The Effect of Exercise on Sleep and Fatigue in Rheumatoid Arthritis: A Randomized Controlled Study

Laura Durcan, Fiona Wilson, and Gaye Cunnane

ABSTRACT. *Objective.* Sleep disturbance and chronic fatigue are common in rheumatoid arthritis (RA) and contribute to disability, symptomatology, and healthcare use. It has long been recognized in other populations that exercise can improve sleep and diminish fatigue. The effect of exercise on sleep quality and fatigue in RA has not been evaluated.

Methods. Ours is a randomized controlled study in RA to determine the effect of an exercise program on sleep quality and fatigue. These were measured using the Pittsburgh Sleep Quality Index and the Fatigue Severity Scale. Patients were randomized to either a 12-week, home-based exercise intervention or usual care. The exercise program consisted of specific exercises to target individual deficiencies identified using the Health Assessment Questionnaire (HAQ) with cardiovascular work as per the guidelines. The intervention group was evaluated on a 3-week basis. Full evaluation was carried out at baseline and at 12 weeks.

Results. Forty patients were randomized to the intervention with 38 controls. In the exercise intervention group, there was a statistically significant improvement in HAQ (p = 0.00), pain (p = 0.05), stiffness (p = 0.05), sleep quality (p = 0.04), and fatigue (p = 0.04). In our control group, there was a statistically significant improvement demonstrated in their overall perceptions of the benefits of exercise, but none of the other variables.

Conclusion. Our study demonstrates that an exercise program resulted in significant improvement in sleep quality and fatigue. This is particularly interesting given the importance of fatigue as an outcome measure in RA and gives us yet another reason to prescribe exercise in this population. (J Rheumatol First Release Aug 15 2014; doi:10.3899/jrheum.131282)

Key Indexing Terms:
RHEUMATOID ARTHRITIS   EXERCISE   FATIGUE   SLEEP QUALITY

Rheumatoid arthritis (RA) is associated with progressive functional disability and accelerated mortality[1,2,3]. Sleep disturbance is common in patients with RA[4]. Multiple causative factors include pain, depression, lack of exercise, restless legs, and corticosteroid use[5,6,7,8,9]. Disordered sleep and fatigue are thought to play important roles in the development of chronic pain[6,7,10]. Poor sleep is a common complaint in the general population[11,12], but is even more common in those with rheumatic diseases[5,7,8]. Chronic insomnia in the general population has been shown to compromise quality of life, psychosocial well-being, and occupational and educational performance[13]. It results in increased morbidity[11], mortality[14], and healthcare use[15]. Pharmacological interventions aimed at improving sleep have shown short-term efficacy, but their longterm usefulness is hindered by dependency, increased mortality[16], and the rapid development of tolerance[17].

Exercise has long been recognized by sleep organizations as a key component in the nonpharmacological management of poor sleep[18]. Experimental studies have also shown that exercise improves sleep quality[19,20]. Patients with RA were previously cautioned regarding participation in cardiovascular (CV) exercise owing to the belief that it was deleterious to joints. For this reason, the role of exercise in improving sleep quality in RA has not been established.

Improvements in sleep quality and associated decreases in subjective fatigue are of particular importance in RA. Fatigue is considered in the Outcome Measures in Rheumatology Clinical Trials (OMERACT)[21] as of 2011 and relates directly to quality of life[22]. A recent Cochrane review examined fatigue in RA and showed that exercise has a modest effect on fatigue; however, the specific issue of sleep quality has not been examined[23].

Our study was undertaken to evaluate the effect of an exercise program on self-reported sleep quality and fatigue in RA.

From the Department of Rheumatology, St. James's Hospital; the Department of Physiotherapy, Trinity College, Dublin, Ireland.

L. Durcan, MD, MB, Bch, BAO, Specialist Registrar in Rheumatology, Department of Rheumatology, St. James's Hospital; F. Wilson, PhD, Assistant Professor and Chartered Physiotherapist, Department of Physiotherapy, Trinity College; G. Cunnane, PhD, Clinical Professor, Trinity College Dublin, Consultant Rheumatologist, St. James's Hospital.

Address correspondence to Dr. L. Durcan, Department of Rheumatology, St. James's Hospital, Dublin 8, Ireland. E-mail: laurajanedurcan@hotmail.com

Accepted for publication June 4, 2014.

