Arthritis & Rheumatism (Arthritis Care & Research)
Vol. 59, No. 10, October 15, 2008, 1488–1494
DOI 10.1002/art.24118

SPECIAL ARTICLE: DISABILITY AND REHABILITATION IN THE RHEUMATIC DISEASES

Strength Training for Treatment of Osteoarthritis of the Knee: A Systematic Review

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Objective. **To assess the effectiveness of isolated resistance training on arthritis symptoms, physical performance, and psychological function in people with knee osteoarthritis.**

Methods. **A comprehensive systematic database search for randomized controlled trials was performed. Two reviewers independently assessed studies for potential inclusion. Study quality indicators, arthritis symptoms, muscle strength, functional performance, and psychological outcomes were extracted. The relative effect sizes (ES) were calculated with 95% confidence intervals.**

Results. **Eighteen studies enrolling 2,832 subjects were reviewed; the mean cohort age range was 55–74 years. In general, the quality of the reviewed literature was moderately robust; on average, 8 out of 12 quality criteria were accounted for in the reviewed literature. Self-reported measures of pain, physical function, and performance, along with muscle strength (mean 17.4%), maximal gait speed and chair stand time, and balance improved significantly following resistance training in 56–100% of studies where they were measured. Limitations included lack of data available for ES calculations and lack of adverse event and compliance reporting, particularly with regard to the actual training intensity versus the prescribed training intensity.**

Conclusion. **Resistance training improved muscle strength and self-reported measures of pain and physical function in over 50–75% of this cohort; 50–100% of the studies reported a significant improvement in all but 1 performance-based physical function measure (walk time). The effects of resistance training on health-related quality of life and depression are yet to be confirmed. More research needs to be conducted to establish dose-response relationships and the effect of resistance training on long-term disability, disease pathology, and progression.**

INTRODUCTION

Knee osteoarthritis (OA) is one of the most common musculoskeletal disorders in the world, affecting 2,693 of every 100,000 women and 1,770 of every 100,000 men (1). Resistance training has beneficial effects on musculoskeletal function and body composition, cardiovascular disease, insulin action, bone health, energy metabolism, psychological health, and functional status (2–4). These adaptations to resistance training are potentially very relevant to knee OA because quadriceps weakness (5), obesity (6), and abnormal mechanical joint forces (7) have been related to the development and progression of knee OA and are potentially modifiable by resistance training (8–10).

Our objectives were 1) to systematically review randomized controlled trials (RCTs) of resistance training interventions in cohorts with knee OA, 2) to evaluate evidence that resistance training is safe and can improve the symptoms of and functional and psychological impairments associated with knee OA, and 3) to provide recommendations for future investigations.

Clinical trials registration: 12605000116628.

Supported by Faculty Postgraduate Funding from the University of Sydney, awarded in December 2007. Ms Lange's work was supported by Faculty Postgraduate Funding, December 2007.

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Submitted for publication February 14, 2008; accepted in revised form July 11, 2008.

MATERIALS AND METHODS

Search protocol. A systematic database search for full-length manuscripts was conducted in December 2007 (by AKL) using the following databases: Ovid Medline (1950 to December 2007), PreMedline (December 2007), Medline Daily Update (December 2007), CINAHL (Nursing and Allied Health; 1982 to December 2007), all Evidence-Based

Medicine Reviews (1991 to December 2007), SportDiscus (1830 to December 2007), AMED (Allied and Complementary Medicine; 1985 to December 2007), Google Scholar (December 10, 2007), Web of Knowledge (1900 to December 2007), and PEDro (Physiotherapy Evidence Database; 1929 to December 2007). The search terms used in all fields for the intervention (category 1) were "resist," "strength," "weight," "muscle," "anabolic," "physical activity," and "exercise." The terms from category 1 were combined using "OR." The search terms in all fields for the condition (category 2) were "arthritis" and "osteoarthrosis," combined using "OR." Category 1 and 2 results were combined using "AND" and duplicates were removed. All abstracts resulting from these combined searches were reviewed for potential inclusion, and retrieved studies were read in full. In addition to the database search, we performed a manual search of authors and reference lists of included studies, review articles, position statements, and consultation with experts in order to extract further studies.

