Eccentric and Concentric Resistance Exercise Comparison for Knee Osteoarthritis

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ABSTRACT

VINCENT, K. R., T. VASILOPOULOS, C. MONTERO, and H. K. VINCENT. Eccentric and Concentric Resistance Exercise Comparison for Knee Osteoarthritis. Med. Sci. Sports Exerc., Vol. 51, No. 10, pp. 1977–1986, 2019. Introduction: This study aimed to compare the efficacy of eccentrically focused resistance exercise (ECC RT) to concentrically focused resistance exercise (CNC RT) on knee osteoarthritis (OA) symptoms and strength. Methods: Ninety participants consented. Participants were randomized to CNC RT, ECC RT, or a wait-list, no-exercise control group. Four months of supervised exercise training was completed using traditional weight machines (CNC RT) or modified-matched machines that overloaded the eccentric action (ECC RT). Main outcomes included one-repetition maximal strength (knee extension, leg flexion, and leg press), weekly rate of strength gain, Western Ontario and McMaster University Osteoarthritis Index (WOMAC) total score and subscores. Results: Fifty-four participants (60–85 yr, 61% women) completed the study. Both CNC RT and ECC RT groups showed 16%–28% improvement relative to the wait-list, no-exercise control group (P = 0.003–0.005) for all leg strength measures. The rate of weekly strength gain was greater for CNC RT than for ECC RT for leg press and knee flexion (by 2.9%–4.8%; both, P < 0.05) but not knee extension (0.7%; P = 0.38). There were no significant differences in WOMAC total and subscores across groups over time. Leg press strength change was the greatest contributor to change in WOMAC total scores (R2 = 0.223). The change in knee flexion strength from baseline to month 4 was a significant predictor of the change in WOMAC pain subscore (F ratio = 4.84, df = 45, P = 0.032). Both modes of strength training were well tolerated. Conclusions: Both resistance training types effectively increased leg strength. Knee flexion and knee extension muscle strength can modify function and pain symptoms irrespective of muscle contraction type. Which mode to pick could be determined by preference, goals, tolerance to the contraction type, and equipment availability. Key Words: JOINT PAIN, STRENGTH TRAINING, SAFETY, ADHERENCE

Knee osteoarthritis (OA) is a major source of pain and disability globally (1). OA is among the top 10 causes of physical disability worldwide (2). Knee pain affects multiple facets of quality of life, impedes physical function, and is related to muscle loss. Pain itself predicts a trajectory of functional decline in well-functioning adults (3). Loss of muscle mass and knee extensor–flexor muscle strength are independently associated with symptomatic progression of OA and reduction in overall health status (4). Isokinetic strength testing indicates that individuals with OA have 11%–56% lower concentric leg extensor strength and 76% lower eccentric strength (5). Pain inhibits corticospinal and intracortical pathways and causes a central activation deficit and strength reduction in the leg muscles about the knee (6). Although no cure exists for this condition, current management strategies for knee OA target potential modifiable symptoms such as pain and contributing risk factors such as strength (1).

Resistance exercise can reduce knee pain severity and leg strength in participants with symptomatic knee OA (7). Exercise interventions using free weights or machines have generally focused on movements with concentric muscle contractions. Previous interventions were developed based on loads lifted during the concentric phase, not the eccentric phase (8). Hence, the eccentric phase is often relatively underloaded compared with the muscle capabilities (8,9). What remains unknown for the population with knee OA is whether increasing the eccentric loading component of resistance training could enhance training benefits on pain and strength. Limited data show that eccentric contractions increase...
muscular strength and hypertrophy at a lower metabolic, cardiac, and neural cost than concentric contractions (8,10). Even among strength-trained young men, accentuated eccentric loading during strength training increases isometric torque and muscle activation more than concentric training (9). Although both types of muscle training can induce hypertrophy in healthy adults, the muscle architecture adaptations for eccentric training largely occur with fascicle length and hypertrophy is more evident in the distal ends of the muscle; after concentric training, muscle hypertrophy occurs largely in the muscle belly and induces changes in pennation angle (11). Moreover, compared with concentric training, eccentric training reduces intracortical inhibition and increases corticospinal excitability by 37%–51%, both of which may promote the documented cross-transfer of strength improvement to opposite limbs (12). The available literature, however, is fraught with methodological variability in training mode, exercise type, unilateral training status, and equipment, which compromises the ability to determine comparative effectiveness for clinical populations such as knee OA. Our laboratory has developed and published an eccentric exercise weight machine model of a well-used concentric weight machine counterpart (13). Until now, there has not been a head-to-head comparison of concentric and eccentric resistance exercise for therapeutic benefit, but our model allows us to perform this comparison.