MATERIALS AND METHODS

Seventy-eight patients with established RA according to the American College of Rheumatology criteria were recruited from the rheumatology outpatient clinic of a large teaching hospital. They were randomized using a preassigned protocol to receive either standard care with information regarding the benefits of exercise in RA or to take part in an exercise program. Forty individuals participated in the exercise program while the remaining 38 received standard care and were given verbal and written instruction regarding the benefits and importance of exercise in RA.

Exclusion. Patients were excluded from participation if they were not independently mobile, were deemed a falls risk or had severe medical conditions that were more limiting than their arthritis. These conditions were congestive heart failure with functional limitation (New York Heart Association level III symptoms or greater), angina, active malignancy, uncontrolled thyroid disease, severe chronic obstructive pulmonary disease (gold stage III or greater), or neurologic condition limiting mobility. Patients were also excluded if they did not speak English or were unable to give informed consent. Because we are a tertiary referral center with patients attending the clinic from distant areas, we limited our study to those who could easily travel for assessments. Those who lived farther than 1 h of travel time were excluded. Ethical approval was granted by the St. James's Hospital Ethics Committee.

Medical assessment. Medical history was reviewed to ensure suitability and current medications were documented. Smoking history was recorded. Disease-specific characteristics were assessed. Disease activity was evaluated using the Disease Activity Score with 28 joint counts[24]. Participants were described as having seropositive disease if either rheumatoid factor or anticyclic citrullinated peptide antibodies were present. If erosions were visible on plain film evaluation of hands or feet, they were described as having erosive disease.

Self-reported measures. For self-reported measures, patients were given the relevant questionnaires to complete while in the clinic waiting room with a doctor available to answer any questions.

Functional limitation was quantified using the Health Assessment Questionnaire (HAQ) Disability Index[25,26]. Both pain and stiffness were determined using visual analog scale (VAS).

Fatigue was assessed using the Fatigue Severity Scale (FSS)[27] and sleep quality was measured using the Pittsburgh Sleep Quality Index (PSQI)[28].

The FSS is widely used across a variety of chronic conditions. It is composed of 9 statements concerning the respondent's fatigue. The scale measures how fatigue affects motivation, exercise, physical functioning, and carrying out of duties, and how it interferes with work, family, and social life. It was originally developed for use in multiple sclerosis and systemic lupus erythematosus (SLE), but has since been used across a broad range of rheumatic and other chronic conditions. Responses are scaled on a 7-point Likert scale from 1 = strongly disagree to 7 = strongly agree. Responses are summed and divided by the number of answers to yield a score with a range of 1–7, with higher scores indicating more fatigue. The FSS has been shown to correlate with VAS and to inversely correlate with the Rand Index of Vitality[29]. The FSS has a clearly outlined minimal clinically important difference. A systemic metaanalysis of the use of this tool in SLE suggested a change of 15% should be considered clinically meaningful[30].

The PSQI is used to measure sleep quality and disturbances over the preceding month[28,31]. It is composed of 7 variables: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. Nineteen items are included in scoring. Five additional items, which are completed by a bed partner, if applicable, are not included in the total score because they may not be available. The PSQI has been used in multiple disease areas and as an outcome in clinical trials. These include, among others, cancer[32,33], restless legs[34], gastroesophageal reflux[35], and obstructive sleep apnea[36]. It has also been used to evaluate sleep quality in RA[37]. The PSQI

has been used to define inclusion criteria for poor sleep quality where a score of over 5 is considered to indicate troublesome sleep. The range for this tool is 0–21, with a higher score indicating worse sleep quality. When scoring this tool, each of the 7 sleep variables are scored separately and then summed to give an overall score. The component scores correlate well with sleep latency, duration, and quality on subsequent polysomnography testing. The PSQI has demonstrated sensitivity to change.

Subjects' opinions regarding exercise and the barriers they encounter that could limit their exercise were evaluated using the Exercise Benefits and Barriers Scale. This was developed by Sechrist, *et al*[38] to determine perceptions of individuals concerning the benefits of and barriers to participating in exercise. It is based on 43 questions. There are 29 benefits items in 5 categories. These are physical performance, preventive health, psychological outlook, social interaction, and life enhancement. There are 14 barriers items in 3 categories: physical exertion, time expenditure, and exercise environment. Individuals rate their agreement to each perceived benefit and barrier item on a Likert scale consisting of 4 answer options from strongly disagree to strongly agree. The possible range of scores on the questionnaire as a whole is 43–172, and higher scores indicate a more positive perception of exercise. For the barriers scale, the range is 14–56, higher scores indicating a greater perception of barriers to exercise.

