J Rehabil Med 2008; 40: 137–144

ORIGINAL REPORT

A RANDOMIZED CONTROLLED TRIAL OF AQUATIC AND LAND-BASED EXERCISE IN PATIENTS WITH KNEE OSTEOARTHRITIS*

Hans Lund, RPT, PhD[1], Ulla Weile, RPT, MSc[1], Robin Christensen MSc[2], Benedicte Rostock, RPT, MSc[3], Anne Downey, RPT[3], Else Marie Bartels, PhD, DSc[2,4], Bente Danneskiold-Samsøe, MD, DMSc[1,2] and Henning Bliddal, MD, DMSc[1,2]

From the [1]Clinical Motor Function Laboratory, [2]Musculoskeletal Statistics Unit and [3]Department of Physiotherapy, The Parker Institute, Frederiksberg Hospital, Fredriksberg and [4]Copenhagen University Library, Copenhagen, Denmark

Objective: **To compare the efficacy of aquatic exercise and a land-based exercise programme vs control in patients with knee osteoarthritis.**

Methods: **Primary outcome was change in pain, and in addition Knee Injury and Osteoarthritis Outcome Score questionnaire (KOOS). Standing balance and strength was also measured after and at 3-month follow-up. Seventy-nine patients (62 women), with a mean age of 68 years (age range 40–89 years) were randomized to aquatic exercise ($n = 27$), land-based exercise ($n = 25$) or control ($n = 27$).**

Results: **No effect was observed immediately after exercise cessation (8 weeks). At 3-month follow-up a reduction in pain was observed only in the land-based exercise group compared with control (–8.1 mm, (95% confidence interval –15.4 to –0.4; $p = 0.039$), but no differences between groups were observed for KOOS; and no improvement following aquatic exercise. Eleven patients reported adverse events (i.e. discomfort) in land-based exercise, while only 3 reported adverse events in the aquatic exercise.**

Conclusion: **Only land-based exercise showed some improvement in pain and muscle strength compared with the control group, while no clinical benefits were detectable after aquatic exercise compared with the control group. However, aquatic exercise has significantly less adverse effects compared with a land-based programme.**

Key words: osteoarthritis, knee, musculoskeletal equilibrium, muscle, skeletal, pain, physical function, hydrotherapy.

J Rehabil Med 2008; 40: 137–144

Correspondence address: Hans Lund, Institute of Sports Science and Clinical Biomechanics. University of Southern Denmark, Campusvej 55, DK-5230 Odense M, Denmark. E-mail: hlund@health.sdu.dk

Submitted January 19, 2007; accepted August 29, 2007.

INTRODUCTION

Primary osteoarthritis (OA) is the most common type of arthritis, with the knee as the most commonly affected joint. Approximately 10% of the population over the age of 65 years have symptoms of OA, and subclinical, radiographic OA may be present in more than half of this age group (1). The most prominent symptom in knee OA is pain. Other symptoms might be due to the various deficits present in patients with knee OA, such as reduced balance (2), muscle weakness (3), decreased joint range of motion (ROM) and joint instability (4). The sum of these deficits is a reduced ability to perform activities of daily living (5). Exercise studies that aimed at improving both strength and endurance have reported improvements on pain relief and physical function (6–8), whereas reviewing data on aquatic exercise alone supports short-term efficacy (9–11); however, others have demonstrated a lack of effect (12–15). Misalignment may be associated with a deterioration of the disease (16), and it may be speculated that weight-bearing exercises can cause adverse effects in knee OA. Indeed, we have seen indications of hydarthrosis in relation to exercise in this group of patients (17).

A possible alternative to land-based exercise is aquatic exercise, where the buoyancy reduces the loading on the damaged joints.

The aim of this study was to compare the efficacy of aquatic exercise and a land-based exercise programme vs control in patients with knee OA, with pain being the primary outcome; in addition physical function, quality of life, balance, and knee muscle strength was monitored and analysed. If a significant difference was found, the 2 interventions was compared *post hoc*, in order to evaluate the relative importance of the different exercise regimes.

METHODS

Design and randomization

The study was a single-blind, randomized, controlled trial with blinded assessment. The 79 patients were randomized (envelope method (opaque) with blocks of 18 (3 × 6) subjects). All 3 groups were asked to continue any other treatment as usual. Informed consent was given prior to randomization, and the baseline measurements were also taken at this point in order to keep the randomization concealed.

Patients

Patients with primary knee OA were recruited from the outpatient clinic, from general practitioners (via letters), and following adver-

*This study was presented as a poster at OARSI, 2005 in Boston, USA.

 ISSN 1650-1977
doi: 10.2340/16501977-0134

tising in local newspapers. A rheumatologist examined the recruited patients to ensure they complied with a definite OA diagnosis at enrolment. All patients fulfilled the OA criteria according to The American College of Rheumatology (18), as well as having C-reactive protein within the reference range, and a negative rheumatoid factor (19). Exclusion criteria were hydrophobia, incontinence, wounds, language or intellectual problems, a history of periarticular knee fracture, total knee replacement, inflammatory joint disease, heart or lung condition and other medical diseases with possible contra-indication of exercise and/or pool therapy, present participation in other clinical or exercise trials, and secondary knee OA. A pre-study power analysis was performed based on a pilot study ($n = 4$, aquatic exercise), performed immediately before the present project, and an earlier study from our laboratory (17) showed an average reduction in the visual analogue scale (VAS) pain score of 22 mm, and a corresponding standard deviation (SD) of 30.25 mm. With an alpha level of 5% and a beta level of 20% (corresponding to 80% power), this indicated that the sample size should be 30 in each group.

Interventions

The intervention started during the week following randomization. Six physiotherapy students instructed the exercise lessons. All students were in the last term of their physiotherapy education and had all passed the examination in "Physical Exercise". The intervention programme was carried out for 8 weeks with 2 sessions per week.

Both the aquatic and land-based exercise programmes consisted of the following parts: warm-up, strengthening/endurance exercise, balance exercise and stretching exercise (Appendix I). Each session lasted 50 min, comprising 10 min warm-up, 20 min resistance exercises, 10 min balance and stabilizing exercises, 5 min lower limb stretches and 5 min cool-down period (Appendix I). The exercises were not individualized within the allocated groups. All patients in the aquatic group and all patients in the land-based group did the same exercises, in order to standardize the procedures used.