Inclusion and exclusion criteria. Studies were included if they were published, full-length RCTs, written in English, investigating adults (age >18 years) with primary knee OA, or resistance training interventions that could take the form of resistance machines, free weights, isometric exercise, other devices such as elastic bands, or a combination of methods, either in isolation or as an adjunct to an alternative treatment, prescribed at any intensity.

Studies were excluded if they included people diagnosed with secondary knee OA (traumatic or postsurgical), rheumatoid arthritis, gouty arthritis, septic arthritis, Paget's disease, or pseudogout within their cohort; were animal studies; were reviews, abstracts, and/or unpublished theses; did not include the training protocol in the study design; included cointerventions such as drugs, diet, other exercise modalities, or physical therapy; or did not include a nonexercise control group.

One author performed the search and extracted all of the data (AKL), with all potentially relevant articles discussed between 2 authors (AKL and MAFS). Quality assessment was based on the Delphi list (11), with the addition of supervision of exercise and adequate exercise description as quality items. In addition, we followed the Cochrane Guidelines for Musculoskeletal Systematic Reviews (12), with the exception of including articles not written in English. If studies had a followup phase within their intervention that included an aerobic mode of training, these data were not included. Additional intervention groups (e.g., ultrasound) and subgroups that did not have knee OA upon entry into the study were not included. Authors were contacted for missing data whenever possible.

Statistical analysis. Relative effect sizes (ES) adjusted via Hedges bias-corrected ES for small sample sizes were calculated according to Formula 1 (13). ES were interpreted according to Cohen's interpretation of trivial (<0.20), small (≥0.20 to <0.50), moderate (≥0.50 to <0.80), and large (≥0.80) ES (13). Caution was taken when using Cohen's interpretations because these were originally based on psychological studies, and 95% confidence intervals for the relative ES were calculated. ES were calculated using the Formula 1 equation (13):

$$ES = \frac{\Delta\text{Treatment} - \Delta\text{Control}}{\text{Pooled SD}}$$

A quantitative data synthesis (meta-analysis) was not conducted due to the heterogeneity of study interventions used and outcomes assessed, which made pooling of data across trials inappropriate.

RESULTS

Category 1 and 2 results were combined to obtain a total of 18,443 studies. Of these, 597 studies were potentially relevant. Eighteen studies met the eligibility criteria, with only 1 of those studies being retrieved via the manual search, highlighting the sensitivity of the search strategy employed.

Study quality assessment. On average, 8 out of 12 quality criteria were accounted for in the reviewed literature (see Appendix A, available at the *Arthritis Care & Research* Web site at http://www3.interscience.wiley.com/journal/7705015/home). Limited data from which to calculate ES was the main difficulty in comparing studies. Only 38% of the studies employed an intent-to-treat analysis, 40% reported study compliance, and only 5 of the 18 studies reported the health status of their subjects apart from knee OA.

Only 3 of 18 studies blinded their participants to the experimental intervention (14–16), and 11 studies reported using blinded assessors for 1 or more of their outcome measures (17–27).

Two-thirds (16 of 18) of the studies were supervised. Four studies performed their intervention under complete supervision (14,18,23,28); 2 other studies reported intermittent supervision (24,29); 3 studies supervised their training/instruction sessions during the clinic/center visits only, whereas the home-based sessions were unsupervised (17,19,25); and 7 studies did not report supervising their participants, although given the equipment and prescription used, some degree of supervision would have been necessary (15,20–22,26,27,30). Two studies were performed solely at home; 1 study visited their subjects on 3 occasions (31), whereas the other did not visit their subjects at all (16).

Cohort characteristics. An overview of the cohort characteristics is provided in Appendix B (available at the *Arthritis Care & Research* Web site at http://www3.interscience.wiley.com/journal/77005015/home). All studies consisted of community-dwelling middle-age or older adults. Eight studies defined knee OA by radiographic criteria (14,16–20,27,28), and 4 studies used radiographic and clinical diagnosis (15,21–23). The 2 main sources of recruitment were via medical/rheumatology clinics (17,18,24,27,29–31) or via referral from a physician (15, 22,26).