The intervention program. A 12-week home exercise program was prescribed for the intervention group. Participants were assessed by a doctor (LD) and senior physiotherapist (FW) at baseline and then every 3 weeks for the duration of the program. Functional limitation was assessed by HAQ. A full physical examination was carried out by a physiotherapist to identify deficiencies or functional limitations in muscular fitness, range of motion, and coordination of affected joints. Specific exercises were prescribed to target the individual deficiencies identified. Resistance exercise was prescribed 3 times per week, and dosage was prescribed and increased according to the American College of Sports Medicine (ACSM) guidelines for healthy individuals, based on their advice for sedentary persons beginning a resistance program[39] (with adaptation where required to avoid aggravation of symptoms where no specific guidelines are available[40]; Table 1). Range of motion exercise was prescribed in functional patterns to be done on a daily basis.

In addition to these strengthening and stretching exercises, a walking program was devised according to ACSM guidelines on physical activity[39]. Based on their CV expenditure prior to our study and their functional capability as measured by a 6-min walk test, a program was devised that included incremental targets for daily walks based on step count and rate of perceived exertion. Patients were given daily step count targets and advised on the level of exertion for which they should be aiming. They were instructed that they should be moderately short of breath on exertion, i.e., unable to comfortably hold a conversation while walking.

The control group. The control group was composed of patients with RA who received advice only on the benefits of exercise in RA. They were assessed at baseline and at 12 weeks.

Statistical analysis. SPSS version 18 was used for analysis. The primary endpoint was sleep improvement, although a lack of consensus on what could be considered a minimum clinically important difference in sleep quality meant that we specifically powered the work to detect a clinically important difference in HAQ. A sample size of 38 patients in each group was calculated to detect a HAQ difference of 0.25 between them with a 90% power and significance level of 0.05. To allow for potential noncompleters, we aimed to recruit 40 individuals per group. Randomization was performed using Excel random numbers. All means are expressed with their SD provided normally distributed and with their interquartile range in the case of non-normal data. Data were assessed for normality using the Kolmogorov-Smirnov test. Before and after scores, provided they were normally distributed, were assessed using a paired t test. The magnitude of changes seen in both the intervention and control group were then compared, and α was set at 0.05.

Table 1. Methods of exercise prescription used in this study.

	Cardiovascular Exercise	Resistance Training	Flexibility and Neuromotor Conditioning
Frequency	5 days of moderate intensity cardiovascular exercise, based on a walking program. With the exception of 1 participant, the participants were sedentary at baseline.	Each major muscle group to be trained 2–3 days per week at 40–50% of 1 RM. In addition, functional exercises were prescribed according to deficiency identified in HAQ.	A daily stretching regimen was devised for each patient. Timed 1 leg stands were prescribed for neuromotor health. These were advised 2–3 days per week.
Intensity	Light to moderate intensity.	1 RM was calculated at baseline assessment using wrist and ankle weights of varying weights. Those who were capable used a dumbbell weight. Weights were provided for the patients for home use. 50% of 1 RM was used as per the ACSM guidelines for deconditioned individuals. Four individuals started with exercises against gravity because they were severely deconditioned.	Stretch to the point of tightness.
Time, type, and repetitions	30–60 min per day to accumulate 150 m/week.	No specific duration was recommended, 15–20 reps were prescribed to target endurance except where specific strength deficits were identified; 8–12 reps of 60–70% 1 RM was prescribed in these cases.	Patients were advised to hold a static stretch for 30 s. Timed 1-leg stands were prescribed where appropriate and with adequate safety awareness for 2–3 min, 2–3 days per week.
Type	Walking (2 individuals chose to swim 2 days per week).	Major muscle groups with specific hand exercises where appropriate. Resistance for hands was prescribed using finger-spring tools.	Each major joint was targeted and specific exercises were prescribed for notable deficits such as hands. Both static and dynamic range of motion exercises were prescribed as appropriate.
Volume	Patients were provided with a step counter to monitor distances.	2 sets, 2–3 days per week.	Prescribed based on individual deficits.
Progression	Daily step targets.	A gradual progression of resistance was prescribed.	Target to increase range of motion to full range.
Pattern	Patients were advised that exercise could be performed in 1 session per day or in multiple sessions of greater than 10 min.	Rest intervals of 2–3 min between sets. Rest of 48 h between muscle groups.	Repetition of each flexibility exercise 2–4 times was recommended.