In the land-based programme, the resistance was the patient's own body weight, a rubber band, or weight resistance (leg press). In water, viscosity, buoyancy and turbulence provided resistance, as did the use of different aqua adjuncts, such as aqua noodles, rings, kick boards and the hands of the physiotherapist. The temperature in the pool was 33.5°C. To create uniform exercising, music was recorded for the purpose and used at each session to ensure that the rhythm and length of performance were exactly the same at all times. The instructor of each session noted drop-outs, adverse reactions, and other comments at each exercise session. Compliance was expressed as the percentage of sessions attended.

Outcome measures

Pain was chosen as the primary outcome (20). All measurements of indicators of improvement were carried out immediately prior to exercise to give a set of baseline data. Following 8 weeks of exercise (post-exercise) the same measurements were performed, and again after 20 weeks (3-month follow-up). All measurements were carried out by 2 independent physiotherapists, who were both experienced in the measuring methods and blinded to the treatment. The various measurements were taken randomly in each session, except for the muscle strength measurement, which was always taken last.

Pain assessment scale. Patients completed a 100-mm VAS (21) based on the degree of (*i*) worst pain at rest, and (*ii*) worst pain at walking. "Worst imaginable pain" was marked at the right extreme of the line, and "No pain at all" at the left extreme of the line. All measurements were taken from left to right. Patients were not permitted to see previous scores.

Knee Injury and Osteoarthritis Outcome Score questionnaire (KOOS). KOOS is a three-dimensional, disease-specific, self-administered health status measure, which assesses 5 indicators: pain, symptoms, physical function, sport and recreation function, and knee-related quality of life. Standardized answer options are given (5 Likert boxes), and each question is scored from 0 to 4. A normalized score (100 indicating no symptoms and 0 indicating extreme symptoms) is calculated for each subscale (22). KOOS is a developmental variant of the WOMAC questionnaire from 1988, which was intended for assessment of elderly people with primary OA (23).

Standing balance. Balance was evaluated using a Balance Master Pro® (Version 6.0, NeuroCom® International Clackamas, OR, USA) as described previously (24). Stability and ankle strategy were expressed as percentage of maximal stability, and mean sway velocity in degrees per second (deg/s).

Each patient was assessed in 4 different conditions: (*i*) eyes open, stable surface (EO); (*ii*) eyes closed, stable surface (EC); (*iii*) eyes open, sway-referenced surface (EOSS); and (*iv*) eyes closed, sway referenced surface (ECSS). Each measurement consisted of 3 sequences, based on which a mean value was calculated. The 3 variables in the analysis are the mean sway velocity, mean percentage maximal stability, and mean percentage ankle strategy. During the measurement the patient was positioned on the platform to face the monitor with feet slightly apart, and with the arms alongside the body. To reduce variability patients had a pre-run prior to each measurement.

Knee muscle strength. Maximal voluntary muscle strength of hamstrings and the quadriceps muscles was measured by isokinetic dynamometry at 30 deg/s, 60 deg/s and 90 deg/s (Biodex System 3 PRO, Biodex Medical System, NY, USA) (25). Isokinetic measurements are applicable for elderly people and patients with rheumatic diseases (26). The dynamometer was calibrated every day, after the warm-up period. The test person was comfortably seated and strapped to the dynamometer chair with leg straps and a body belt. The lower part of the test leg was placed in the foot support so that the axis of the rotation corresponded to the axis of the knee's flexion and extension. Prior to the measurements a correction for gravity was made by placing the test person's lower leg in the ROM position closest to horizontal. The dynamometer registered the leg's weight, which was then used for gravity correction of the obtained force during the further measurements. The best of the 3 results was chosen as maximal isokinetic muscle strength. During the test procedure each patient was required to fold their arms across their chest and was given verbal encouragement in an attempt to achieve a maximal effort level. Prior to each test the purpose and procedure were verbally explained to the patients and they were asked to perform a submaximal test in order to familiarize them with the test.

Statistical analyses

The primary analysis was based on General Linear Models with the outcome measures applied as dependent variables (i.e. VAS pain, KOOS, balance and muscle strength for each individual at a particular time point). The factor *treatment* (3 levels) was applied as a fixed factor, and in each analysis the individual patient's baseline level was used as covariate in the corresponding 1-way analysis of covariance (ANCOVA). Thus any random difference between the groups at baseline was implicitly adjusted for. All data are presented as mean ± standard error (SE), unless stated otherwise. We used SAS statistical software (SAS® version 9.1).

In addition, an intention-to-treat analysis was included as recommended (27), using the last observation carried forward methodology, as it tends to produce more conservative estimates independent of drop-out rates between the groups (28).

The isokinetic knee muscle strength measurements were taken at 3 different velocities (30, 60 and 90 deg/s), both for flexion and extension. Thus the total number of muscle strength expressions was $3 \times 2 = 6$ repeated (assumed mutually correlated) measures. In order to minimize the number of different expressions of the muscle strength we performed a linear mixed model procedure in which the 3 different velocities were analysed together: based on the resulting estimates from the 2-group comparisons from (*i*) aquatic exercise vs control and (*ii*) land-based exercise vs control, which was handled as the standardized mean difference (SMD) – supplied with the corresponding variances ($\sigma^2 \approx [SE]^2$). These individual outcomes (subjects clustered within multiple expressions) were used to calculate the inverse-variance weighted effect size (i.e. pooled SMD), based on a maximum-likelihood method in analogy to the recommended approach for meta-analysis (29, 30). This analogy to meta-analyses has previously been introduced for the analysis of cluster randomized trials (31). The level of significance was defined (a priori) as $p \leq 0.05$ (2-tailed); however, the clustered data analyses (muscle strength and balance) is presented with 95% confidence intervals (95% CI) based on a Gaussian distribution ($\pm 1.96 \times SE_{pooled}$). Whereas 95% CI for pain scores etc. is based on the *t*-distribution.

The pooled clustered empirical analyses were only carried out on a *per-protocol* basis, since we were investigating the changes in muscle strength and balance as a result of exercise (aquatic or land-based, compared with a control group not adding exercise therapy).