Mean ± SD age ranged from 55.3 ± 13.6 to 74.6 ± 5.2 years, and the majority of studies had more women than men in their cohort (14–16,19,21–25,27,29–31). All cohorts were overweight or obese on average. Only 3 studies described knee OA medication use (14,16,30). Among the studies that reported comorbidities, hypertension, diabetes, and heart disease were the most common (14,16, 19,20,29).

Intervention characteristics. An overview of the training interventions is provided in Appendix C (available at the *Arthritis Care & Research* Web site at http://www3.interscience.wiley.com/journal/77005015/home). Dynamic or isotonic training was the most common exercise modality (14,16,19,20,23,24,27). Machine-based resistance training was used in 44% of studies (15,20–22,26–28,30), whereas 44% of studies used free weights (14,16,17,19), Therabands, and/or other items around the home (chairs, stairs, etc.) (18,24,29,31). One study (23) used machines and Therabands, and another did not state the type of equipment used (25).

Trial duration ranged from 1 to 30 months. The majority of studies were between 1 and 6 months (14–18,20–22, 24,25,27,28,30,31), and 3 studies were between 18 and 30 months (19,23,32).

Training sessions lasted between 10 and 60 minutes, although most studies did not report the duration of each session (14,20–23,25–29,30,31). The majority of studies prescribed 3 sets (15,16,18,20,23,26,29), but sets ranged from 1 to 10. Five (16,21,22,30), 10 (17,18,20,27), and 12 repetitions (15,19,23,28,29) per set were most commonly prescribed; repetitions ranged from 3 to 20 per set. Three training sessions per week was most commonly prescribed (14,19–23,26–29), but the range was from 2 to 7 sessions per week (15,16,18,24,31).

Among the 13 dynamic exercise trials, 7 were light to moderate intensity (16,17,19,21,22,27,29), 3 were high intensity (14,20,23), and the reviewers were unable to determine the intensity in 3 studies (18,24,31). Among the 8 studies that included an isokinetic and isometric component, 3 studies were maximal intensity (15,28,29), 1 study was submaximal intensity (22), and 4 studies did not explicitly state the intensity (25,26,30,31).

Most (14 of 18) studies were progressive; the most common method was via increasing resistance (14,17, 19,20,23–25,28). In 3 studies, progression was stopped after the first 6 sessions (21,22,30). Four studies did not report any progression in their intervention (15,18,26,28).

Only 6 of the 18 studies provided the average attendance rate of their participants as a percentage, ranging from 50–84% (average 74%) (14,19–23). Therefore, reported compliance was moderate, and true overall compliance across the 18 studies is unknown but likely to be lower. None of the studies indicated whether prescribed training intensity was ever achieved or maintained throughout the trial. One study reported the percentage of participants (60%) who were able to train at the maximum weight (17).

Most (11 of 18) studies did not report the incidence of adverse events (15,17,18,20–22,25,28,29–31). One study provided an a priori definition for an adverse event (19), and another study stated that any injuries were recorded (20). All reported adverse events were minor musculoskeletal injuries. Two studies reported no adverse events (26,28), 3 reported events that could be attributed to the training intervention (19,23,24), 1 reported events that were unrelated to the training intervention (14), and 1 study did not provide any details of their events (16).

Drop-out rates were reported in 17 of the 18 studies, ranging from 0% (15,17,25,28–30) to 36% (mean ± SD 8.3% ± 9.7%) (23). The reasons for dropouts included increased knee pain (21,22), increased pain in general/other areas (24,26), time or travel constraints (23), or personal reasons (20,27). Four studies did not provide any reasons for their dropouts (14,16,19,31).

Control groups: type of intervention. Six studies instructed control groups to continue usual activities (17,24,28–31), with 2 offering exercise sessions at the completion of the trial (24,29). Six studies had placebo interventions, including sham electrical stimulation (15,18), range of motion exercises (23), non–weight-bearing exercises without progression (16), health education (27), and nutritional education booklets plus home visits (14). One study had an active control group that prescribed hyaluronic acid injections (25). Three studies used an enhanced form of usual OA care as part of their study (18,19,26). One study had an attention control group (only telephone contact every 2 weeks) (20), and 2 studies did not provide any details of their control intervention (21,22). Three studies reported having equal contact time between the intervention and control groups (15,18,23).