RM: repetition maximum; HAQ: Health Assessment Questionnaire; ACSM: American College of Sports Medicine.

RESULTS

Four hundred potential participants with RA were assessed for eligibility. Of the 400, 220 lived within an easily accessible distance. From these 220 potential participants, 136 were suitable for the program based on our exclusion criteria. One hundred thirty-six patients were approached and given information regarding the exercise program. Eighty individuals were interested in taking part. All were given at least 24 h "opt out time" as per our protocol. They were then randomized to either intervention or control group (Figure 1). Forty-two participants were randomized for intervention; however, 2 of them had abnormalities at their initial assessment, which meant they were unable to take part. One individual described exertional chest pain and another was found to have a new diagnosis of uncontrolled hyperthyroidism.

All participants were assessed at baseline and following the 12-week exercise program. Interim evaluations were carried out at 3 weeks, 6 weeks, and 9 weeks. All participants who completed the program attended at least 2 of the 3 interim assessments. Three individuals (7.5%) missed 1 assessment.

The demographics and disease-specific characteristics of the group are outlined in Table 2.

Sleep quality as measured by the PSQI was 5.6 in the control group and 7.2 in the intervention group. This was not statistically significant. The level of perceptual barriers to exercise was comparable in both groups at 31.2 and 28.6. Their overall opinions of the benefits of exercise were also similar at 126.3 in the control group and 125.8 in those who took part in the exercise intervention. Levels of fatigue were similar in both groups at 30.5 and 29.5 in the control and intervention groups.

In both groups, the most commonly reported statement relating to fatigue and quality of life was "Fatigue is among my three most disabling symptoms". This was reported as being greater than 5 (on a scale of 0–7) by 75%. The second most commonly reported statement was "I am easily
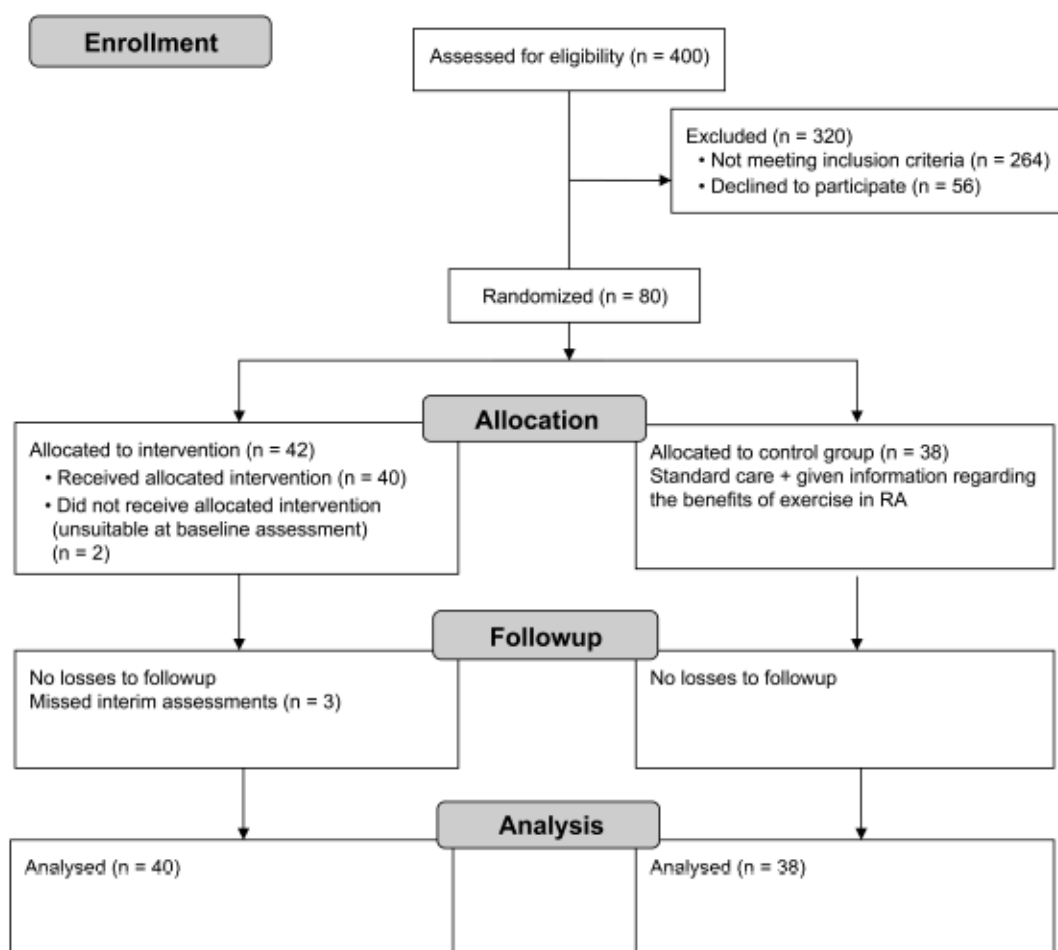
Enrollment

