adverse events were observed.

Conclusion. Tai Chi reduces pain and improves physical function, self-efficacy, depression, and health-related quality of life for knee OA.

INTRODUCTION

Knee osteoarthritis (OA) is an increasing problem in the elderly population, resulting in pain, functional limitation, disability, reduced quality of life, and substantial health care costs (1,2). The pathophysiologic basis of knee

ClinicalTrials.gov identifier: NCT00362453.

Supported by the National Center for Complementary and Alternative Medicine of the NIH (grant R21AT002161).

¹Chenchen Wang, MD, MSc, Christopher H. Schmid, PhD, Robert Kalish, MD, Timothy McAlindon, MD, MPH: Tufts Medical Center, Tufts University School of Medicine, Boston, Massachusetts; ²Patricia L. Hibberd, MD, PhD: Tufts University School of Medicine, Boston, Massachusetts; ³Ronenn Roubenoff, MD, MHS: Tufts Medical Center, Tufts University School of Medicine, Boston, Massachusetts, and Biogen Idec, Cambridge, Massachusetts; ⁴Ramel Rones, BS: Mind-Body Therapies, Boston, Massachusetts.

Address correspondence to Chenchen Wang, MD, MSc, Division of Rheumatology, Tufts Medical Center, Box 406, Tufts University School of Medicine, Boston, MA 02111. E-mail: cwang2@tuftsmedicalcenter.org.

Submitted for publication January 30, 2009; accepted in revised form June 22, 2009.

OA is multifaceted and includes degeneration of articular structures, impaired muscle function, and psychological traits of chronic pain (3–5). To our knowledge, no feasible preventive intervention strategies or effective disease-modifying remedies currently exist for knee OA. Recommended core treatments include physical therapy such as aerobic and muscle strengthening exercise (2,3,6), but these have modest benefits for pain and physical function and may not affect psychological outcomes (7).

Tai Chi is a traditional Chinese mind-body exercise that enhances balance, strength, flexibility, and self-efficacy, and reduces pain, depression, and anxiety in diverse patient populations with chronic conditions (8). As a complementary mind-body approach, Tai Chi may be an especially applicable treatment for older adults with knee OA. The physical component provides exercise consistent with current recommendations for OA (range of motion, flexibility, muscle conditioning, and aerobic cardiovascular exercise) (9); the mental component could address the chronic pain state through effects on psychological wellbeing, life satisfaction, and perceptions of health (10).

Although Tai Chi has spread worldwide over the past 2 decades, scientific evidence to support its efficacy for knee OA has been inconclusive (11). Some benefits were shown in one large-scale randomized controlled trial (RCT), but interpretation of its results was limited by methodologic

The contents of this manuscript are solely the responsibility of the authors and do not necessarily represent the official views of the National Center for Complementary and Alternative Medicine or the NIH.

issues, including enrollment of individuals with hip as well as knee OA, absence of radiographic confirmation, short followup, and poor adherence (12).

A well-designed study may overcome the previous limitations, and we therefore conducted a 12-week RCT with a 1-year followup to test the effects of Tai Chi on pain (a marker of disease activity), functional independence (a marker of impairment), and health-related quality of life in elderly people with knee OA. We hypothesized that participants receiving Tai Chi would show greater improvement in knee pain, physical and psychological functioning, and health status than participants treated with an attention control intervention consisting of wellness education and stretching, and that the benefits would be mediated by effects on muscle function, musculoskeletal flexibility, and mental health.

PATIENTS AND METHODS

Setting and participants. The study was conducted at Tufts Medical Center, an urban tertiary care academic hospital in Boston, Massachusetts. It received ethics approval from the Tufts Medical Center/Tufts University Human Institutional Review Board. A detailed version of the study protocol was reported in 2008 (13).

Patients with knee OA were recruited from the greater Boston area. To ensure adequate enrollment of underrepresented groups, we placed advertisements in local media. We also used the rheumatology clinic patient database at Tufts Medical Center to identify patients with knee OA. For interested respondents, we determined eligibility through a brief, scripted interview that posed questions with predictive values for knee OA that were known from population-based data. Applicants who screened positive on the telephone interview were scheduled for eligibility visits, when written informed consent was obtained.

The eligibility criteria consisted of age \geq 55 years, body mass index (BMI) $\leq 40 \text{ kg/m}^2$, Western Ontario and Mc-Master Universities Osteoarthritis Index (WOMAC) pain subscale score (visual analog version) >40 (range 0-500), and fulfillment of the American College of Rheumatology criteria for knee OA (14) with radiographic Kellgren/ Lawrence scale knee OA grade ≥ 2 (15). We excluded individuals who had prior Tai Chi training or similar types of alternative medicine like Qi Gong or yoga; individuals with serious medical conditions, limiting their ability for full participation as determined by primary care physicians; individuals with intraarticular steroid injections in the previous 3 months, or reconstructive surgery on the affected knee and any intraarticular hyaluronate injections in the previous 6 months; and individuals unable to pass the Mini-Mental examination (score <24) (16).

To avoid bias in favor of the Tai Chi intervention, we informed participants that we were studying the effects of 2 different types of exercise training programs, one of which was combined with nutrition education. Participants were allowed to continue routine medications and maintain their usual visits with their primary care physicians or rheumatologists throughout the study.

Randomization. Participants were randomly assigned to Tai Chi (n = 20) or to an attention control group (n =

20). Randomization assignments were designated by the statistician (CHS), using computer-generated numbers to randomize permuted blocks of sizes 2 and 4 so that each block was complete. They were provided in sealed, opaque envelopes and opened on the patient's agreement to participate. The block size was randomly assigned to minimize correct prediction of assignments, while preserving approximate balance between the groups. Outcomes that required an analysis of knee strength were based on evaluation of the knee reported as most painful at baseline. If both knees were equally affected (which occurred in 2 participants), one knee was chosen at random as the affected knee.