Ethics

The experimental protocol was in accordance with ethical standards on human experimentation and with the Helsinki Declaration of 1975 as revised in 1983, it was approved by The Scientific-Ethical Committee for Copenhagen and Frederiksberg (J.nr. KF 01-056/02), and each patient gave signed informed consent.

RESULTS

Recruitment started in January 2003 and was completed in April 2004. A total of 134 persons responded to the advertising and 50 were referred from general practitioners. Of the 184 persons who were interested in taking part in the trial, 98 were, by means of telephone interviews, considered eligible patients in accordance with the inclusion and exclusion criteria (Fig. 1). Fifteen of these were excluded following the clinical examination performed by the rheumatologist and 4 decided not to participate after being fully informed about the randomized design. Finally, 79 patients were randomized to the aquatic exercise group ($n = 27$), the land-based exercise group ($n = 25$) or a control group (no exercise) ($n = 27$). The demographic characteristics of the patients are given in Table I.

Of the 79 patients randomly allocated, 8 dropped out during the exercise period: 5 from the land-based exercise group, 3 due to increased pain, one due to a fracture not related to the exercise programme, and one due to work; 2 from the control group, one dropped out at baseline, one moved abroad, and one did not showed up att follow-up; and one from the aquatic exercise group due to work. Seventy-one patients completed the programme: 26 in the aquatic exercise group, 20 in the land-based exercise group and 25 in the control group. Compliance in the aquatic exercise

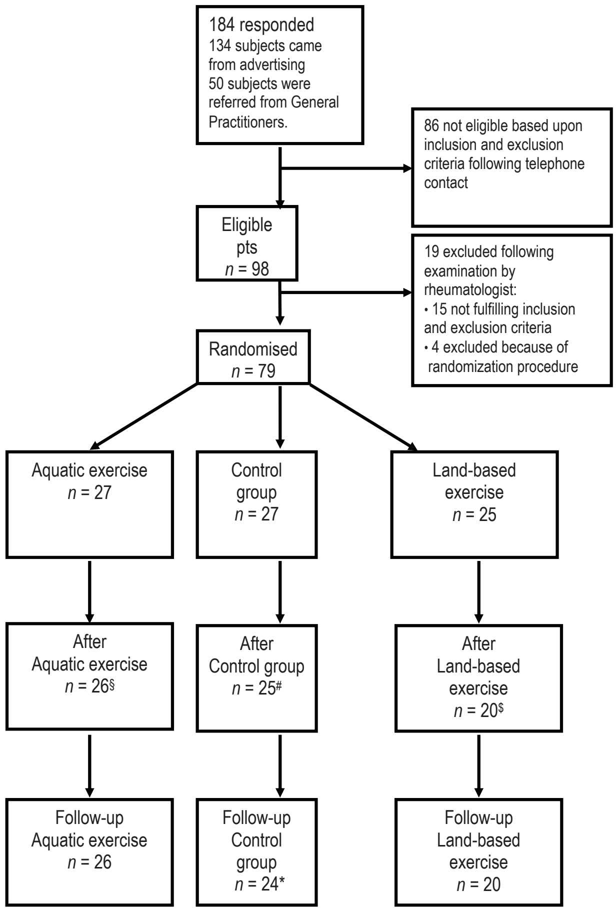

Fig. 1. Patients in the present study. §One stopped due to work. #One stopped due to moving abroad, and one dropped out at baseline. $Three patients stopped due to increased pain. One patient stopped due to an antebrachium fracture, and one stopped due to work. *One did not showed up at follow-up.

group was 92%, and 85% in the land-based exercise group. A significant difference between all 3 groups was found for body weight ($p = 0.03$, Table I), but a *post-hoc* analysis showed that this difference was only between the aquatic exercise group and the land-based exercise group ($p = 0.05$). Baseline values for all dependent variables are presented in Table II.

Pain assessment scale. No difference in pain was observed immediately following exercise for any of the groups (Table III). A significant reduction in pain at rest at 3 months follow-up

Table I. *Demographic characteristics. Values are mean (SD) unless otherwise stated*

	Aquatic ($n = 27$)	Control ($n = 27$)	Land-based ($n = 25$)	*p*-value
Females, *n* (%)	22 (83)	18 (66)	22 (88)	0.13
Age (years)	65 (12.6)	70 (9.9)	68 (9.5)	0.17
Weight (kg)	81.1 (19.2)	77.3 (8.5)	67.6 (11.5)	0.03
Height (cm)	172.0 (7.1)	172.0 (10.4)	168.8 (9.1)	0.29
Duration of OA (median, 1st and 3rd quartile, years)	8.5 (3.4–10.8)	4.5 (3.6–10.8)	7.8 (4.6–20.3)	0.18
Lequesne score (1–26)	11.8 (2.8)	10.8 (4.0)	11.1 (2.8)	0.59
Blood pressure (Systolic/diastolic; mmHg)	143/88 (88/30)	146/84 (11/11)	144/83 (19/9)	0.95/0.18

OA: osteoarthritis; SD: standard deviation.

Table II. Baseline values for aquatic, control and land-based groups. Values are mean (SD) unless otherwise stated