Assessed for eligibility (n = 400)

Excluded (n = 320)
- Not meeting inclusion criteria (n = 264)
- Declined to participate (n = 56)

Randomized (n = 80)

Allocation

Allocated to intervention (n = 42)
- Received allocated intervention (n = 40)
- Did not receive allocated intervention (unsuitable at baseline assessment) (n = 2)

Allocated to control group (n = 38)
Standard care + given information regarding the benefits of exercise in RA

Followup

No losses to followup
Missed interim assessments (n = 3)

No losses to followup

Analysis

Analysed (n = 40)

Analysed (n = 38)

Figure 1. Diagram outlining patient recruitment. RA: rheumatoid arthritis.

Table 2. Comparison of characteristics of intervention group to RA controls at baseline.

	Mean (SD) Control	n (%) Control	Mean (SD) Intervention	n (%) Intervention
Age, yrs	59 (12)		61 (8.0)	
Female		20 (52.6)		30 (75)
Seropositive for RF ± anti-CCP		30 (78.9)		33 (82.5)
Erosive		21 (55.2)		33 (82.5)
Disease duration, yrs	11 (11.2)		16 (10.9)	
Biologic therapy		12 (31.5)		10 (25)
Smoker		20 (52.6)		17 (42.5)
HAQ	0.9 (0.4)		0.8 (0.4)	
Pain (VAS 0–100)	41.4 (25.5)		29 (21.5)*	
Stiffness (VAS 0–100)	43.8 (23.7)		32 (22.6)	
PSQI	5.6 (5.2)		7.2 (4.4)	
Barriers	31.2 (5.1)		28.6 (3.2)	
EBBS	126.3 (21.2)		125.8 (5.5)	
FSS	30.5 (15.4)		29.5 (17.8)	

*Indicates significant difference between the groups, other differences are nonsignificant. RA: rheumatoid arthritis; RF: rheumatoid factor; anti-CCP: anticyclic citrullinated peptide antibodies; HAQ: Health Assessment Questionnaire; VAS: visual analog scale; PSQI: Pittsburgh Sleep Quality Index; EBBS: Exercise Benefits and Barriers Scale; FSS: Fatigue Severity Scale.

Table 3. Pittsburgh Sleep Quality Index, components, and no. participants.

Component of Sleep	Participants with a Problem (%)	Intervention Group, n = 40 (%)	Control Group, n = 38 (%)
Subjective sleep quality	70 (90)	34 (85)	36 (94)
Sleep latency	56 (72)	27 (67)	29 (76)
Sleep duration	56 (72)	28 (70)	28 (74)
Habitual sleep efficacy	29 (37)	15 (38)	14 (37)
Sleep disturbances	71 (91)	36 (90)	35 (92)
Requiring medication to sleep	23 (29)	11 (28)	12 (32)
Daytime dysfunction	65 (83)	33 (83)	32 (84)

fatigued". This was reported as greater than 5/7 by 70%. A score of greater than 36 is thought to represent debilitating fatigue. This was present in 27 participants (35%).