The Tai Chi intervention. Subjects participated in 60minute Tai Chi sessions twice weekly for 12 weeks instructed by a Tai Chi master (Ramel Rones) with more than 20 years of teaching experience. In the first session, we explained Tai Chi theory and procedures and provided the patients with printed teaching materials, including a welltested, validated Institutional Review Board-approved Tai Chi program that described Tai Chi principles, practicing techniques, and safety precautions for knee OA (13,17). For the remaining sessions, each subject practiced Tai Chi under the instruction of the Tai Chi master. Every session included 1) 10-minute self-massage and a review of Tai Chi principles, 2) 30 minutes of Tai Chi movement, 3) 10 minutes of breathing technique, and 4) 10 minutes of relaxation. The program consisted of 10 forms from classic Yang style Tai Chi (18), with minor modifications that were suitable for people with knee pain. This involved eliminating stances that require greater than 90° knee flexion and can cause excess knee joint stress (19). We also provided a Tai Chi DVD published by Ramel Rones. Patients were instructed to practice Tai Chi at least 20 minutes per day at home and encouraged to maintain their usual physical activities, but not to participate in additional new strength training or exercise programs other than Tai Chi. After completing the 24 treatment sessions, we instructed the subjects to continue practicing Tai Chi at home following the DVD and handouts until the 48-week followup visit.

The attention control intervention. The wellness education and stretching program provided an active control for the attention being paid to the Tai Chi group (13,20). The control group attended two 60-minute class sessions per week for 12 weeks. In the first session, research staff explained the program and procedures. A variety of health professionals provided nutrition and medical information in the following sessions. Every session included 40 minutes of didactic lessons on 1) OA as a disease, 2) diet and nutrition, 3) therapies to treat OA, or 4) physical and mental health education (e.g., recognizing and dealing with stress). The nutrition education was based on Dietary Guidelines for Americans (21) and focused on general knowledge of nutrition, cooking, and shopping, but not on specific nutrients and supplements. The final 20 minutes consisted of stretching exercises involving the upper body, trunk, and lower body, with each stretch being held for 10-15 seconds. Participants were instructed to practice at least 20 minutes of stretching exercises per day at home.

They were encouraged to maintain their usual physical activities, but not to participate in additional strength and mind-body exercise programs other than their stretching exercise. The stretching and health information was compiled using materials from our previous program (17) and the Web site of the National Institute of Arthritis and Musculoskeletal and Skin Diseases at the National Institutes of Health (22).

Throughout the 12-week period, we tracked the reasons for missed sessions and the number of missed sessions, and asked the subjects to complete daily logs indicating the amount of time they practiced Tai Chi or stretching exercises.

Outcome measures and followup. Our knee OA outcome measurements were drawn from the core set recommended by the Osteoarthritis Research Society International (23), and focused on pain, physical function, and patients' overall assessment of their knee OA severity. The primary outcome measure was the change in the WOMAC pain subscale between baseline and 12 weeks. The WOMAC is a validated, self-administered instrument specifically designed to evaluate knee and hip OA (24,25). It has 3 subscales that we analyzed separately: pain (score range 0-500), stiffness (score range 0-200), and function (score range 0-1,700), with higher scores indicating more severe disease. Secondary outcomes included weekly WOMAC pain scores during the 0-12-week intervention and assessments of WOMAC function, WOMAC stiffness, and global knee pain status assessed separately by the participant and a study physician (RK) who was blinded to group assignment (visual analog scale score range 0-10, where 0 = no pain) (26). We evaluated physical performance using the timed chair stand (measured in seconds) (27), 6-minute walk test (measured in yards) (28), and standing balance (score range 0-5, where 0 = worst balance) (29). Additional measures included the Center for Epidemiologic Studies Depression Scale (CES-D; score range 0-60, where 0 = no dysphoria) (30), outcome expectations for exercise (score range 1-5, where 1 = nooutcome expectations) (31), self-efficacy (score range 1-5, where 1 = no self-efficacy (32), and the physical component summary and mental component summary of the Short Form 36 to assess quality of life (score range 0-100, where 0 = worst health state) (33). Adherence and occurrence of adverse events were also assessed.

We instructed participants to maintain their regular medications, including nonsteroidal antiinflammatory drugs (NSAIDs) and acetaminophen. We recorded any change of medication use at each assessment. To test durability of response, we repeated outcome measures at the 24- and 48-week followups.

Statistical analysis. We determined the sample size of 40 patients using the results of an RCT conducted at Tufts University that tested an exercise intervention among older adults with knee OA (19). That study enrolled 46 patients and randomized them to either 4-month home-based progressive strength training or an attention control group. The strength training group experienced a 36% decrease in WOMAC pain (the primary outcome; mean \pm SD change of 79 \pm 91) compared with an 11% decrease (mean \pm SD change of 20 \pm 77) in the attention control



Figure 1. Study flow chart. OA = osteoarthritis; BMI = body mass index; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.

group. Based on those numbers, a sample size of 20 per group at an alpha level of 0.05 would have 60% power to detect an expected difference of 59 points. Although we recognized that our study was underpowered for a definitive comparison, we were primarily directed toward gathering preliminary data in order to evaluate this research direction.

We analyzed the data on an intent-to-treat basis. We compared between-group changes in outcomes across all times at 0, 12, 24, and 48 weeks with mixed models, using time and group as categorical fixed factors with random intercepts and first-order autocorrelation of the errors. Similar mixed models were used to examine weekly WOMAC pain analyses from baseline to 12 weeks. Also, we evaluated for potential effects of confounding or interaction with treatment by covariates, including age, sex, BMI, disease duration, disease severity (pain, function, and radiograph score), comorbidities, health status, and use of pain medications. A 2-sided P value less than 0.05 was considered to indicate statistical significance. Results are shown as the between-group differences with 95% confidence intervals (95% CIs) of the differences.