Recent meta-analysis showed that exercise reduces OA pain severity similarly to traditional analgesic agents (14). Regimens that maximize strength with relatively less physiological stress are highly attractive for the older adult with debilitating OA. Evidence from the Osteoarthritis Initiative shows that as knee OA progresses and pain increases over time, knee flexor and extensor muscle strength declines linearly in both men and women (15). This strength loss seems to be independent of radiographic stage of the disease (16) and is minimally explained by comorbidities or depression (15). Pain reduction and reduction of pain impact on physical functioning are related to strength gains from a variety of exercises (17,18). Previous investigations have documented improvements in joint disease-specific instruments such as the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), up to 54% with resistance exercise (19), and that changes in knee extensor strength mediate WOMAC scores (20). What remains unclear is whether eccentric- or concentric-based resistance training is more effective for reducing knee OA pain symptoms and reversing the OA-related strength decline. We performed a randomized, controlled study to compare the effectiveness of eccentrically focused resistance exercise (ECC RT) and concentrically focused resistance exercise (CNC RT) on knee OA symptoms and leg muscle strength for 4 months. We hypothesized that ECC RT would elicit superior improvements in knee pain, perceived function, and leg maximal strength compared with CNC RT.

METHODS

Study Design

This was a 4-month randomized, controlled, single-blinded study of two different resistance exercise training programs on knee OA symptoms. This study followed the Consolidated Standards of Reporting Trials 2010 guidelines for reporting parallel-group randomized trials. The study was registered as a clinical trial NCT00187863.

Participants

Older adults with knee OA were recruited from study flyers and newspaper advertisements posted in the Gainesville area and surrounding regions using the UF Orthopaedics Clinics, the Clinical Trials Register, and a list of older adults provided by the UF Claude Pepper Aging Center. Recruitment occurred from November 2010 to December 2012. Inclusion criteria were as follows: men and women age 60–85 yr, presence of OA of the knee (using American College of Rheumatology criteria) for ≥6 months (21), knee pain primarily due to tibiofemoral OA and not from patellofemoral OA, bilateral standing anterior–posterior radiograph demonstrating Kellgren and Lawrence OA grade 2 or 3 out of the target knee (22), willing and able to participate in regular exercise for 4 months, free from musculoskeletal limitations that would preclude resistance exercise participation (i.e., joint contractures, fractures), and free of abnormal cardiovascular responses during the screening graded maximal walk test. Exclusion criteria were as follows: any surgery to either knee within the last 12 months, lumbar radiculopathy, or vascular claudication; significant anterior knee pain due to diagnosed isolated patella–femoral syndrome or chondromalacia in either knee; had corticosteroid or hyaluronic acid injections administered within 3 months of study participation; and have added new over-the-counter or prescription pain medication within 2 months of study participation. Knee OA eligibility criteria were first reviewed on each potential participant by the study coordinator and the principal investigator (physician) on the study to ensure that the appropriate participants were enrolled. This study was approved by the University of Florida Institutional Review Board, and all procedures on human subjects were conducted in accordance with the Helsinki Declaration of 1975, as revised in 1983. All participants provided written, informed consent to participate. The Consolidated Standards of Reporting Trials study flow diagram is shown in Figure 1.

Additional Screening Measures and Study Visits

All study measures were collected at the University of Florida Human Dynamics Laboratories. Visit 1 included an orientation to the laboratory testing area and a familiarization with the machines. Participants completed the WOMAC for knee pain–related quality of life impact. Before clearance, the participant’s maximal rate of oxygen consumption was determined using a walking symptom–limited graded exercise test at baseline (incremental treadmill Naughton test). All procedures followed the American College of Sports Medicine guidelines with electrocardiogram heart monitoring and blood pressure measures. Open-circuit spirometry was used to determine the rate of oxygen use and carbon dioxide production using a metabolic cart (VIASYSCareFusion Corp., San Diego, CA). The test was stopped at voluntary exhaustion or when knee
pain prevented further walking. RPE values were collected at rest, at each exercise stage, and during recovery. If no abnormal cardiovascular responses occurred, the participant continued in the study. Visit 2 involved maximal strength testing of major muscle groups to develop a training program. First, participants were familiarized to each exercise machine, and the settings of each machine were individually customized to match the anthropometry of each participant. Once the strength values for each exercise were determined, a training schedule was established. After the training period, participants completed a third visit for posttraining measures.

Randomization Procedure

Participants were randomly assigned to one of three study groups: a concentrically based resistance exercise training program (CNC RT), an eccentrically based resistance exercise training program (ECC RT), or a wait-list, nonexercise control group (CON). Randomization was achieved using a computer-generated list and hidden sequencing of the individual assignment. The assignments per participant number were placed in numbered sealed envelopes. Each new enrolled participant opened an envelope to receive the group assignment. One study coordinator issued the assignment, and the principal investigator and other investigators were blinded to the allocation sequence. A total of 90 participants were enrolled into the study.

Resistance Exercise Interventions

CNC RT was performed on traditional commercial dynamic resistance exercise machines (MedX®). ECC RT was performed on modified MedX® machines that contained a novel design that resistance loads during the eccentric phase of the contraction, while “assistance” was provided by the machine during the concentric phase. This allowed for each type of contraction to use a load that more appropriately matched its respective force-producing capabilities when compared with CNC RT machines. Exercise training sessions were performed in a supervised laboratory setting over a 4-month period. All participants were familiarized with all the testing equipment and performed a light exercise set on each of the exercise machines to configure the machine seat position. Participants in the trained groups reported to the laboratory two times a week for one-on-one training sessions with an experienced exercise physiologist. Work performed during each exercise session was recorded in a personalized training chart.