Outcome measures. *Effects on arthritis.* Pain was measured in all of the reviewed studies (see Appendix D, available at the *Arthritis Care & Research* Web site at http://www3.interscience.wiley.com/journal/77005015/home); 56% (10 of 18) of the studies reported a significant improvement in pain in the resistance training group (14,16,19,21,22,24,28–31). Two studies had inconsistent significant improvements in pain; in 1 study, only half of their self-reported pain measures improved significantly (25), and although the second study found that more people improved their pain score in the exercising group compared with the control group (65% versus 36%; $P = 0.007$), the between-group difference in the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain score did not reach statistical significance (26). Five of the 18 studies assessed joint stiffness, and 2 studies (24,30) found a significant improvement in the resistance training group.

Physical disability significantly improved in the resistance training group in 79% (11 of 14) studies where it was measured (14,16,19,21,22,24,27–31) (see Appendix D, available at the *Arthritis Care & Research* Web site at http://www3.interscience.wiley.com/journal/77005015/home). Penninx and colleagues (33) from the Fitness, Arthritis, and Seniors Trial (FAST) study reported a relative risk of 0.60 for incident activities of daily living disability.

Relative ES for symptom reduction were very large on average (−2.11, range 0.05 [15] to −6.47 [29] across the studies in which they could be calculated). Relative ES for physical disability reduction were smaller on average, although the range of ES was very broad (0.31, range −3.58 to 2.15). One study had a large ES for the change in physical function (ES −1.57; isometric training group), but the result did not reach statistical significance for the group by time effect even though it was sufficiently powered (29). In 3 of the studies where self-reported pain and disability did not significantly change, no ES were able to be calculated, limiting the reviewers' ability to assess whether or not a Type II error may have precluded demonstration of statistical significance.

Only 4 studies provided results of clinical or radiologic disease severity following their intervention (14,19,23,26) (see Appendix D, available at the *Arthritis Care & Research* Web site at http://www3.interscience.wiley.com/journal/77005015/home). Clinical knee examination improved in 1 study (14), 2 studies reported nonsignificant improvements in joint space narrowing (23) and knee joint effusion (14%) (26), and 1 study reported no change in radiograph score (19).

Muscle function and morphology. In general, muscle strength improved significantly in the resistance training groups (mean improvement of 17.4%, range 10.5% decrease to 49.5% increase), with 9 out of 14 studies reporting significant improvements (see Appendix E, available at the *Arthritis Care & Research* Web site at http://www3.interscience.wiley.com/journal/77005015/home). Relative ES for strength outcomes ranged from −0.04 (14) to 1.52 (30), with an average of 0.38 (small to moderate).

Positive associations were found between increased muscle strength and walking self-efficacy ($r = 0.383$) (14), reduced pain ($P < 0.05$) (26), improved function ($r = -0.336$ [14], $P < 0.05$ [26]), and total WOMAC score ($P < 0.05$) (26). Additionally, Baker and colleagues (14) pooled results of several strength training studies and found a significant association between improvements in knee extension strength and self-reported disability ($r = 0.877$, $P = 0.02$). Passive knee range of motion increased in only 1 (16) of 6 (16–18,25,27,30) studies reporting this outcome.

Physical performance. In general, challenging physical tasks improved significantly in the resistance training groups relative to controls (see Appendix F, available at the *Arthritis Care & Research* Web site at http://www3.interscience.wiley.com/journal/77005015/home), whereas measures of habitual gait or aerobic capacity did not consistently improve.

Walking endurance, measured via the 6-minute walk test, improved significantly in the resistance training group in 1 of the 2 studies where it was measured (19), and time taken to complete a specified distance significantly improved in 1 of the 4 studies where it was measured (16).

Maximal gait speed improved significantly following resistance training in all 4 of the studies where it was assessed (20–22,27). In addition, Lin and colleagues (27) tested maximal gait speed on stairs, walking in a figure 8, and habitual gait on a compliant surface, and found that speed increased significantly after resistance training. Maximal stair climb/descent time was assessed in 5 studies (14,16,19,28,29) and significantly improved with resistance training in 3 studies (14,16,28). Maximal chair stand time was assessed and significantly improved after resistance training in 2 studies (14,28).