RESULTS

Between October 2005 and February 2006, 366 individuals were screened by telephone and 62 were identified for further evaluation. Forty participants (65%) were found eligible and were randomized to the Tai Chi or attention control group. The remaining participants were excluded for a variety of reasons (Figure 1), the major one being absence of radiographic evidence of knee OA.

Baseline data. Table 1 shows the baseline data of the 40 participants before randomization to the intervention groups. The participants had a mean age of 65 years and

Table 1. Baseline characteristics of the study participants*					
Variable	Tai Chi (n = 20)	Attention control $(n = 20)$	Total (n = 40)		
Demographics					
Women, no. (%)	16 (80)	14 (70)	30 (75)		
Age, years	63 ± 8.1	68 ± 7.0	65 ± 7.8		
White, no. (%)	14 (70)	14 (70)	28 (70)		
Greater than or equal to high school education, no. (%)	20 (100)	19 (95)	39 (98)		
Body mass index, kg/m ²	30.0 ± 5.2	29.8 ± 4.3	29.9 ± 4.8		
Disease condition					
Duration of knee pain (on study knee), years Radiograph score, no. (%)	9.7 ± 7.0	9.7 ± 8.3	9.7 ± 7.6		
K/L grade 2	4 (20)	3 (15)	7 (18)		
K/L grade 3	7 (35)	3 (15)	10 (25)		
K/L grade 4	9 (45)	14 (70)	23 (58)		
Knee surgery, no. (%)	6 (30)	8 (40)	14 (35)		
Knee replacement, no. (%)	1 (5)	1 (5)	2 (5)		
Patient VAS (range 0–10 cm)†	4.2 ± 2.1	4.8 ± 2.0	4.5 ± 2.0		
Physician VAS (study knee; range 0–10 cm)†	4.8 ± 1.7	5.8 ± 2.2	5.3 ± 2.0		
WOMAC pain (range 0-500 mm)†	209.3 ± 58.5	220.4 ± 101.0	214.8 ± 81.7		
WOMAC physical function (range 0–1,700 mm)†	707.6 ± 246.9	827 ± 258.8	767.3 ± 256.9		
WOMAC stiffness (range 0–200 mm)+	105.7 ± 37.3	120.7 ± 50.4	113.2 ± 44.4		
Receiving NSAIDs prior to study, no. (%)	9 (45)	13 (65)	22 (55)		
Receiving analgesics prior to study, no. (%)	4 (20)	6 (30)	10 (25)		
Self-reported comorbidities, no. (%)					
Congestive heart disease	1 (5)	4 (20)	5 (13)		
Hypertension	7 (35)	12 (60)	19 (48)		
Diabetes mellitus	0 (0)	4 (20)	4 (10)		
Health-related quality of life and others					
SF-36 PCS (range 0–100)‡	37.5 ± 8.5	32.0 ± 8.8 §	34.8 ± 9.0		
SF-36 MCS (range 0–100)‡	51.4 ± 12.2	50.8 ± 12.6	51.1 ± 12.3		
CES-D (range 0–60)†	13.6 ± 11.7	9.3 ± 9.2	11.5 ± 10.6		
Self-efficacy score (range 1–5)‡	3.1 ± 1.1	3.3 ± 1.0	3.2 ± 1.0		
Outcome expectation score (range 1–5)¶	4.1 ± 0.6	4.3 ± 0.4	4.2 ± 0.5		
Physical performance					
6-minute walk test, yards	$500.1 \pm 114.3 \#$	488.9 ± 109.2	$494.3 \pm 110.4 * *$		
Balance score (range 0–5)	4.0 ± 0.7	3.8 ± 0.8	3.9 ± 0.7		
Chair stand score, seconds	40.8 ± 13.4	$35.6\pm9.2 \text{\#}$	38.3 ± 11.7 **		

* Values are the mean ± SD unless otherwise indicated. P values were calculated by t-test for continuous variables and by chi-square test or Fisher's exact test for categorical variables. K/L = Kellgren/Lawrence scale; VAS = visual analog scale; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; NSAIDs = nonsteroidal antiinflammatory drugs; SF-36 = Short Form 36; PCS = physical component summary; MCS = mental component summary; CES-D = Center for Epidemiologic Studies Depression Scale.

+ Lower scores indicate improved state.

‡ Higher scores indicate improved state.

P = 0.05.

¶ Higher scores indicate high outcome expectations.

N = 19. ** N = 39.

were mainly women (75%) and white (70%). On average, participants had 10 years of knee pain and a BMI of 30.0 kg/m². There were 2 patients, 1 in each group, who were enrolled with a self-reported asymptomatic total knee replacement (one knee), but also with a symptomatic nonoperated knee (study knee). Baseline characteristics were reasonably well balanced between the groups, although there was somewhat greater knee OA severity and comorbidity in the control group.

Adherence. Attendance for the interventions was 85% for Tai Chi and 89% for attention control over 12 weeks. No patient withdrew from the study (40 of 40 participants completed followup at 12, 24, and 48 weeks). We followed our rigorous study protocol to achieve high levels of adherence and attendance (14). We built a highly experienced and dedicated research team, selected participants who were interested and reliable, accommodated patient preference when scheduling evaluation visits, randomized patients after the baseline evaluation to have a large enough pool for replacements, engaged in friendly personal contact with patients, organized interesting classes, conducted a rigorous quality control program, and prepared a detailed description of the training sessions that we pilot tested prior to the initiation of this study. We offered subjects a monetary incentive to maximize participation and rigorously adhered to the Manual of Operations to enhance compliance.