	Aquatic (n = 27)	Control (n = 27)	Land-based (n = 25)	p-value
VAS pain at rest (0–100 mm)	29.8 (23.5)	15.5 (20.1)	23.3 (18.8)	0.14
VAS pain during walking (0–100 mm)	59.8 (18.4)	48.5 (31.9)	53.0 (32.6)	0.43
KOOS symptom (0–100)	50.5 (13.6)	50.1 (13.6)	50.9 (12.7)	0.89
KOOS pain (0–100)	47.1 (15.2)	37.9 (15.0)	41.0 (14.8)	0.12
KOOS ADL (0–100)	44.7 (18.1)	39.6 (13.2)	40.6 (13.6)	0.51
KOOS sport (0–100)	79.1 (18.4)	70.0 (22.8)	75.6 (20.3)	0.38
KOOS quality of life (0–100)	63.7 (11.8)	60.8 (13.1)	57.0 (12.4)	0.18
Muscle strength (extension 30/sec, Nm)	81.0 (24.8)	91.2 (27.8)	89.4 (35.7)	0.41
Muscle strength (extension 60/sec, Nm)	70.9 (26.1)	81.2 (23.0)	82.6 (31.3)	0.23
Muscle strength (extension 90/sec, Nm)	63.0 (20.1)	73.4 (21.0)	73.3 (26.3)	0.16
Muscle strength (flexion 30/sec, Nm)	38.0 (14.0)	45.6 (16.8)	41.7 (18.4)	0.24
Muscle strength (flexion 60/sec, Nm)	35.2 (14.0)	43.1 (16.7)	39.2 (17.8)	0.20
Muscle strength (flexion 90/sec, Nm)	30.9 (12.4)	38.0 (15.2)	33.0 (18.2)	0.22
Balance (V, EO) (%)	0.33 (0.13)	0.34 (0.11)	0.39 (0.16)	0.20
Balance (V, EC) (%)	0.56 (0.28)	1.02 (2.5)	0.71 (0.42)	0.51
Balance (V, EOSS) (%)	0.71 (0.39)	0.75 (0.30)	0.80 (0.32)	0.70
Balance (V, ECSS) (%)	1.54 (0.56)	1.56 (0.44)	1.66 (0.58)	0.70
Balance (MaxStab, EO) (%)	93.15 (3.60)	93.23 (2.12)	92.20 (3.04)	0.41
Balance (MaxStab, EC) (%)	89.44 (3.67)	89.44 (3.28)	87.45 (5.47)	0.16
Balance (MaxStab, EOSS) (%)	76.10 (14.64)	75.80 (14.35)	75.96 (12.86)	0.99
Balance (MaxStab, ECSS) (%)	49.41 (24.42)	50.70 (19.93)	52.11 (20.11)	0.90
Balance (AnkleStr, EO) (%)	95.38 (2.21)	94.88 (2.55)	95.65 (2.46)	0.50
Balance (AnkleStr, EC) (%)	92.00 (4.50)	91.73 (5.20)	92.36 (6.85)	0.92
Balance (AnkleStr, EOSS) (%)	81.21 (11.26)	83.16 (5.38)	81.92 (9.51)	0.73
Balance (AnkleStr, ECSS) (%)	64.87 (13.13)	61.41 (17.07)	64.08 (13.92)	0.67

KOOS: Knee injury and Osteoarthritis Outcome Score; ADL: activities of daily living; VAS: visual analogue scale; V: velocity; MaxStab: maximal stability; AnkleStr: ankle strategy; EO: eyes open; EC: eyes closed; EOSS: eyes open sway surface; ECSS: eyes closed sway surface.

was observed in the land-based exercise group compared with the control group (group mean difference –8.1 mm (95% CI –15.8 to –0.4 mm; p = 0.039, Table IV)).

Knee Injury and Osteoarthritis Outcome Score (KOOS) questionnaire. No significant differences between groups were observed in the self-reported daily symptoms, pain, physical function, sports activities or quality of life. This was the case both immediately after the end of treatment and at 3 months follow-up (Table III and Table IV).

Knee muscle strength. A significant overall effect on muscle strength was found for the land-based exercise programme compared with control (SMD 0.20; 95% CI 0.02–0.38), while

Table III. *Clinical outcome measures (Knee injury and Osteoarthritis Outcome Score (KOOS) and Visual Analog Scale (VAS) pain at rest and while active) immediately after 8 weeks of exercise. Intention to treat results and the per protocol results are presented*

	Aquatic Mean (SE)	Control Mean (SE)	Land-based Mean (SE)	Aquatic vs control GMD (95% CI)	Land-based vs control GMD (95% CI)	Aquatic vs land-based GMD (95% CI)
Intention to treat						
VAS pain at rest	20.3 (3.2)	27.2 (3.2)	18.8 (3.3)	–3.9 (–13 to 5.2)	–5.5 (–14.6 to 3.6)	1.5 (–7.6 to 10.7)
VAS pain during walking	55.8 (4.0)	58.1 (4.0)	51.5 (4.1)	–2.3 (–13.6 to 8.9)	–6.6 (–18.0 to 4.8)	4.3 (–7.2 to 15.7)
KOOS symptom	64.6 (2.31)	61.4 (2.3)	66.9 (2.3)	3.3 (–3.3 to 9.8)	5.5 (–1.1 to 12.1)	–2.3 (–8.8 to 4.4)
KOOS pain	60.2 (2.4)	60.3 (2.4)	62.0 (2.5)	–0.2 (–7 to 6.7)	1.7 (–5.2 to 8.5)	–1.8 (–8.7 to 5.1)
KOOS ADL	62.7 (2.3)	61.1 (2.2)	64.1 (2.3)	1.6 (–4.7 to 8.0)	3.1 (–3.4 to 9.5)	–1.5 (–0.8 to 5.0)
KOOS sport	26.2 (3.0)	21.8 (3.0)	28.4 (3.1)	4.4 (–4.1 to 12.9)	6.6 (–2.0 to 15.2)	–2.2 (–10.8 to 6.3)
KOOS quality of life	43.0 (2.4)	43.1 (2.3)	43.8 (2.5)	–0.1 (–6.7 to 6.5)	0.7 (–6.1 to 7.5)	–0.9 (–7.7 to 6.0)
Per protocol						
VAS pain at rest	17.6 (5.2)	23.5 (6.6)	14.5 (4.8)	–6.0 (–23.2 to 11.3)	–9.0 (–25.8 to 7.7)	3.1 (–11.4 to 17.6)
VAS pain during walking	51.1 (8.1)	55.6 (7.6)	43.5 (7.1)	–4.5 (–27.3 to 18.4)	–12.1 (–33.4 to 9.2)	7.6 (–14.5 to 29.7)
KOOS symptom	62.4 (4.0)	67.4 (3.7)	63.2 (4.5)	–5.1 (–16.0 to 5.8)	–4.2 (–16.0 to 7.5)	–0.8 (–12.9 to 11.2)
KOOS pain	57.9 (3.0)	64.0 (3.4)	60 (4.4)	–6.1 (–15.3 to 3.0)	–4.0 (–15.2 to 7.2)	–2.1 (–12.9 to 8.6)
KOOS ADL	61.7 (3.6)	62.3 (3.0)	63.6 (4.3)	–0.6 (–10.1 to 8.8)	1.3 (–9.2 to 11.9)	–1.9 (–13.3 to 9.4)
KOOS sport	24.0 (4.6)	24.2 (4.2)	28.1 (4.5)	–0.3 (–12.7 to 12.2)	3.9 (–8.5 to 16.3)	–4.1 (–17.0 to 8.8)
KOOS quality of life	41.1 (3.4)	43.3 (3.8)	44.7 (3.1)	–2.1 (–12.4 to 8.1)	1.5 (–8.4 to 11.3)	–3.6 (–12.8 to 5.6)

GMD: group mean difference; SE:standard error; CI: confidence interval; ADL: activities of daily living.