Overall, 38 individuals (49%) had a score of greater than 5 indicating problematic sleep. Table 3 outlines the specific sleep problems encountered. With regard to the individual components of sleep where disturbances were identified, 70 (90%) reported poor sleep quality subjectively, 56 (72%) had problems with sleep latency, 56 (72%) had disturbed duration of sleep, 29 (37%) had problems with habitual sleep efficacy, 71 (91%) reported disturbed sleep, 23 (29%) required sleeping tablets, and 65 (83%) reported daytime dysfunction as a result of sleep disturbance. The intervention and control groups demonstrated similar proportions of patients with difficulty in the individual components of sleep.

Table 4 demonstrates the differences seen after 12 weeks

in both the intervention and control groups. In those who took part in the exercise intervention, there was a statistically significant improvement in HAQ, pain, stiffness, and perceptions regarding the benefits of exercise, sleep quality, and fatigue. In our control group, there was a statistically significant improvement demonstrated in their overall perceptions of the benefits of exercise, but there were no benefits observed for any of the other variables.

In Table 5, the changes seen in both the control and intervention groups are analyzed. On comparison of the control group to the intervention group, there were significantly greater improvements in pain, stiffness, subjective sleep quality, and fatigue in the intervention group. There was a nonsignificant difference in the subject's feelings regarding their barriers to exercise and their opinions regarding its benefits.

Table 4. Difference in self–reported outcomes in the intervention and control groups at baseline and following 12 weeks. Pain is the level of pain measured on the visual analog scale (VAS). Stiffness is the level of stiffness measured on the VAS. "Barriers" is the perceptual barriers to exercise as measured by the Exercise Benefits and Barriers Scale (EBBS). EBBS indicates the overall perception of exercise. FSS is the level of fatigue as measured by the Fatigue Severity Scale.

	Baseline (SD)	12 Weeks (SD)	Difference	Significance
Intervention group				
HAQ	0.8 (0.4)	0.5 (0.5)	0.3	< 0.001*
Pain	29 (21.5)	21 (18)	7.8	< 0.001*
Stiffness	32 (23)	24 (24)	7.9	< 0.001*
PSQI	7.2 (4.4)	6.2 (3.6)	1.0	< 0.001*
Barriers	28.6 (3.2)	25.2 (3.4)	3.5	< 0.001*
EBBS	125.8 (5.5)	131.6 (9.4)	5.6	< 0.001*
FSS	29.5 (17.8)	21.4 (18.8)	11.2	< 0.001*
Control group				
HAQ	0.9 (0.4)	0.8 (0.7)	0.2	0.635
Pain	41.4 (25.5)	39.8 (29.3)	1.6	0.494
Stiffness	43.8 (23.7)	42.4 (32.2)	1.3	0.060
PSQI	5.6 (5.2)	5.4 (3.7)	0.2	0.077
Barriers	31.2 (5.1)	29.5 (6.12)	1.6	0.180
EBBS	126.3 (21.2)	129.4 (18.8)	3.1	< 0.001*
FSS	30.5 (15.4)	30.6 (16.8)	0.1	0.980

* Indicates statistical significance. HAQ: Health Assessment Questionnaire; PSQI: Pittsburgh Sleep Quality Index.

Table 5. Comparison of intervention group to control group, and changes seen in clinical measures. Pain is the level of pain measured on the visual analog scale (VAS). Stiffness is the level of stiffness measured on the VAS. "Barriers" is the perceptual barriers to exercise as measured by the Exercise Benefits and Barriers Scale (EBBS). EBBS indicates the overall perception of exercise. FSS is the level of fatigue as measured by the Fatigue Severity Scale.

	Change in Control Group (95% CI)	Change in Intervention Group (95% CI)	Significance
HAQ	0.02 (−0.05–0.08)	0.3 (0.2–0.3)	< 0.001*
Pain	3.1 (−3.1–6.3)	7.8 (4.3–11.2)	0.050*
Stiffness	1.6 (0.1–2.5)	7.9 (4.0–11.7)	0.050*
EBBS	1.6 (1.4–4.7)	5.6 (−8.3–−2.9)	0.160
Barriers	1.3 (0.3–0.3)	3.5 (2.3–4.6)	0.360
PSQI	0.2 (−0.02–0.5)	1.0 (0.6–1.6)	0.040*
FSS	0.1 (−0.01–0.2)	11.2 (7.6–14.9)	0.040*

* Indicates statistical significance. EBBS: Exercise Benefits and Barriers Scale; FSS: Fatigue Severity Scale; HAQ: Health Assessment Questionnaire; PSQI: Pittsburgh Sleep Quality Index.