	Table 2. Changes in prima	ry and secondary outcomes [*]	k						
Improvement from baseline									
Variable	Tai Chi (n = 20)	Attention control (n = 20)	differences, Tai Chi vs. attention control	Pt					
Primary outcome: WOMAC pain (range 0–500 mm)‡									
Week 12	-157.25(-203.11, -111.39)	-38.45(-84.31, 7.41)	-118.80(-183.66, -53.94)	0.0005					
Week 24	-131.55 (-177.41, -85.69)	-64.60(-110.46, -18.74)	-66.95(-131.81, -2.09)	0.05					
Week 48	-115.35(-161.21, -69.49)	-69.20(-115.06, -23.34)	-46.15(-111.01, 18.71)	0.2					
Secondary outcomes	,,	,	,,						
WOMAC physical function (range 0-1 700 mm) [±]									
Week 12	-506.75(-640.66) -372.84)	$-182\ 15\ (-316\ 06\ -48\ 24)$	$-324\ 60\ (-513\ 98\ -135\ 22$	0.001					
Week 24	-44050(-57441 - 30659)	-257.30(-301.21, -123.30)	-183.20(-372.58, 6.18)	0.06					
Week 48	-405.85(-530.76) -271.94)	-30055(-43446, -16664)	-105.20(-204.68.84.08)	0.00					
WOMAC stiffnoss	403.03 (333.70, 271.34)	300.33 (434.40, 100.04)	105.50 (234.00, 04.00)	0.5					
$(range 0-200 \text{ mm})^{\ddagger}$									
Wook 12	-73.05(-94.36, -51.74)	-50.15(-71.46)(-28.84)	-22.90(-53.04, 7.24)	0.1					
Week 24	-65.00(-86.31, -43.69)	-50.20(-71.51, -28.89)	-14.80(-44.94, 15.34)	0.1					
Week 24 Wook 49	-64.15(-95.46, -42.94)	-60.50(-91.91, -20.10)	-2.65(-22.70, 26.40)	0.3					
Dhysician VAS (range 0, 10 cm)	-04.15 (-05.40, -42.04)	-60.50 (-61.61, -39.19)	-3.65 (-33.79, 26.49)	0.0					
Mash 12	+	1 44 (0 10 0 70)		0.000					
Week 12	-3.14(-3.88, -2.41)	-1.44(-2.18, -0.70)	-1.71(-2.75, -0.66)	0.002					
Week 24	-2.59(-3.33, -1.86)	-2.06(-2.80, -1.32)	-0.53(-1.58, 0.51)	0.3					
Week 48	-2.53(-3.27, -1.80)	-1.50(-2.25, -0.75)	-1.03(-2.09, 0.02)	0.06					
(range 0-10 cm)	<i>,</i>		<i>.</i>						
Week 12	-2.98(-4.16, -1.80)	-0.83(-2.00, 0.35)	-2.15(-3.82, -0.49)	0.01					
Week 24	-2.36(-3.53, -1.18)	-1.71 (-2.89 , -0.53)	-0.65 (-2.31 , 1.02)	0.4					
Week 48	-1.65(-2.83, -0.48)	-1.70(-2.87, -0.52)	0.04(-1.62, 1.70)	1.0					
6-minute walk test, yards¶									
Week 12	48.33 (11.15, 85.50)#	-1.76 $(-50.70, 47.18)$	50.08 (-10.34, 110.50)	0.1					
Week 24	53.12 (10.04, 96.21)§	9.41(-33.48, 52.30)	43.71(-15.07, 102.50)	0.1					
Week 48	35.17(-17.29, 87.64)§	20.56 (-20.73, 61.85)	14.61 (-49.36, 78.59)	0.7					
Balance score (range 0–5)¶									
Week 12	0.15(-0.16, 0.46)	0.25(-0.06, 0.56)	-0.10(-0.54, 0.34)	0.7					
Week 24	0.15(-0.16, 0.46)	0.08(-0.24, 0.39)	0.07 (-0.37, 0.52)	0.7					
Week 48	0.35 (0.04, 0.66)	0.46 (0.14, 0.77)§	-0.11 (-0.55 , 0.34)	0.6					
Chair stand time, seconds‡									
Week 12	-12.03(-15.60, -8.46)§	-1.15(-4.70, 2.40)§	-10.88(-15.91, -5.84)	0.00005					
Week 24	-9.87(-13.44, -6.30)§	-4.75(-8.30, -1.20)§	-5.12(-10.15, -0.08)	0.05					
Week 48	-9.22(-12.79, -5.65)§	-3.24(-6.85, 0.37)#	-5.98(-11.06, -0.91)	0.02					
Body mass index, kg/m ²									
Week 12	0.04(-0.27, 0.36)	-0.17(-0.51, 0.17)	0.21(-0.23, 0.66)	0.34					
Week 24	0.10(-0.37, 0.57)	-0.02(-0.38, 0.34)	0.13(-0.45, 0.70)	0.66					
Week 48	-0.07(-0.54, 0.40)	-0.29(-0.72, 0.15)	0.22(-0.40, 0.84)	0.48					
SF-36 MCS (range 0–100)¶									
Week 12	2.14(-2.35, 6.64)	1.93(-2.56, 6.43)	0.21(-6.15, 6.57)	0.9					
Week 24	4.39(-0.11, 8.89)	4.50 (0.00, 9.00)	-0.11(-6.47, 6.25)	1.0					
Week 48	5 80 (1 31 10 30)	1.00(-3.46.5.53)	477(-159,1113)	0.1					
SE-36 PCS (range 0-100)¶	0.00 (1.01, 10.00)	1.01 (0.10, 0.00)	1.77 (1.00, 11.10)	0.1					
Week 12	11 57 (8 08 15 06)	4 14 (0.65, 7.63)	7 43 (2 50 12 36)	0 004					
Week 24	10.80(7.31, 14.20)	6 29 (2 80 9 77)	451(-042.945)	0.001					
Wook 48	10.00(7.01, 14.20) 10.41(6.02, 13.00)	4 10 (0.61, 7.58)	6.32(1.38, 11.25)	0.00					
$CES-D$ (range 0_60)t	10.11 (0.32, 13.30)	1.10 (0.01, 7.30)	0.02 (1.00, 11.20)	0.01					
Wook 12	-740(-1099 - 202)	-0.70(-4.19, 2.79)	-6.70(-11.62 - 1.77)	0.000					
WOOK 12	-6.40(-0.82, -3.92)	-1.10(-4.59, 2.20)	-5.20(-10.22, -0.27)	0.009					
Week 24	0.40 (-9.00, -2.92)	1.10 (-4.00, 2.00) 1.65 (-1.92, 5.12)	-9.00(-12.92, -0.37)	0.04					
Solf officeour coore (7.20 (-10.73, -3.77)	1.05 (=1.65, 5.15)	0.90 (-13.03, -3.97)	0.0000					
Wook 12	0.60 (0.12, 1.02)		0.71 (0.02, 1.20)	0.04					
Week 12	0.00(0.12, 1.00) 0.68(0.20, 1.16)	-0.11(-0.09, 0.07)	0.71(0.03, 1.39) 0.95(0.17, 1.59)	0.04					
Week 24	0.00 (0.20, 1.10) 0.72 (0.24, 1.20)	-0.24 (-0.72, 0.24)	0.00(0.17, 1.33)	0.02					
WEEK 40	0.72 (0.24, 1.20)	-0.24 (-0.72, 0.24)	0.90 (0.28, 1.64J	0.007					