Blinding to Treatment

Coordinators and exercise physiologists conducted the testing sessions and the assessments for the study. The physiologists and the physicians who provided coverage and interpretation of the testing were blinded to the randomization, group allocation, and related interventions.

Body Composition

Body composition was tracked using air plethysmography (BODPOD; Life Measurement, Concord, CA) from pretraining to posttraining. This is a reliable technique of body volume and composition measurement and is highly correlated with the reference standard of underwater weighing (23). The intraclass coefficient for body density was 0.996 for a heterogeneous sample. The test–retest correlation for body mass measurement is \( r = 0.999 \) (23).

Strength Testing

Resistance loads were set using a percentage of the one-repetition maximum (1RM) technique for each exercise. The 1RM was determined using the following protocol: for each exercise, a warm-up of five repetitions at a low weight was followed by three repetitions at a higher weight of each dynamic exercise. One lift was performed at progressively higher
loads until the dynamic exercise could not be performed or performed with good form. 1RM values were secondary outcomes. Recovery periods between each lift were 60 s. Specific training appointment times were established for each participant during the week to avoid exposure to other participants and contamination of data. All adverse events and unanticipated events were tracked during the study.

**CNC RT.** For clarity, we define here that the phase of the motion that involves pushing the weight away from the body is the concentric phase, and the phase of the motion that involves controlled weight return toward the body is the eccentric phase. We modified our exercise protocol that was successfully used on our older adult population of a similar age range using MedX® machines and is in accord with the guidelines prescribed by the American College of Sports Medicine. Participants randomized to this group performed two resistance exercise sessions per week, and one set of each exercise was completed in each session: leg press, knee flexion, knee extension, chest press, seated row, overhead press, biceps curl, and calf press. A description of the exercise details can be found in Supplemental Table 1 (Supplemental Digital Content 1, Exercise start and end positions, directions and cues for MedX® resistance exercise machines, http://links.lww.com/MSS/B592). Each set contained 12 repetitions performed at a resistance load of 60% of the concentric 1RM for that exercise. Participants subjectively rated the effort of the exercise set using a 6- to 20-point Borg scale. As the participant adapted, the effort was less, and the resistance load was increased for the set to keep the RPE value at approximately 17–18 for the exercise over the study duration.

**ECC RT.** The resistance strategy for enhanced eccentric training is therefore to continually perform the eccentric muscle action or weight return with the equivalent of the concentric 1RM. During the pushing or concentric phase of each lift here, the resistance was set at 60% of 1RM. Each set consisted of eight repetitions, and the participants subjectively rated the effort of the exercise set using a 6- to 20-point Borg scale. Progression of loading over time was identical to that of the CNC RT group described earlier. The repetition structure on the eccentric exercise machine and comparative concentric exercise machine was adjusted to equalize the work performed on a given exercise between the study groups.

**CON.** Participants continued participating in their normal activities during the 4-month study period if assigned to this group. This group was offered the opportunity to complete either the CNC RT or ECC RT program after the control period. Telephone contact was made weekly to help encourage adherence to the knee symptom management guidelines and to provide attention to this group. Finally, all participants wore dual-axis accelerometers for 7 d before and after the training period (StepWatch activity monitors (SAM); Cyma, Seattle, WA) to track whether habitual activity changed.

### Main Outcomes

The main study outcomes included patient-reported knee symptoms and function, dynamic muscle strength, and ambulatory knee pain severity.

**WOMAC.** The WOMAC is a disease-specific, reliable, and valid measure of patient-reported knee or hip status. A total of 24 items were grouped into three subscales, including pain (5 items), stiffness 2 items), and physical function (17 items). Questions were asked in 4-point Likert scale format. The point range for this format was 0 points (no difficulty, pain, or stiffness) to 100 points (worst pain, stiffness, and worst function). Internal consistency for this instrument is high with Cronbach α values for pain, stiffness, and subscale scores ranging from 0.86 to 0.55 (24). WOMAC test–retest reliability intraclass correlation coefficient for these WOMAC subscales ranges from 0.90 to 0.9 (25). The minimum clinically important improvement in the WOMAC global with treatment is −39.0%.

The minimum clinically important improvements for pain and physical function are −40.8% and −26.0%, respectively (26). The study was powered based on the WOMAC as the primary study outcome.

**Muscle strength.** The 1RM values for knee extension, knee flexion, and leg press on the MedX® machines represented the dynamic muscle strength values. Strength of muscles around the knee joint is clinically important because lower strength is associated with higher WOMAC pain score (15). The test–retest reliability intraclass correlation coefficient for 1RM measures in the lower extremity ranges from 0.94 to 0.99 in other older populations (27) and persons with mobility limitations (28). The knee flexor-to-extensor ratio was calculated before and after the training period. This ratio has been used to estimate knee function and muscle balance; higher flexor-to-extensor rations indicate lower quadriceps strength (29). Muscle strength values for other muscle groups are reported in Supplemental Table 2 (Supplemental Digital Content 2, Maximal strength measurements across intervention groups for other muscle groups, http://links.lww.com/MSS/B593).