Table IV. *Clinical outcome measures (Knee injury and Osteoarthritis Outcome Score (KOOS) and Visual Analogue Scale (VAS) pain at rest and while active) at 3 months follow-up. Intention to treat results and the per protocol results are presented*

	Aquatic Mean (SE)	Control Mean (SE)	Land-based Mean (SE)	Aquatic vs control GMD (95% CI)	Land-based vs control GMD (95% CI)	Aquatic vs land-based GMD (95% CI)
Intention to treat						
VAS pain at rest	18.1 (2.7)	23.8 (2.7)	15.6 (2.8)	–5.7 (–13.3 to 2.0)	–8.1 (–15.8 to –0.4)	–2.5 (–5.2 to 10.2)
VAS pain during walking	52.9 (3.8)	58.3 (3.5)	50.1 (4.0)	–5.4 (–16.2 to 5.4)	–8.2 (–19.7 to 2.7)	2.8 (–8.2 to 13.8)
KOOS symptom	64.1 (2.5)	63.7 (2.5)	66.1 (2.6)	20.5 (–6.6 to 7.6)	2.4 (–4.8 to 9.5)	–1.9 (–9.0 to 5.2)
KOOS pain	60.7 (2.6)	62.6 (2.5)	62.0 (2.6)	–1.5 (–8.7 to 5.8)	–0.3 (–7.5 to 7.0)	–1.2 (–8.5 to 6.1)
KOOS ADL	63.0 (2.6)	61.4 (2.6)	63.9 (2.7)	1.6 (–5.7 to 8.9)	2.5 (–5.0 to 9.9)	–0.9 (–8.3 to 6.6)
KOOS sport	24.2 (3.5)	23.5 (3.5)	31.6 (3.6)	0.7 (–9.3 to 10.7)	8.1 (–2.0 to 18.2)	–7.4 (–17.5 to 2.7)
KOOS quality of life	42.8 (2.4)	41.4 (2.4)	43.1 (2.5)	1.7 (–5.4 to 8.2)	1.7 (–5.3 to 8.7)	–0.3 (–7.4 to 6.7)
Completers						
VAS pain at rest	14.7 (4.2)	21.9 (4.4)	10.8 (4.0)	–7.2 (–19.5 to 5.1)	–11.1 (–23.1 to 0.9)	3.9 (–7.8 to 15.6)
VAS pain during walking	48.7 (5.8)	55.4 (7.2)	39.3 (6.7)	–6.7 (–25.5 to 12.1)	–16.1 (–36.1 to 3.9)	9.4 (–8.6 to 27.4)
KOOS symptom	63.0 (4.4)	69.4 (3.2)	62.1 (4.7)	–6.4 (–17.3 to 4.5)	–7.3 (–18.7 to 4.1)	0.9 (–12.0 to 13.8)
KOOS pain	59.5 (3.4)	65.6 (3.4)	58.9 (4.8)	–6.1 (–15.8 to 3.6)	–6.7 (–18.5 to 5.1)	0.6 (–11.2 to 2.4)
KOOS ADL	62.6 (4.1)	62.2 (2.8)	61.1 (5.0)	0.4 (–9.5 to 10.3)	–1.1 (–12.6 to 10.4)	1.5 (–11.4 to 14.4)
KOOS sport	22.8 (4.9)	24.8 (5.4)	32.1 (5.2)	–2.0 (–16.6 to 12.6)	7.3 (–7.8 to 22.4)	–9.3 (–23.6 to 5.0)
KOOS quality of life	41.5 (2.9)	41.5 (3.9)	43.0 (3.6)	0.0 (–9.8 to 9.8)	1.5 (–9.2 to 12.2)	–1.5 (–10.9 to 7.9)

GMD: group mean difference; SE: standard error; CI: confidence inerval; ADL: activities of daily living.

a significant decrease in muscle strength was found for the aquatic exercise programme (SMD –0.22; 95% CI –0.38 to –0.05) (Table V, Fig. 2A). This overall effect following land-based exercise was probably because of a significant effect during follow up (SMD 0.26; 95% CI 0.00–0.52) (Table V), Fig. 2 (A and B)). The decreased muscle strength was also observed in the follow-up measurement for the aquatic exercise programme compared with control (SMD –0.28; 95% CI –0.51 to –0.04) (Table V, Fig. 2 (A and B)). As presented in the figure, the land-based exercise programme had a significant effect on muscle strength (improvement) – compared with the control group; while aquatic exercise have a detrimental effect on muscle strength compared with control (i.e. muscle strength was significantly decreased at follow-up).

Table V. *Totals and subtotals for the meta-view analysis for muscle strength and balance. Results presented as the standardized mean difference (SMD) between control and aquatic and land-based exercise respectively with corresponding 95% confidence intervals (95% CI)*