* Values are the mean (95% confidence interval). WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; VAS = visual analog scale; SF-36 = Short Form 36 health survey; MCS = mental component summary; PCS = physical component summary; CES-D = Center for scale; SI-36 = Short Form 36 health survey; MCS = ment Epidemiologic Studies Depression Scale. *P* values were calculated by *t*-test for continuous variables. *Lower* scores indicate improved state.
§ N = 19.
¶ Higher scores indicate improved state. *#* N = 18.



Figure 2. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale over a 12-week intervention period by treatment group. Values are the unadjusted mean. Measurements were obtained weekly over a 12-week period. Error bars show the 95% confidence interval (95% CI), but the data are slightly offset in the figure for clarity. Means with 95% CIs are shown at each line for each group. Linear treads between weeks are indicated by the connected graph. Lower scores indicate improvement in outcome.

At the 24-week followup, 13 (65%) of 20 participants in the Tai Chi group continued to practice Tai Chi, and 12 (60%) of 20 in the control group continued to practice stretching exercises. At the 48-week followup, these rates were 9 (45%) of 20 for Tai Chi and 8 (40%) of 20 for the control group.

Primary outcome: WOMAC pain at 12 weeks. At 12 weeks, the Tai Chi arm exhibited a statistically significant decrease in knee pain, as measured by the WOMAC pain scale, compared with the attention control group. The between-group mean difference was -118.80 (95% CI -183.66, -53.94; P = 0.0005) (Table 2).

Secondary outcomes. Figure 2 shows that the betweengroup mean difference gradually increased during the 12week intervention, based on the nearly linear decline in pain with Tai Chi. Table 2 compares changes in all of the secondary outcomes between groups from baseline to 12, 24, and 48 weeks. These changes are illustrated in Figure 3.

WOMAC pain at 24 and 48 weeks. At 24 and 48 weeks, there remained a large WOMAC pain reduction from baseline, although not as large as at 12 weeks. The reduction was borderline statistically significant at 24 weeks (P = 0.05) but was not statistically significant at 48 weeks (P = 0.2).

WOMAC physical function and stiffness at 12, 24, and 48 weeks. At 12 weeks, participants in the Tai Chi arm exhibited greater improvement in WOMAC physical function compared with the attention control group (mean difference -324.60 [95% CI -513.98, -135.22; P =0.001]). There were non-statistically significant improvements at both 24 and 48 weeks. Tai Chi participants showed more improvement at all times for WOMAC stiffness, although it was not statistically significant.

Patient and physician global assessments. At 12 weeks, compared with the attention control group, participants in the Tai Chi group improved in the subjective self-report patient global assessment by -2.15 (95% CI -3.82, -0.49;

P = 0.01) and in the objective physician global assessment by -1.71 (95% CI -2.75, -0.66; P = 0.002). These changes did not remain statistically significant at 24 and 48 weeks.

Physical performance and BMI. The chair stand time was statistically significantly reduced by -10.88 seconds (95% CI -15.91, -5.84; P = 0.00005) at 12 weeks, 5 seconds at 24 weeks, and 6 seconds at 48 weeks. The Tai Chi group was also able to walk 50, 44, and 15 yards further in 6 minutes at 12, 24, and 48 weeks, respectively, although none were statistically significant. Notably, changes in BMI and balance test at each assessment were not statistically significant.

Quality of life and psychological variables. At 12 weeks, the Tai Chi group improved compared with the control group on the mean physical component summary score by 7.43 (95% CI 2.50, 12.36; P = 0.004), the CES-D by -6.70 (95% CI -11.63, -1.77; P = 0.009), and the self-efficacy score by 0.71 (95% CI 0.03, 1.39; P = 0.04). Small non-statistically significant improvements were seen in both groups on the mental component summary score. Notably, statistically significant improvements on self-efficacy and depression were maintained for Tai Chi at 24 and 48 weeks.

Evaluation for confounding by participant group characteristics. Regression adjustment for baseline characteristics, including radiographic severity and number of comorbidities, revealed no confounding variables or interactions with treatment assignment.