### Feasibility and Safety

The feasibility of the training interventions was examined by the weekly rate of strength gain. Safety was tracked by adverse events related to the intervention, and included but was not limited to worsening of knee pain, falls, knee joint swelling, and onset of other joint pain. Adverse events were documented from the time of enrollment to completion of the 4-month study for each participant and were reviewed as they occurred and on a monthly basis with the study team.

### Statistics

All analyses were conducted in JMP Pro 12.0 (SAS Institute, Inc., Cary, NC). Differences in baseline categorical measures across concentric (CNC RT), eccentric (ECC RT), and control (CON) groups were assessed using χ² tests. Differences in baseline continuous measures across the CNC RT, and ECC RT groups were assessed with ANOVA, using the Tukey–Kramer test for pairwise comparisons, which also adjusted for multiple comparisons using the Bonferroni method. Nonnormal measures were log transformed before analyses. For primary
outcomes, data were analyzed by intent-to-treat approach, using linear-mixed models. These models included time (pre or post) and study group as main effects, with an interaction model between time and group. A significant time–group interaction would indicate that change in outcome from pre to post differed among groups. Mixed models use maximal likelihood estimation to handle missing data, including full information from all individuals randomized in the study.

General linear models were also run and compared, which gains in strength (calculated as preimprovement to postimprovements in leg press, knee flexion, and knee extension) best-explained improvements in WOMAC total scores. The first model (model 1) included preintervention WOMAC total score as the independent variable and postintervention WOMAC total score as the dependent variable to model change in total WOMAC score. Subsequent models (models 2a–2c) added each strength measure (leg press change, knee flexion change, knee extension change) separately and then all together (model 3). Model fit and parsimony were assessed with $R^2$ (% variance explained in WOMAC total score) and Akaike information criteria (AIC). A reduction in AIC would indicate greater model parsimony and better model fit.

Sample size estimation. Power analysis was calculated using previously published data regarding differences elicited for the WOMAC pain subscale (30–33). This variable was chosen because it is a primary reason for people with knee OA to undergo a total knee arthroplasty for OA (31–33). The minimum clinically relevant decrease in the WOMAC pain subscale is 1.2 cm on a 10-cm scale (34). For this investigation, 1.5 cm represents a 30% difference between the two exercise interventions. Sample size estimation using a mean of 5 cm with an SD of 2 cm and a desired effect size of 1.5 cm indicated that 20 participants per group were needed to have a power of 0.80 at an α level of 0.05. With our past experience, we anticipated a 30% dropout rate and increased the number of participants in each group to 30.

RESULTS

Participant characteristics. Figure 1 shows the study flow diagram. A total of 351 people were screened by phone, and 237 candidates did not meet all the inclusion criteria or met one or more exclusion criteria. A total of 114 candidates were offered initial appointments, and 90 were enrolled. Table 1 provides the baseline characteristics of the three study groups. The proportion of participants who used pain medications for knee pain or the mean number of pain medications used by the three groups was not different from pretraining to posttraining. Mean pain medication numbers after training were 0.8 ± 0.5 (CNC RT), 0.8 ± 0.6 (ECC RT), and 1.2 ± 1.1 (CON; $P = 0.347$). Mean step counts from the activity monitors were not different across groups over time, indicating no change in habitual activity levels (CNC RT, 3600–3496 steps per day; ECC RT, 4652–4643 steps per day; and CON, 5002–4851 steps per day; $P = 0.962$).

Adherence to the intervention. From the initial 90 who consented to participate, 88 were randomized into a study group and 54 completed the study. Figure 1 provides the details for dropouts. For the two groups who trained, the percentages of exercise training sessions completed was 94.8% and 96.4% in the CNC RT and ECC RT, respectively ($P = 0.533$). The average training durations, or days to complete the training sessions, were 126 ± 21 d (95% confidence interval (CI), 114–137 d) for the CNC RT and 130 ± 12 d (95% CI, 123–135 d) for the ECC RT ($P = 0.628$).

Body composition. There were no significant changes in body mass or composition among the three groups from pretraining to posttraining. Posttraining body weight for the CNC RT, ECC RT, and CON were 93.2 ± 20.0, 79.5 ± 5.0, and 87.7 ± 19.2 kg, respectively ($P = 0.509$). The percent fat-free mass values were also not different among the three groups (57.0% ± 11.4% [CNC RT], 59.6% ± 9.8% [ECC RT], and 61.5% ± 11.2% [CON]; $P = 0.715$).