	Aquatic SMD (95% CI)	Land-based SMD (95% CI)
Muscle strength		
After subtotal extension	–0.14 (–0.46 to 0.19)	0.26 (–0.09 to 0.60)
After subtotal flexion	–0.18 (–0.51 to 0.15)	0.03 (–0.31 to 0.37)
After subtotal	–0.16 (–0.39 to 0.07)	0.14 (–0.10 to 0.38)
Follow-up subtotal extension	–0.32 (–0.65 to 0.01)	0.24 (–0.13 to 0.61)
Follow-up subtotal flexion	–0.24 (–0.57 to 0.10)	0.28 (–0.09 to 0.66)
Follow-up subtotal	–0.28 (–0.51 to –0.04)	0.26 (0.00 to 0.52)
Total (combined)	–0.22 (–0.38 to –0.05)	0.20 (0.02 to 0.38)
Balance		
After subtotal velocity	0.19 (–0.09 to 0.47)	–0.27 (–0.56 to 0.03)
After subtotal maximal stability	0.08 (–0.20 to 0.36)	–0.10 (–0.40 to 0.20)
After subtotal ankle strategy	0.14 (–0.14 to 0.42)	0.13 (–0.17 to 0.42)
After subtotal	0.14 (–0.02 to 0.30)	–0.08 (–0.25 to 0.09)
Follow-up subtotal velocity	–0.03 (–0.32 to 0.27)	–0.22 (–0.54 to 0.10)
Follow-up subtotal maximal stability	–0.11 (–0.41 to 0.19)	–0.16 (–0.48 to 0.16)
Follow-up subtotal ankle strategy	0.09 (–0.21 to 0.38)	0.11 (–0.20 to 0.43)
Follow-up subtotal	–0.02 (–0.19 to 0.16)	–0.09 (–0.27 to 0.09)
Total (combined)	0.07 (–0.05 to 0.18)	–0.08 (–0.21 to 0.04)

Standing balance: None of the pooled (meta-view) analyses indicates a significant effect on balance parameters, but as indicated in Fig. 2B aquatic exercise may have a more beneficial effect on balance than the applied land-based exercise programme.

Adverse reactions

In the land-based exercise group, 11 patients reported adverse effects of the exercise (44%), 8 patients (32%) reported increased pain during and after exercise, 3 patients (12%) reported swollen knees. Among them, 3 patients decided to drop out. In the aquatic exercise group 3 patients (11%) reported pain during exercise, but none from the aquatic exercise group stopped the intervention due to adverse effects of the treatment. Based on Fisher's exact test, these numbers corresponded to significantly more adverse effects in the land-based exercise group compared with aquatic exercise ($p = 0.012$); with adverse events being 6 times more likely following land-based exercise therapy (exact odds ratio = 6.3 (95% CI 1.3–39.6)).

DISCUSSION

Out of our 2 knee OA exercise groups following a relatively intense aquatic or land-based exercise programme, only patients

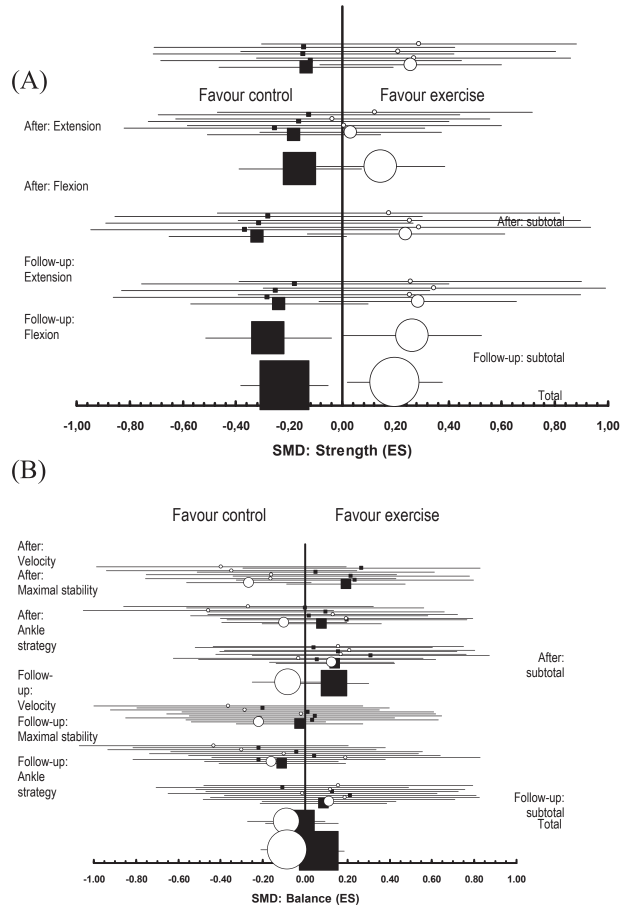

Fig. 2. A graphic presentation of the meta-view analysis for muscle strength (A) and balance (B). Aquatic exercise is presented as ■ with horizontal lines representing the 95% confidence interval. Subtotals with a bigger ■ and total with the biggest ■. Land-based exercise is presented as O with horizontal lines representing the 95% confidence interval. Subtotals with a bigger O and total with the biggest O. The upper half of each figure represents the measurements immediately after 8 weeks of exercise (After), while the lower half represents the follow-up measurements 3 months after cessation of exercise (Follow-up). Estimates on the left side of the ordinate favour control and estimates on the right side favour exercise.

from the land-based exercise group showed a decrease in pain from baseline at 3 months follow-up. No effect was seen on self-reported symptoms, physical functions or quality of life in either of the groups. These results are partly contradictory to the conclusion of a meta-analysis based on studies of effects of exercise therapy for patients with knee OA, which shows that land-based exercise therapy reduces pain and improves physical function in knee OA patients (32). However, a risk of a type II error could not be excluded, since a power analysis before starting this project indicated 30 patients in each group.

When designing the exercise programme for this study we aimed at finding a balance between a high exercise dose/ exercise intensity, whilst providing an exercise programme that was not too demanding for the individual patient. The exercise programme comprised 16 sessions of either land-based or aquatic exercise spread over 8 weeks to ensure a physiological effect (33). The basis for the design was that moderate levels of physical activity are not associated with radiographic progression seen in knee OA, but that a high level of physical activities are related to increased risk of developing the radiographic progression usually seen with knee OA (34).

Previously we have observed signs of adverse effects of land-based exercises for patients with knee OA (17). The compliance in our present study was good, 92% for aquatic and 85% for land-based exercise, and all patients participated fully in the exercise programme when present. With 11 patients from the land-based exercise group who complained of adverse effects of the exercise, we can argue that the amount of exercise could not be characterized as too low.

We designed our programme to obtain a definite effect on strength (35) by combining balance, aerobic exercises and stretching exercises with a moderate intensity as recommended by the American Geriatrics Society (36). The question that these mixed programmes rise, is whether each type of exercise has too little to give to an optimal dosage. So far, no one has been able to define a clear objective when prescribing exercise for patients with knee OA.