Adverse events. One participant in the Tai Chi group reported an increase in knee pain at the 2-week assessment. This was resolved following modification of that participant's Tai Chi technique. One participant in each assignment group reported newly diagnosed cancer (1 breast cancer, 1 colon cancer) during the 12-week intervention period (the patient in the Tai Chi group missed 4 intervention visits but completed her followup evaluations). No other adverse events were reported.

Analgesics and NSAID use. At baseline, 11 (55%) of 20 participants in the Tai Chi group were receiving analgesics and NSAIDs compared with 14 (70%) of 20 in the attention control group. The numbers decreased to 6 (30%) of 20 for the Tai Chi group and 10 (50%) of 20 for the control group at the 12-week assessment (Table 3). We found no statistically significant differences between the groups who were using any of the 2 categories of medications.

DISCUSSION

Overall, Tai Chi appears to reduce pain and improve physical function for people with knee OA. The measures of benefit include patient-reported outcomes, as well as physician assessments and several physical function tests. We also observed significant benefits in the measures of depression and self-efficacy that appeared durable for participants who continued to practice Tai Chi beyond the 12week intervention period. Therefore, in this first long-term followup trial of Tai Chi for knee OA, the Tai Chi group seems to have developed a general sense of well-being, suggesting that there may be synergy between the physical and mental components of this discipline. These findings



Figure 3. Mean changes of secondary outcomes by treatment group at baseline and 12, 24, and 48 weeks. Values are the unadjusted mean \pm SD. Error bars show the 95% confidence interval. Measurements were obtained at baseline and 12, 24, and 48 weeks, but the data are slightly offset in the figure for clarity. * = lower scores indicate improvement in outcome; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; VAS = visual analog scale; CES-Depression = Center for Epidemiologic Studies Depression Scale; \dagger = higher scores indicate improvement in outcome; SF-36 = Short Form 36 health survey; MCS = mental component summary; PCS = physical component summary.

are promising because there are few efficacious longlasting treatments for knee OA (2,6).

There have been several previous trials testing the effects of Tai Chi for OA (12,34–37). However, interpretation of their results is limited by low levels of adherence (12,35), short followup (12,36,37), deployment of varying Tai Chi styles (12,35), and inclusion of heterogeneous types of OA (12). Nevertheless, our results are consistent with some of their positive findings for improvements

Table 3. Use of analgesics and nonsteroidal antiinflammatory drugs (NSAIDs)						
	Tai Chi	Tai Chi (n = 20),		(n = 20),		
	no.	no. (%)		(%)		
Medication	Baseline	12 weeks	Baseline	12 weeks		
Analgesics	4 (20)	3 (15)	6 (30)	4 (20)		
NSAIDs	9 (45)	5 (25)	13 (65)	9 (45)		

in pain (34,35) and function (12,35,37). Our findings are also consistent with prior studies showing the benefits of Tai Chi on self-efficacy, depression, and quality of life (8). However, our study did not show any improvement in balance tests, as was shown in a number of other studies (8).

Recent efforts have suggested that there is a minimum clinically important difference for WOMAC scores from both pharmacologic and rehabilitation trials (38,39). In our trial, the Tai Chi group had a 75% improvement of WOMAC pain over baseline (57% greater than controls) and a 72% improvement of WOMAC function over baseline (46% greater than controls). Therefore, our study shows that Tai Chi gives more than the minimally perceptible improvement for patients.

Most of our participants were significantly overweight, with an average BMI of 30 kg/m². It is well known that significant weight reduction can improve symptoms of knee OA (40). However, there was no significant weight reduction for either group during the trial. In addition, the 2 groups did not differ in medication use, and it is unlikely that the difference in outcomes between the groups was attributable to changes in medication patterns occurring over the course of the trial.

Explanatory theories from Eastern and Western literature provide a supposed rationale for the effectiveness of Tai Chi to treat knee OA (41–43). Although the biologic mechanisms by which Tai Chi may improve the clinical consequence of knee OA still remain unknown, synergy between its physical and mental components likely plays a major role. First, Tai Chi may enhance cardiovascular benefits, muscular strength, balance, coordination, and physical function (8). All of these are thought to be able to reduce joint pain. Because the severity of pain is directly correlated with the degree of muscle weakness (41), stronger muscles and better coordination improve the stability of the joints and lessen pain. Increased periarticular muscle strength may also protect joints from traumatic impacts. Second, evidence suggests that the mind-body component may influence immune, endocrine, neurochemical, and autonomic functioning (43). Third, controlled breathing and movements promote a restful state and mental tranquility. These influences may help break the arthritis pain cycle (42). Improving self-efficacy, social function, and depression can also help people build confidence, get support, and overcome fears of pain. Together, these can lead to improved physical, psychological, and psychosocial well-being and overall quality of life (44).

Our study had some limitations. First, the attention group appears to have had more severe knee OA, as measured by WOMAC physical function, radiography scores, and self-reported comorbidities at baseline. This difference likely occurred by chance as a result of the relatively small sample size, rather than as a problem with the randomization procedures. Regression adjustment for these baseline differences did not change any of the conclusions. The possibility exists that some unidentified confounding factors were not measured in our trial, such as socioeconomic status and knee malalignment, and these factors will be considered in our future work. Second, we could not mask the participants to treatment assignment. Although an elaborate sham treatment might accomplish such blinding, no validated approach for this currently exists. As a result, participants' a priori beliefs and expectations with respect to Tai Chi could have biased their subjective outcome assessments. Therefore, we attempted to minimize such expectations by maintaining a stance of equipoise regarding the likely benefits of the 2 interventions. By deemphasizing our specific interest in Tai Chi, participant expectations would have been reduced. In addition, we tested to see if expectations might have produced any bias. We found that the baseline outcome expectations of benefit from an exercise intervention were similar in both groups (Tai Chi mean \pm SD 4.1 \pm 0.6, control mean \pm SD 4.3 \pm 0.4). Furthermore, total session attendance was similar in both groups (89% control, 85% Tai Chi), indicating that our neutral presentation of the interventions may have succeeded. A third limitation, instruction by a single Tai Chi master, might limit generalizability. However, we only made minor modifications to the movements of the classic Yang style to avoid knee injury. Therefore, this modified Yang-style Tai Chi should

not be difficult for other instructors to implement and for participants to practice at home, so that the benefits of Tai Chi may be extended to the general population. Finally, although the patients were instructed not to communicate with the blinded assessors about their treatment assignments, there is the possibility that leakage of information did occur even though the study physician reported no such leakage.