Balance was analyzed in 1 study (34). Static balance in the eyes-closed double-leg stance condition improved significantly after resistance training and tended to improve for the single-leg stance eyes-open condition ($P = 0.074$).

Psychological health outcomes. The psychological domains of the Short Form 36 and the overall effect of resistance training on health-related quality of life was measured in 6 studies with inconsistent results (14,20,23,24,26,31) (see Appendix G, available at the *Arthritis Care & Research* Web site at http://www3.interscience.wiley.com/journal/77005015/home).

Physical self-efficacy was reported in 2 studies; walking self-efficacy score (14) and satisfaction self-efficacy (20) improved significantly in their respective resistance training groups.

Effect of compliance on outcome measures. Five studies ([16,19,23,31] and an additional analysis from the FAST study [33]) performed a secondary analysis and reported significant positive effects of increasing compliance with the lowest risk of incident activities of daily living disability (33) and self-reported disability (19), and improvement in pain (16,19,31), walking endurance (16,19), stair-climbing performance (16), and muscle strength (23,31).

Cost-effectiveness. Four studies assessed the costs associated with their interventions. Sevick and colleagues (35) did a cost-effectiveness analysis of the FAST study and found that compared with health education, resistance training was more economically efficient than aerobic training for improving self-reported disability and various other observed physical function outcomes.

Thomas et al also published the cost-effectiveness of their interventions (32). The exercise intervention cost more (£112 [$227] per patient) than the telephone contact (control group; £61 [$124] per patient), but the exercise was significantly more effective in improving pain. Callaghan and Oldham (18) found that the functional exercises performed without supervision (i.e., enhanced OA care) were more cost-effective than the exercises performed under the supervision of a physiotherapist. Finally, Maurer and colleagues (26) indicated that although the exercise intervention was effective, the educational program still provided substantial benefits over time, including significant improvements in isometric and isokinetic knee extension strength and self-reported disability at a much cheaper cost, although no cost-effectiveness data was reported.

DISCUSSION

Eighteen RCTs enrolling a total of 2,832 patients with knee OA have been identified. In general, the quality of the reviewed literature is moderately robust; on average, 8 out of 12 quality criteria were present. The most common deficiencies were lack of blinding of assessors, lack of reporting concealment, adverse events, exercise supervision, and training intensity compliance. Limited ES calculations due to incomplete data presentation restricted thor-

Table 1. Summary of significant improvement in outcome measures in the strength training group relative to the control group

Outcome	Studies that measured the outcome	Studies with significant improvement in the strength training group compared with control	
		No. (%)	Ref.
Self-reported			
Pain	18	10 (56)	14, 16, 19, 21, 22, 24, 28–31
Stiffness	5	2 (40)	24, 30
Physical disability	14	11 (79)	14, 16, 19, 21, 22, 24, 27–31
Quality of life	6	2 (33)	14, 23
Self-efficacy	2	2 (100)	14, 20
Depression	2	0 (0)	
Muscle function			
Strength	14	9 (64)	14, 19–22, 24, 27, 28, 31
Range of motion	6	1 (17)	16
Physical performance			
Walking endurance	2	1 (50)	19
Walk time	4	1 (25)	16
Maximal/challenging gait speed	4	4 (100)	20–22, 27
Habitual gait speed	2	1 (50)	44
Stair climb	5	3 (60)	14, 16, 28
Sit-to-stand	2	2 (100)	14, 28

ough comparisons of outcomes across studies and assessment of the possibility of Type II errors. Study quality did not appear to be related to the magnitude of benefits reported.

Generalizability of the findings to clinical cohort characteristics is unclear, given that the majority of studies did not present a detailed description of medical comorbidities. Although strength improvements were generally greater in studies of women and younger subjects, no such trends were evident for knee OA symptom relief.

Table 1 provides a summary of significant results for the resistance training group. Specifics of the resistance training prescription used (modality, duration, volume, frequency, intensity) did not appear to be related to study outcomes, although an analysis of overall effectiveness of strength training for different severities of knee OA was not included in any of the reviewed studies. However, in the studies where none of the relevant outcomes were significant, 3 of the 4 (15,18,26) did not employ a progressive element in their training intervention.