In a recent meta-analysis the effect of aerobic and strengthening exercise was found to be the same (37). The overall effect of exercise therapy given to patients with knee OA was improvement in pain and physical function (32–37). However, results vary in the literature and of 17 studies included by Fransen et al. (32) in the analysis, 11 studies observed no effect on physical function and 4 no effect on pain.

The effect of a programme is presumably dependent on type of exercise, and standards have not been developed for exercises. Thus differences between programmes are likely to be a significant confounder.

In a Cochrane review only one study (38) tried to answer the question about optimal intensity, and Fransen et al. (32) conclude that specific recommendations cannot be made either for optimal dosage or optimal programme content.

The land-based exercise group showed improved muscle strength compared with the control group at follow-up, but not immediately following therapy. A possible explanation for this delay could be that the land-based exercise group continued some kind of strengthening exercise at home, and that 3 months further exercise was necessary to show a significant result. The aquatic exercise, on the other hand, showed no effect on muscle strength, possibly due to too little resistance exercise, which is necessary to improve strength. No development in strength was observed in this group during follow-up and the aquatic programme may not in itself have stimulated to higher physical activity at home. Another explanation could be the difference in initial body weight. The land-based exercise group had a lower initial body weight compared with both the aquatic exercise group and the control group. A recent review clearly indicates that weight loss improves not only pain, but also physical function (39). This seems to be a possible explanation since the mean difference between the aquatic and land-based exercise group was 13.5 kg. However, this difference is not based on a weight change, as it is a result of (concealed) random allocation from the random sample (n = 79) of knee OA patients in Denmark. But since a heavier person often has a higher muscle strength, the improved strength in the land-based (lighter group) could not be explained by the difference in body weight alone. Finally, the difference in weight was only observed between the aquatic exercise group and the land-based exercise group, between whom no further difference was observed, thus indicating that the weight difference was not important when analysing the results from the present study.

In conclusion, only land-based exercise showed slight improvement of pain and strength compared with the control group, while no changes were detectable after aquatic exercise compared with the control group. Nevertheless, aquatic exercise showed significantly less adverse effects. We argue that to increase compliance and decrease the number of withdrawals and adverse events, a combination of aquatic and land-based exercise should be the preferred exercise regimen in knee OA.

ACKNOWLEDGEMENTS

The study was supported by The Oak foundation, The Research Foundation of the Danish Physiotherapy Association, The Danish Rheumatism Association, The Spies Foundation and H:S Central Research Fund. Skilful and much-appreciated assistance was given by Jette Nielsen, Salomea Hirschorn, Reidun Mansour, Sofie Bliddal, Tove Riis, Sobia Tanwer, Linn Weile, Vibeke Heltborg and Dorthe Nielsen. Mette Gad, MA, provided linguistic revision. In addition, we would like to thank the physiotherapy students who were in charge of the exercise sessions, and at last we would like to thank all the knee OA patients who participated in the study.

REFERENCES

1. Lane NE, Thompson JM. Management of osteoarthritis in the primary-care setting: an evidence-based approach to treatment. Am J Med 1997; 103: 25S–30S.
2. Hinman, RS. Balance impairments in individuals with symptomatic knee osteoarthritis: a comparison with matched controls using clinical tests. J Rheumatol 2002; 41: 1388–1394.
3. O'Reilly S, Jones A, Doherty M. Muscle weakness in osteoarthritis. Curr Opin Rheumatol 1997; 9: 259–262.
4. Baker K, McAlindon T. Exercise for knee osteoarthritis. Curr Opin Rheumatol 2000; 12: 456–463.
5. Minor MA. Exercise in the management of osteoarthritis of the knee and hip. Arthritis Care Res 1994; 7: 198–204.
6. Deyle GD, Henderson NE, Matekel RL, Ryder MG, Garber MB, Allison SC. Effectiveness of manual physical therapy and exercise in osteoarthritis of the knee. A randomized, controlled trial. Ann Intern Med 2000; 132: 173–181.
7. Ettinger WH, Jr., Burns R, Messier SP, Applegate W, Rejeski WJ, Morgan T, et al. A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis. The Fitness Arthritis and Seniors Trial (FAST). JAMA 1997; 277: 25–31.
8. Peloquin L, Bravo G, Gauthier P, Lacombe G, Billiard J-S. Effects of a cross-training exercise program in persons with osteoarthritis of the knee. A randomized controlled trial. J Clin Rheumatol 1999; 5: 126–136.
9. Wang T-J, Belza B, Thompson E, Whitney JD, Bennett K. Effects of aquatic exercise on flexibility, strength and aerobic fitness in adults with osteoarthritis of the hip and knee. J Adv Nurs 2006; 57: 141–152.
10. Belza B, Topolski T, Kinne S, Patrick DL, Ramsey SD. Does adherence make a difference? Results from a community-based aquatic exercise program. Nurs Res 2002; 51: 285–291.
11. Minor MA, Hewett JE, Webel RR, Anderson SK, Kay DR. Efficacy of physical conditioning exercise in patients with rheumatoid arthritis and osteoarthritis. Arthritis Rheum 1989; 32: 1396–1405.
12. Hopman-Rock M, Westhoff MH. The effects of a health educational and exercise program for older adults with osteoarthritis for the hip or knee. J Rheumatol 2000; 27: 1947–1954.
13. Maurer BT, Stern AG, Kinossian B, Cook KD, Schumacher HR. Osteoarthritis of the knee: Isokinetic quadriceps exercise versus educational intervention. Arch Phys Med Rehabil 1999; 80: 1293–1299.
14. Schilke JM, Johnson GO, Housh TJ, O'Dell JR. Effects of muscle-strength training on the functional status of patients with osteoarthritis of the knee joint. Nurs Res 1996; 45: 68–72.
15. Bautch JC, Malone DG, Vailas AC. Effects of exercise on knee joints with osteoarthritis: A pilot study of biologic markers. Arthritis Care Res 1997; 10: 48–55.
16. Sharma L. Proprioceptive impairment in knee osteoarthritis. Rheum Dis Clin North Am 1999; 25: 299–314, vi.
17. Rogind H, Bibow-Nielsen B, Jensen B, Moller HC, Frimodt-Moller H, Bliddal H. The effects of a physical training program on patients with osteoarthritis of the knees. Arch Phys Med Rehabil 1998; 79: 1421–1427.
18. Altman R, Asch E, Bloch D, Bole G, Bortenstein 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: 1039–1049.
19. Altman R, Brandt K, Hochberg M, Moskowitz R, Bellamy N, Bolch 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: 217–243.
20. 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.
21. Huskisson EC. Measurement of pain. Lancet 1974; 2: 1127–1131.
22. Roos EM, Roos HP, Ekdahl C, Lohmander LS. Knee injury and Osteoarthritis Outcome Score (KOOS)-validation of a Swedish version. Scand J Med Sci Sports 1998; 8: 439–448.
23. 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: 1833–1840.
24. Rogind H. Comparision of Kistler 9861 A platform and Chattecx Balance System for measurement of postural sway: correlation and test-retest reliability. Scand J Med Sci Sports 2003; 13: 106–114.
25. Lund H, Sondergaard K, Zachariassen T, Christensen R, Bulow P, Henriksen M, et al. Learning effect of isokinetic measurements in healthy subjects, and reliability and comparability of Biodex and Lido dynamometers. Clin Physiol Funct Imaging 2005; 25: 75–82.
26. Danneskiold-Samsoe B, Grimby G. Isokinetic and isometric muscle strength in patients with rheumatoid arthritis. The relationship to clinical parameters and the influence of corticosteroid. Clin Rheumatol 1986; 5: 459–467.
27. Altman DG, Schulz KF, Moher D, Egger M, Davidoff F, Elbourne D, et al. The revised CONSORT statement for reporting randomized trials: explanation and elaboration. Ann Intern Med 2001; 134: 663–694.