In conclusion, 12-week Tai Chi appears to reduce pain and improve physical function, self-efficacy, depression, and health status for knee OA. These observations emphasize a need to further evaluate the biologic mechanisms and approaches of Tai Chi to extend its benefits to a broader population. Further studies should replicate these results and deepen our understanding of this therapeutic modality.

ACKNOWLEDGMENTS

We gratefully acknowledge the Data Safety Monitoring Board members Drs. Karen H. Costenbader, Kristin Baker, Wenjun Li, and Ms. Resa Arovas for their insightful suggestions for the study protocol. We are grateful to Jun Wang, Marcie Griffith, Aghogho Okparavero, Xiaoyan Chen, Melynn Nuite, Erica McAdams, Xiaogang Gao, Steve Wong, Ian Schmid, and the Clinical Research Center nurses for their help with different aspects of the study, and to Drs. Haewook Han and Harry Pino for their expertise in teaching the control group. We also thank Judith L. Ramel for her assistance in preparing this manuscript. We gratefully acknowledge the participation of our study subjects; their cooperation, encouragement, and enthusiasm were an inspiration to the investigators.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. Wang had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. **Study conception and design.** Wang, Schmid, Hibberd, Kalish,

Roubenoff, Rones, McAlindon.

Acquisition of data. Wang, Schmid, Hibberd, Kalish, McAlindon. Analysis and interpretation of data. Wang, Schmid, Hibberd, Kalish, Roubenoff, McAlindon.

ROLE OF THE STUDY SPONSOR

The National Center for Complementary and Alternative Medicine of the National Institutes of Health had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

REFERENCES

- 1. Felson DT. Clinical practice: osteoarthritis of the knee. N Engl J Med 2006;354:841-8.
- 2. Zhang W, Moskowitz RW, Nuki G, Abramson S, Altman RD, Arden N, et al. OARSI recommendations for the management of hip and knee osteoarthritis. Part II. OARSI evidence-based, expert consensus guidelines. Osteoarthritis Cartilage 2008;16: 137–62.
- 3. Van Baar ME, Dekker J, Lemmens JA, Oostendorp RA, Bijlsma JW. Pain and disability in patients with osteoarthritis of hip or knee: the relationship with articular, kinesiological, and psychological characteristics. J Rheumatol 1998;25:125–33.

- 4. Slemenda C, Brandt KD, Heilman DK, Mazzuca S, Braunstein EM, Katz BP, et al. Quadriceps weakness and osteoarthritis of the knee. Ann Intern Med 1997;127:97–104.
- 5. Rejeski WJ, Miller ME, Foy C, Messier S, Rapp S. Self-efficacy and the progression of functional limitations and selfreported disability in older adults with knee pain. J Gerontol B Psychol Sci Soc Sci 2001;56:S261–5.
- Zhang W, Moskowitz RW, Nuki G, Abramson S, Altman RD, Arden N, et al. OARSI recommendations for the management of hip and knee osteoarthritis. Part I. Critical appraisal of existing treatment guidelines and systematic review of current research evidence. Osteoarthritis Cartilage 2007;15:981– 1000.
- Jamtvedt G, Dahm KT, Christie A, Moe RH, Haavardsholm E, Holm I, et al. Physical therapy interventions for patients with osteoarthritis of the knee: an overview of systematic reviews. Phys Ther 2008;88:123–36.
- 8. Wang C, Collet JP, Lau J. The effect of Tai Chi on health outcomes in patients with chronic conditions: a systematic review. Arch Intern Med 2004;164:493–501.
- Jordan KM, Arden NK, Doherty M, Bannwarth B, Bijlsma JW, Dieppe P, et al. EULAR Recommendations 2003: an evidence based approach to the management of knee osteoarthritis. Report of a Task Force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT). Ann Rheum Dis 2003;62:1145–55.
- Axford J, Heron C, Ross F, Victor CR. Management of knee osteoarthritis in primary care: pain and depression are the major obstacles. J Psychosom Res 2008;64:461–7.
- 11. Lee MS, Pittler MH, Ernst E. Tai Chi for osteoarthritis: a systematic review. Clin Rheumatol 2008;27:211-8.
- Fransen M, Nairn L, Winstanley J, Lam P, Edmonds J. Physical activity for osteoarthritis management: a randomized controlled clinical trial evaluating hydrotherapy or Tai Chi classes. Arthritis Rheum 2007;57:407–14.
- Wang C, Schmid CH, Hibberd PL, Kalish R, Roubenoff R, Rones R, et al. Tai Chi for treating knee osteoarthritis: designing a long-term follow up randomized controlled trial. BMC Musculoskelet Disord 2008;9:108.
- Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, et al. Development of criteria for the classification and reporting of osteoarthritis: classification of osteoarthritis of the knee. Arthritis Rheum 1986;29:1039-49.
- Kellgren JH, Lawrence JS. Radiological assessment of osteoarthrosis. Ann Rheum Dis 1957;16:494–502.
- Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189–98.
- Wang C, Lau J, Roubenoff R, Kalish R, Christopher S, Hibberd P. Tai Chi improves pain and functional status in adult with rheumatoid arthritis [abstract]. Arthritis Rheum 2003;48: 3656-8.
- China Sports. Simplified "Taijiquan." Beijing (China): China Publications Center; 1983.
- Van Baar ME, Assendelft WJ, Dekker J, Oostendorp RA, Bijlsma JW. Effectiveness of exercise therapy in patients with osteoarthritis of the hip or knee: a systematic review of randomized clinical trials. Arthritis Rheum 1999;42:1361–9.
- Baker KR, Nelson ME, Felson DT, Layne JE, Sarno R, Roubenoff R. The efficacy of home based progressive strength training in older adults with knee osteoarthritis: a randomized controlled trial. J Rheumatol 2001;28:1655–65.
- US Department of Health and Human Services. Dietary guidelines for Americans. 2005. URL: http://www.health.gov/ DietaryGuidelines/dga2005/document/default.htm.
- 22. National Institute of Arthritis and Musculoskeletal and Skin Diseases. Osteoarthritis. 2006. URL: http://www.niams.nih. gov/Health_Info/Osteoarthritis/default.asp.
- Bellamy N, Kirwan J, Boers M, Brooks P, Strand V, Tugwell P, et al. Recommendations for a core set of outcome measures for future phase III clinical trials in knee, hip, and hand osteoarthritis: consensus development at OMERACT III. J Rheumatol 1997;24:799-802.
- Bellamy N. WOMAC osteoarthritis index: a user's guide. London (Ontario): University of Western Ontario; 1995.