WOMAC responses. There were no statistically significant differences in WOMAC measures across groups (Table 2). Fifty-four patients had postintervention assessments. Figure 2 shows change in WOMAC scores from pretraining to postintervention. As shown in Figure 2A–D, there were no statistically significant group differences in this change for WOMAC total scores ($F_{2,50} = 2.1, P = 0.13$), WOMAC stiffness scores ($F_{2,51} = 0.01, P = 0.98$), and WOMAC function scores ($F_{2,51} = 1.0, P = 0.37$), although there was a trend for differences for WOMAC pain scores ($F_{2,51} = 2.6, P = 0.08$). A total of 50% and 68.4% of the CNC RT and ECC RT achieved the minimum clinically relevant reduction in the WOMAC pain subscore, respectively. There were no main effects ($P > 0.050$) of age or sex on any WOMAC measure.

Muscle strength. There were statistically significant group differences for pretraining to postintervention change

Table 1. Baseline characteristics of older adults with knee OA.

<table>
<thead>
<tr>
<th></th>
<th>CNC RT (n = 29)</th>
<th>ECC RT (n = 30)</th>
<th>CON (n = 32)</th>
<th>P (Significance)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>69.5 ± 6.5</td>
<td>66.8 ± 5.4</td>
<td>68.6 ± 7.2</td>
<td>0.287</td>
</tr>
<tr>
<td>Body mass, kg</td>
<td>92.7 ± 19.7</td>
<td>79.5 ± 20.7</td>
<td>86.9 ± 19.7</td>
<td>0.203</td>
</tr>
<tr>
<td>BMI, kg·m⁻²</td>
<td>32.8 ± 7.4</td>
<td>28.7 ± 6.6</td>
<td>30.1 ± 6.2</td>
<td>0.069</td>
</tr>
<tr>
<td>Fat-free mass, %</td>
<td>57.3 ± 11.8</td>
<td>61.0 ± 9.6</td>
<td>61.7 ± 10.8</td>
<td>0.486</td>
</tr>
<tr>
<td>Sex, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>67.0 ± 0.5</td>
<td>70.0 ± 0.0</td>
<td>66.0 ± 0.0</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>33.0 ± 0.0</td>
<td>30.0 ± 0.0</td>
<td>34.0 ± 0.0</td>
<td>0.381</td>
</tr>
<tr>
<td>Race/ethnicity, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>85.0 ± 93.0</td>
<td>93.0 ± 81.0</td>
<td>81.0 ± 93.0</td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>11.0 ± 7.0</td>
<td>7.0 ± 6.0</td>
<td>6.0 ± 7.0</td>
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<tr>
<td>Other</td>
<td>4.0 ± 0.0</td>
<td>0.0 ± 13.0</td>
<td>13.0 ± 0.0</td>
<td>0.439</td>
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<tr>
<td>Work status, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Working</td>
<td>40.0 ± 23.0</td>
<td>23.0 ± 34.0</td>
<td>34.0 ± 23.0</td>
<td></td>
</tr>
<tr>
<td>Not working</td>
<td>4.0 ± 7.0</td>
<td>7.0 ± 13.0</td>
<td>13.0 ± 7.0</td>
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<tr>
<td>Retired</td>
<td>52.0 ± 70.0</td>
<td>70.0 ± 50.0</td>
<td>50.0 ± 70.0</td>
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<tr>
<td>Disabled</td>
<td>4.0 ± 0.0</td>
<td>0.0 ± 3.0</td>
<td>3.0 ± 0.0</td>
<td>0.981</td>
</tr>
<tr>
<td>Duration of pain, median (Q1–Q3)</td>
<td>4.5 (2–11)</td>
<td>10 (2.75–20)</td>
<td>5 (2–10)</td>
<td>0.150</td>
</tr>
<tr>
<td>Location of knee pain, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>18.0 ± 20.0</td>
<td>20.0 ± 9.0</td>
<td>9.0 ± 20.0</td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>15.0 ± 17.0</td>
<td>17.0 ± 28.0</td>
<td>28.0 ± 17.0</td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td>67.0 ± 63.0</td>
<td>63.0 ± 63.0</td>
<td>63.0 ± 63.0</td>
<td></td>
</tr>
<tr>
<td>Pain medications, no.</td>
<td>1.0 ± 0.5</td>
<td>0.9 ± 0.5</td>
<td>1.1 ± 1.1</td>
<td>0.863</td>
</tr>
</tbody>
</table>

Values are means ± SD or % of the group.
in leg press, knee flexion, and knee extension (Fig. 3; all, \(P < 0.05\)). Specifically, for all leg strength measures, both CNC RT and ECC RT groups showed greater improvement relative to the CON group (\(P = 0.003–0.005\)), but there were no statistically significant differences between the CNC RT and ECC RT groups. The percent changes in the leg press strength from pretraining to posttraining in the CON, CNC RT, and ECC RT were \(-2.2\% (95\% CI, -18.7\% to 14.2\%)\), \(33.5\% (95\% CI, 16.1\% to 50.9\%)\), and \(32.8\% (95\% CI, 17.2\% to 48.4\%)\), respectively. The percent changes in the knee extension strength from pretraining to posttraining in the CON, CNC RT, and ECC RT were \(-7.4\% (95\% CI, -19.8\% to 5.1\%)\), \(29.2\% (95\% CI, 7.1\% to 51.2\%)\), and \(20.2\% (95\% CI, 4.1\% to 36.4\%)\). Finally, the percent changes in the knee flexion strength values in these same three groups were \(-0.5\% (95\% CI, -10.2\% to 9.3\%)\), \(20.8\% (95\% CI, 10.7\% to 30.9\%)\), and \(13.3\% (95\% CI, 10.2\% to 28.2\%)\), respectively. Maximal strength values for all other muscle groups are reported in Supplemental Table 2 (Supplemental Digital Content 2, Maximal strength measurements across intervention groups, other muscle groups, http://links.lww.com/MSS/B593). There were no statistically significant group–time interactions for strength for chest press, shoulder press, and seated row. There were significant main effects (\(P < 0.05\)) of both age and sex on strength measures.