The development and progression of knee OA is multifactorial, with quadriceps weakness being one of the main factors that is modified by resistance training according to this review. It appears that all modes of resistance training can improve strength in this cohort. Muscle strength improved by a mean of 17.4%, which is in the lower range of strength improvements seen in non-OA cohorts (4% to <150%) (36). The low overall percentage of strength improvement may be due to the low to moderate training intensity prescribed in the majority (15 of 18) of studies, because maximal isokinetic (21,22,30,37) and high-intensity dynamic training (14) yielded higher relative strength gains (20.4–49.5%).

Although limited, the reviewed studies suggest that participation in a resistance training program can potentially counteract the functional limitations seen in knee OA; positive associations were found between increased muscle strength and walking self-efficacy, reduced pain, improved function, and total WOMAC score. Notably, improvements were greater in maximal versus submaximal effort testing, possibly due to a ceiling effect.

Fifty-six percent of the studies reviewed found an improvement in self-reported measures of pain and physical disability/mobility following the training intervention. It is difficult to establish whether or not the studies that had insignificant changes in self-reported pain and disability were due to Type II error due to a lack of ES data available.

The minimal clinically important difference for WOMAC (10-point scale) is between 17% and 22% (38), and minimally perceptual clinical improvement is 14–16% (100-mm normalized visual analog scale) (39). Although the studies reviewed did not necessarily use those exact scales, out of the 8 studies that used the WOMAC questionnaire and for which a percentage change score was able to be calculated, 5 studies had percentage change scores in their resistance training groups within or higher than the above ranges for 1 or more of the WOMAC subscores (14,26,27,29,31). One of the studies did not have a statistically significant improvement in its WOMAC subscores, but did show a clinically relevant improvement (26). Three studies were below the ranges specified (20,23,24), with 1 of those studies reporting a statistically significant difference following their intervention (24).

Clinical trials in the future should include not only the physical function and self-reported outcomes, but should also assess long-term changes in the morphology of the articular cartilage and surrounding bone. Imaging techniques (e.g., magnetic resonance imaging) have been validated for this purpose (40), and, along with cartilage biomarker analysis, would provide further insight into the mechanisms of benefit of long-term exercise interventions in knee OA. Up until now, the research on knee OA and exercise has centered on the self-reported measures of disability and rarely objective measures (medication use, nursing home admissions, health care use, progression to joint replacement, and cost-effectiveness), which require further study to assess efficacy of resistive exercise for these important clinical outcomes. In older adults, aerobic exercise has been demonstrated to decrease total habitual physical activity levels (41), whereas we (42,43) have shown, by contrast, that PRT in older adults is associated with an increase in overall habitual physical activity levels. Therefore, structured aerobic exercise may substitute for walking and other lifestyle activities, but progressive resistance training may actually enable adults with muscle weakness, mobility impairment due to OA, or other causes to increase their overall activity level. This needs to be explored specifically in cohorts selected for OA as the limiting factor in their sedentary behavior.

The inclusion of adverse event reporting, session and intensity compliance reporting, and more complete data sets to calculate ES are needed in order to fully establish the efficacy and feasibility of resistance training.

There is reasonably large and robust literature supporting the efficacy of resistance training in patients with knee OA. Over 50–75% of the studies included in this review found knee OA symptoms, physical function, and strength improved by clinically meaningful amounts with resistance training when compared with usual care. Because strength changes have been shown by several authors to be related to symptoms and physical function at various training intensities, large trials comparing different intensities of PRT would be needed to answer this question fully. Although more safety data is needed, it appears that resistance training administered in a variety of modes and intensities is tolerable and effective in this cohort. However, at this stage there is insufficient data available to comment on the efficacy of resistance training on measures of health-related quality of life and psychological outcomes or disease progression and overall health care use, and extrapolation of the findings to patients with severe knee OA, multiple comorbidities, or frailty should be made with caution until further long-term studies in these higher-risk cohorts are conducted.

AUTHOR CONTRIBUTIONS

Ms Lange 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 design. Lange, Vanwanseele, Fiatarone Singh.
Acquisition of data. Lange, Fiatarone Singh.
Analysis and interpretation of data. Lange, Vanwanseele, Fiatarone Singh.
Manuscript preparation. Lange.
Statistical analysis. Lange.

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