- 1553
- 25. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. J Rheumatol 1988;15:1833–40.
- 26. Altman R, Brandt K, Hochberg M, Moskowitz R, Bellamy N, Bloch DA, et al. Design and conduct of clinical trials in patients with osteoarthritis: recommendations from a task force of the Osteoarthritis Research Society. Results from a workshop. Osteoarthritis Cartilage 1996;4:217–43.
- Csuka M, McCarty DJ. Simple method for measurement of lower extremity muscle strength. Am J Med 1985;78:77–81.
- Guyatt GH, Sullivan MJ, Thompson PJ, Fallen EL, Pugsley SO, Taylor DW, et al. The 6-minute walk: a new measure of exercise capacity in patients with chronic heart failure. Can Med Assoc J 1985;132:919–23.
- Messier SP, Royer TD, Craven TE, O'Toole ML, Burns R, Ettinger WH Jr. Long-term exercise and its effect on balance in older, osteoarthritic adults: results from the Fitness, Arthritis, and Seniors Trial (FAST). J Am Geriatr Soc 2000;48:131–8.
- Radloff LS. The CES-D scale: a new self-report depression scale for research in the general population. Appl Psychol Meas 1977;1:385-40.
- Resnick B, Zimmerman SI, Orwig D, Furstenberg AL, Magaziner J. Outcome expectations for exercise scale: utility and psychometrics. J Gerontol B Psychol Sci Soc Sci 2000;55: S352-6.
- Marcus BH, Selby VC, Niaura RS, Rossi JS. Self-efficacy and the stages of exercise behavior change. Res Q Exerc Sport 1992;63:60-6.
- Ware JE Jr, Sherbourne CD. The MOS 36-item Short-Form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992;30:473–83.
- Brismee JM, Paige RL, Chyu MC, Boatright JD, Hagar JM, McCaleb JA, et al. Group and home-based Tai Chi in elderly subjects with knee osteoarthritis: a randomized controlled trial. Clin Rehabil 2007;21:99–111.
- 35. Song R, Lee EO, Lam P, Bae SC. Effects of Tai Chi exercise on pain, balance, muscle strength, and perceived difficulties in physical functioning in older women with osteoarthritis: a randomized clinical trial. J Rheumatol 2003;30:2039–44.
- Hartman CA, Manos TM, Winter C, Hartman DM, Li B, Smith JC. Effects of Tai Chi training on function and quality of life indicators in older adults with osteoarthritis. J Am Geriatr Soc 2000;48:1553–9.
- Lee HY, Lee KJ. Effects of Tai Chi exercise in elderly with knee osteoarthritis. Taehan Kanho Hakhoe Chi 2008;38:11–8. In Korean.
- 38. Zhao SZ, McMillen JI, Markenson JA, Dedhiya SD, Zhao WW, Osterhaus JT, et al. Evaluation of the functional status aspects of health-related quality of life of patients with osteoarthritis treated with celecoxib. Pharmacotherapy 1999;19:1269–78.
- 39. Angst F, Aeschlimann A, Stucki G. Smallest detectable and minimal clinically important differences of rehabilitation intervention with their implications for required sample sizes using WOMAC and SF-36 quality of life measurement instruments in patients with osteoarthritis of the lower extremities. Arthritis Rheum 2001;45:384–91.
- Rogers MW, Wilder FV. The association of BMI and knee pain among persons with radiographic knee osteoarthritis: a crosssectional study. BMC Musculoskelet Disord 2008;9:163.
- O'Reilly SC, Jones A, Muir KR, Doherty M. Quadriceps weakness in knee osteoarthritis: the effect on pain and disability. Ann Rheum Dis 1998;57:588–94.
- 42. Yocum DE, Castro WL, Cornett M. Exercise, education, and behavioral modification as alternative therapy for pain and stress in rheumatic disease. Rheum Dis Clin North Am 2000; 26:145–59.
- National Center for Complementary and Alternative Medicine. Tai Chi: an introduction. 2006. URL: http://nccam.nih. gov/health/taichi/.
- Wilson IB, Cleary PD. Linking clinical variables with healthrelated quality of life: a conceptual model of patient outcomes. JAMA 1995;273:59-65.