There were significant differences in weekly strength gains between the CNC RT and ECC RT groups (Fig. 4). Specifically, the CNC RT had greater mean weekly gains compared with the ECC RT for leg press (\(7.2\% \pm 2.0\%\) vs \(2.3\% \pm 0.7\%; P < 0.001\)) and knee flexion (\(5.0\% \pm 1.5\%\) vs \(2.1\% \pm 0.7\%; P < 0.001\)), but not for knee extension (\(4.3\% \pm 1.2\%\) vs \(3.6\% \pm 1.2\%; P = 0.38\)). Finally, the knee flexor-to-knee-extensor strength ratio was not different across groups over time (\(P = 0.109\)). The mean strength flexor-to-knee extensor ratios for the three groups from pretraining and posttraining were CNC RT (from 1.11 to 1.00), ECC RT (from 1.01 to 1.00), and CON (from 1.03 to 1.14).

Relationship between muscle strength and WOMAC pain scores. Model fitting procedures examined the relationship between the individual strength leg gains on the change in WOMAC pain score, the results of which are shown in Supplemental Table 2 (Supplemental Digital Content 2, Maximal strength measurements across intervention groups for other muscle groups, http://links.lww.com/MSS/B593). Models accounted for age, sex, baseline strength value, and study group. Among the three leg strength measures, knee flexion was a significant predictor of pain reduction (\(P = 0.033\)). Model fitting procedures also examined the relationship between gains in leg strength (for overall sample of patients) and improvements in WOMAC total scores (Supplemental Table 3, Supplemental Digital Content 3, Fixed effects results for the relationship between gains in leg strength and change in WOMAC Pain scores, http://links.lww.com/MSS/B594). The best-fitting, most parsimonious model (in terms of combined \(R^2\) and AIC) resulted from the inclusion of the leg press strength as an independent predictor of improvement in WOMAC total scores.

### Table 2: Baseline WOMAC and maximal leg strength measurements across intervention groups.

<table>
<thead>
<tr>
<th></th>
<th>CNC RT ((n = 28))</th>
<th>ECC RT ((n = 30))</th>
<th>CON ((n = 32))</th>
<th>(P) (Significance)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WOMAC pain</td>
<td>5.9 ± 3.2</td>
<td>6.2 ± 2.8</td>
<td>5.3 ± 3.2</td>
<td>0.496</td>
</tr>
<tr>
<td>WOMAC stiffness</td>
<td>4.3 ± 1.6</td>
<td>3.6 ± 1.5</td>
<td>4.1 ± 1.5</td>
<td>0.588</td>
</tr>
<tr>
<td>WOMAC physical function</td>
<td>25.6 ± 11.1</td>
<td>20.2 ± 10.0</td>
<td>19.2 ± 10.2</td>
<td>0.061</td>
</tr>
<tr>
<td>WOMAC total</td>
<td>35.9 ± 14.7</td>
<td>30.1 ± 13.2</td>
<td>28.0 ± 13.7</td>
<td>0.115</td>
</tr>
<tr>
<td>Leg press</td>
<td>528.9 ± 207.9</td>
<td>597.4 ± 207.7</td>
<td>672.4 ± 179.6</td>
<td>0.701</td>
</tr>
<tr>
<td>Knee flexion</td>
<td>230.6 ± 65.3</td>
<td>281.9 ± 110.2</td>
<td>303.6 ± 98.2</td>
<td>0.211</td>
</tr>
<tr>
<td>Knee extension</td>
<td>322.8 ± 106.9</td>
<td>314.1 ± 178.8</td>
<td>332.9 ± 172.8</td>
<td>0.091</td>
</tr>
</tbody>
</table>

Values are mean ± SD. WOMAC scores are expressed in points, and strength values are expressed in N·m.

FIGURE 2—Change (pretraining to postintervention) in WOMAC scores for CNC RT group (dashed line), ECC RT group (dotted line), and CON group (solid gray line). Error bars represent 95% CI. A, WOMAC total scores. B, Pain subscores. C, Stiffness subscores. D, Physical Function subscores.
scores. This model explained nearly 30% of the variance in the outcome (Supplemental Table 4, Supplemental Digital Content 4, Model fitting results for the relationship between gains in strength and improvement in total WOMAC scores, model 2a, http://links.lww.com/MSS/B595). Greater gains in the leg press exercise result in greater decreases (improvements) in WOMAC total score ($\beta = -0.29$, SE = 0.13, $P = 0.027$).