28. Wright CC, Sim J. Intention-to-treat approach to data from randomized controlled trials: a sensitivity analysis. J Clin Epidemiol 2003; 56: 833–842.
29. van Houwelingen HC, Arends LR, Stijnen T. Advanced methods in meta-analysis: multivariate approach and meta-regression. Stat Med 2002; 21: 589–624.
30. Wang MC, Bushman BJ. Integrating Results through meta-analytic review using SAS Software. Cary: NC: SAS Institute Inc.; 1999.
31. Thompson SG, Pyke SD, Hardy RJ. The design and analysis of paired cluster randomized trials: an application of meta-analysis techniques. Stat Med 1997; 16: 2063–2079.
32. Fransen M, McConnell S, Bell M. Exercise for osteoarthritis of the hip or knee. Cochrane Database Syst Rev 2001; CD004286.
33. Franklin, BA, editor. Guidelines for Exercise Testing and Prescription. ACSM's guidelines for exercise testing. Philadelphia: Lea & Febiger: 2000.
34. Thorstensson CA, Roos EM, Petersson IF, Ekdahl C. Six-week high-intensity exercise program for middle-aged patients with knee osteoarthritis: a randomized controlled trial [ISRCTN20244858]. BMC Musculoskelet Disord 2005; 6: 27.
35. Pelland, L.Brosseau L. Efficacy of strengthening exercises for osteoarthritis (part 1): a meta-analysis. Phys Ther Rev 2004; 9: 77–108.
36. American Geriatrics Society Panel on Exercise and Osteoarthritis. Exercise prescription for older adults with osteoarthritis pain: consensus practice recomendations. JAGS 2001; 49: 808–823.
37. Roddy E, Zhang W, Doherty M. Aerobic walking or strengthening exercise for osteoarthritis of the knee? A systematic review. Ann Rheum Dis 2005; 64: 544–548.
38. Brosseau L, MacLeay L, Robinson V, Wells G, Tugwell P. Intensity of exercise for the treatment of osteoarthritis. Cochrane Database Syst Rev 2003; CD004259.
39. Christensen R, Bartels EM, Astrup A, Bliddal H. Effect of weight reduction in obese patients diagnosed with knee osteoarthritis: a systematic review and meta-analysis. Ann Rheum Dis 2007; 66: 433–439.

APPENDIX I. *Description of the aquatic and land-based exercise programmes in the present study. Even though the programmes are very different due to different environments, the aim for each group of exercises was the same*

	Land			Aquatic		
Aims	Exercise	Time	Progression	Exercise	Time	Progression
Aerobic training – warm-up	Cycling on stationary bike	10 min	A larger number of kilometres	Aquatic running with belt	10 min	The speed
Strengthening and endurance exercises	1. Leg press (40% of 1 RM) 2. Raising / sitting down on a chair (42 cm high) 3. Forward up and backward down steps on a step bench (20 cm high) 4. Sideward up and down steps on a step bench (20 cm high) 5. Patient lying on mattress, with bended hips and knees – extending both hips 6. Leg abduction by a rib, with a rubber- band against the ankle	20 min. Each exercise lasts for 3.5 min	1.Increased number of repetitions and a higher weight 2. As 1 plus a lower chair 3. As 1 plus a higher step 4. As 1 plus extending and abduction of the non-weight-bearing leg at the same time 6. A tighter rubber-band.	1. Knee extension and flexion. The patient has a ring around the foot, which she/he presses down to the bottom of the pool 2. "Bad Ragaz" resistance exercise, where the physiotherapist give resistance to the working extremity 3. Patient lying supine on a pool bar. Legs presses alternate into extension 4. Patient lying lateral on a pool bar. The lower leg presses down into abduction 5. Running and jumping forward/ backward with hand weights 6. Standing posture – pressing a kickboard up/down and anterior/ posterior in the water	20 min. Each exercise lasts for 3.5 min	Increased number of repetitions
Balance exercises	Trampoline Balance board Balance cushion	10 min. Each exercise lasts for 3 min	From eyes open standing on 2 legs – to eyes closed standing on one leg	The patient is carrying an aqua belt around the waist, and she/he stays in the deep part of the pool (1.58 m). Different types of movements with the lower part of the body, staying erect		Higher severity level of the exercises
Stretching exercises	M. triceps surae (gastrocnemius and soleus) M. quadriceps Hamstrings M. iliopsoas	Approximately 30 sec/muscle group		1. M. triceps surae (gastrocnemius and soleus) 2. M. quadriceps 3. Hamstrings 4. M. iliopsoas	About 30 sec/muscle group	
Cool-down	Lie down on the floor, with the lower part of the body elevated	5 min		Lie down in a pool corner "cycling" slowly with the legs in the water surface	5 min	

RM: repetition maximum.