**Safety and feasibility.** The dropout rates in the CNC RT, ECC RT, and CON groups were 39%, 36%, and 45%, respectively. The proportions of patients experiencing a nonserious adverse event were 10.7% in the CNC RT (arm ligament strain, fall unrelated to study), 3.3% in the ECC RT group (increased hip pain), and 0% in the CON group. The proportion of patients experiencing a severe adverse event was 1.7% (1/58 total exercisers), and this was not related to the study (broken hip due to fall in the home). A total of 13.7% of participants were lost to follow-up because of “personal reasons” (lost interest, assumed care for family member or spouse). Among the others lost to follow-up in the two exercising groups, 6.8% ($n = 4$) were nonadherent to the exercise program, one participant moved away, and one was unexpectedly diagnosed with cancer. In the CON group, seven participants cited personal reasons for stopping the study and decided not to wait for their opportunity to train, and five sought other treatment options for the knee pain.

**DISCUSSION**

We compared the efficacy of ECC RT to traditional CNC RT on knee pain, perceived function, and leg maximal strength for 4 months compared with a control group. Maximal strength improved with both resistance exercise programs, but the rate of strength gain was higher in the CNC RT group. The ECC RT was well tolerated and safe. These findings indicate that ECC RT provides comparable strength benefits to strength or pain reduction compared with CNC RT for 4 months.

We found wide variability in the pain and strength responsiveness to resistance exercise among these participants, with individual knee pain changes ranging from −65% to 78%, and strength improvements ranging from 4% to 54%. Because neither training program seemed superior to the other with respect to mean strength gains and perceived function and pain, there is flexibility for the patient with OA and the care provider to determine which training program best matches the patient’s goals in light of other health considerations.

Data from the Osteoarthritis Initiative show that with disease progression, for each increase in WOMAC pain, knee extensor and flexor strength linearly decrease by 1.6%–1.9% to 1.6%–2.5%, respectively (15). We anticipated that pain severity would be reduced in parallel with training-induced strength gains. The mean group changes in the WOMAC pain scores
over the 4-month period were not statistically different. However, we did find that there was a subset of individuals who responded better to the training than others. Specifically, approximately 50% of the exercising participants in the ECC RT and CNC RT groups achieved clinically significant pain reduction represented by a 30% reduction in WOMAC pain subscore from baseline (2- to 2.8-point reduction). A recent systematic review and meta-regression from 45 varied exercise trials in knee OA revealed that detection of pain improvement or knee function is unlikely unless leg muscle strength gains were ≥30% from pretraining values (18). In our present study, both resistance training groups made gains in leg strength ranging from 13.3% (knee flexion) to 33.5% (leg press). Variability existed in the pain responsiveness to training, where some patients achieved clinically meaningful improvements to pain, whereas others did not. These collective findings suggest that the overall gains made here may not have been sufficient for all exercising participants to obtain clinically meaningful pain relief. Alternatively, the findings could mean that (1) strength gain is but one part of the exercise benefit on pain relief in knee OA, or (2) that contraction type may differentially affect pain depending on individual variations in OA grade, location, and size of cartilage deficits. Recent evidence indicates that eccentric quadriceps strength compared with concentric strength is lower in persons with focal cartilage lesions (35). These areas warrant further study to identify which patients would respond best to which contraction mode depending on OA joint morphology.

Published studies of total body strength training and WOMAC scores in knee OA are limited. One study that used weight machines and free weights reported that a 26%–43% increase in knee flexors/extensors strength paralleled a WOMAC pain score reduction of 9–4.9 points (36). Another study that used Keiser pneumatic machines as the training stimulus did not find training group–time interactions for total WOMAC scores and subscores (37). Pain reductions in the sham and training groups were 1.2–1.8 WOMAC points, respectively (21%–32% pain reductions). The authors explained these findings in part due to the fact that their control group (“sham exercise”) was more than a sham because it consisted of low-volume knee extensions (37). Hence, resistance exercise even in low volumes may positively improve WOMAC scores.

Despite a significantly higher rate of weekly strength gain in the CNC RT group compared with ECC RT, we found that the maximal leg strength gains were not different between training groups. Our findings are similar to studies showing no difference in strength gain and torque between eccentrically and concentrically focused protocols after 5 wk of training (9), but disagree with other evidence that superior strength gains are achieved after 5–12 wk of eccentric resistance training than concentric training (38). One possibility to explain this finding is that the regular resistance exercise, irrespective of type of contraction, may prepare an individual to perform maximal lifts during posttesting. Familiarity with the machines and the sensations experienced during maximal lifts could have mitigated adverse perceptions of the strength testing (e.g., temporary knee pain, fatigue, and elevated heart rate) so that maximal loads were better tolerated and improved in both groups after 4 months. Alternatively, ECC RT may have improved volitional drive by reducing corticospinal inhibition to muscle more than CNC RT (10), enabling participants to achieve similar maximal lifts during strength testing to those in the CNC RT group. The therapeutic application of these findings lies in the ability to individualize strength protocols depending on the goals of the patient, as both were equally effective in terms of improving function while decreasing pain. There is the possibility that there are sex differences in the strength gains and muscle adaptations to different forms of resistance exercise, and thus, individualizing strength protocols may be important. Although data to support this point are limited, Miller et al. (39) reported sex differences in the mitochondrial content and improved contractility of muscle fibers after training in men than in women and believed that much of the strength and functional adaptation in women was related to neural mechanisms. Potentially, the eccentric and concentric stimulus affects strength and function differently in women and men. Future studies should consider sex as a factor in responsiveness to training protocols. The relative contribution of the gains in leg press, knee extension, and knee flexion on OA symptom changes is not clear. Previous intervention studies showed that strengthening exercise involving both knee extensors and flexors produces better WOMAC pain symptom relief than knee extension alone (40). Here, knee flexor strength gain was a significant predictor of pain reduction. This is in contrast to most of the published cross-sectional work of the relationships between leg muscle strength and pain symptoms (38). The hamstring-to-quadriceps ratio (knee flexor/knee extensor) has not been found to be associated with pain severity during daily tasks including stair climb, lying down, standing up, and sitting cross-legged on the floor (38). Our pretraining knee flexor/extensor strength ratios were close to 1, indicating that there was not a relative quadriceps to hamstrings strength deficit in the in our cohort, as has been shown in other knee OA groups. The potential significance of the role in hamstrings to pain reduction could be in part due to favorable shifting of the femoral and tibial contact points relative to the location of the cartilage lesions. Regression modeling revealed that greater gains in the leg press exercise resulted in better WOMAC total scores (β = −0.29, SE = 0.13, P = 0.027). The importance of this finding may lie in the translation of leg press strength to the functionality of the knee. Tevald et al. (41) and Aalund et al. (42) showed that leg press power contributed to the ability to perform physical function tasks such as 10-m fast walks, stair climb, get up and go tests, and chair rise time. Hence, leg press may be more functionally relevant than knee extension or curl in this group. Achievement of strength gain did not seem to be superior in the ECC RT to the CNC RT. This suggests that either mode of training would provide benefit to leg muscles in knee OA. The choice of which strengthening machines to use in the clinical setting can thus be decided by the patient and practitioner depending on the goals of the treatment plan.
For those patients who have OA and issues with hypertension or cardiovascular disease, a program that emphasizes the eccentric phase may prove to be the preferable option, as the cardiovascular cost of this type of contraction is lower compared with the concentric phase.

**Limitations and strengths.** There are several limitations to the present study. In contrast to our expectations, our control group was very healthy and demonstrated similar patterns of WOMAC physical function and stiffness improvements (Fig. 2). Also, our CNC RT group tended to have higher BMIs and lesser fat-free mass, and more were working; it is possible that at baseline, WOMAC functional scores were greater as a consequence. Only \( n = 54 \) patients completed postintervention measurements. There was also greater variability in the pain responsiveness to the training than initially expected. Thus, a greater sample size may have been required to detect statistical significance in both the pain and strength outcomes; follow-up calculations show that \( n = 66 \) patients with completed postintervention data would be needed to detect the observed differences in WOMAC pain scores at statistically significant at \( \alpha = 0.05 \). We used maximal likelihood estimation to handle missing data and used full information for all patients, and this is in line with an intent-to-treat approach. The number of dropouts to the final number of 54 participants was due to a combination of factors including inability to commit to an intensive four month schedule, inability to follow study procedures, personal reasons, and sought other procedures for knee pain. The percent dropouts were not different among the three study groups, ranging from 36.6% to 41.3%, which was 6.6%–11.3% higher than we anticipated at the outset. We were unable to obtain radiographic images of joint space changes and differences in tibiofemoral contact points, which would have provided insight into mechanisms of exercise effects. Study strengths included a rigorous randomized controlled trial design, matched exercise equipment models for head-to-head comparison of muscle contraction type (13), and use of validated, reliable instruments (24,25). A strong finding from this study is that overall, both exercise programs were well tolerated and there were no adverse events related to the exercise that required medical intervention. The machines for the CNC RT are readily available in most fitness and therapy centers, and the protocol is highly feasible. As more companies develop eccentrically focused machines, the ECC RT will also become more feasible for the general public.

**CONCLUSIONS**

ECC RT and CNC RT were both effective in increasing leg muscle strength. WOMAC pain reduction was related to knee flexion strength gains in people with knee OA, and overall WOMAC scores were predicted in part by leg press strength gains. These data indicate that programs that use either traditional modes of resistance training or those that emphasize the eccentric component of the contraction cycle can be well tolerated in this population. Neither proved to be advantageous compared with the other, allowing the provider and the patient to determine which method is best tolerated and fits the patient’s goals and other health considerations most appropriately. The reduced cardiovascular stress associated with eccentric contractions may make this mode more appropriate for patients with cardiovascular disease allowing strength and functional gains while minimizing cardiovascular stress.

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**REFERENCES**