DISCUSSION

Our study evaluated the effect of a targeted exercise intervention on sleep quality and fatigue in RA. It showed that an exercise program focusing on functional disability with CV targets had a significant and clinically important effect on fatigue and sleep quality. This intervention also yielded significant improvements in pain, stiffness, and functional disability.

Fatigue is an important outcome measure and is experienced in up to 90% of patients with RA[41,42]. This high prevalence is likely multidimensional, reflecting disease severity, inflammatory burden, functional limitation, pain, stiffness, and depression[22,41,43,44,45,46]. Fatigue relates directly to quality of life[22] and is considered in the outcome measures in OMERACT[21] quality of care domains. It is one of the variables used in assessing response to treatment in clinical trials. A metaanalysis evaluating the effect of biologic therapies on fatigue demonstrated a modest effect at best[47]. This makes any intervention that influences fatigue particularly important.

Fatigue and poor sleep are known to associate with chronic pain. Studies based in pain clinics commonly link poor sleep with higher levels of pain in those who have sleep disturbances[48]. This has been shown across a wide variety of chronic pain conditions. In fibromyalgia, poor sleep is almost universal and those who sleep badly have a higher burden of symptoms[49]. Patients with RA commonly have disturbed sleep[5,7,37], which is likely multifactorial and influenced by pain, corticosteroid use, depression, lack of exercise, and restless legs. This contributes to fatigue, symptomatology, healthcare use, and poor quality of life.

In keeping with our findings, a study evaluating sleep quality in RA demonstrated PSQI scores over 5 in 50% of the participants[10]. A score of 5 or greater has high diagnostic specificity for detecting clinical sleep impairment as defined by the diagnostic criteria for insomnia in the general population. The findings are also in keeping with those seen in ankylosing spondylitis (AS). A study demonstrated 35.4% of patients with AS had poor sleep as measured by the PSQI with a mean total score of 6.62[50].

The current guidelines for physical activity from the ACSM and the World Health Organization are at least 150 min per week of moderate-intensity aerobic exercise. These recommendations also include advice on muscular strength, endurance, flexibility, and balance. They appear to be sufficient to improve subjective sleep quality in other populations[20,51,52]. Generally, in those who have dysfunctional sleep, exercise is beneficial. This has been shown in many studies. A study by Irwin, *et al*, which examined the effects of tai chi on older adults, found improvements among poor sleepers engaging in this form of exercise[53]. King, *et al* examined the effect of CV exercise on sleep quality in older, inactive adults with moderate sleep complaints. They found significant improvements in sleep quality as measured by the PSQI[52]. Further study by King, *et al* examined the effect of a year-long exercise intervention on sleep quality in sedentary adult caregivers. They found significant improvements in the PSQI with inverse correlations with self-perceived stress[51]. These findings are in keeping with our work, which demonstrates a significant improvement in sleep quality and fatigue as a result of a physical activity intervention.

Sleep professionals have long advocated exercise. There are many proposed mechanisms by which exercise improves sleep. Exercise has well-described antidepressant effects and it reduces anxiety, which contributes to hyperarousal and is an important factor in insomnia. Exercise is also thought to improve circadian rhythms and thermoregulation, both of which affected sleep quality. Santos, *et al* suggested in a recent review that exercise affects sleep through modest elevations in the levels of proinflammatory cytokines, interleukin (IL)-1, IL-6, and tumor necrosis factor-α[54]. Modest concentrations are thought to promote sleep while higher volumes are associated with increased nighttime

wakefulness[54]. This is in keeping with the findings of poor sleep in our patients with inflammatory arthritis and is consistent with other research suggesting that acute ultra-endurance activity causes greater elevations in inflammatory cytokines and can increase nighttime wakefulness[55]. Further, exercise has been shown in recent metaanalyses to decrease the erythrocyte sedimentation rate in RA[56] and C-reactive protein in heterogeneous populations[57]. This supports the theory that physical activity can have antiinflammatory properties.

In our study, sleep quality was poor in 50% (n = 20) of the intervention and 47.4% (n = 18) of the control group. This improved significantly as a result of the exercise intervention. Consistent with this, fatigue also declined. These changes remained significant when changes in the control group were taken into account and is, to the best of our knowledge, the first time that the effect of exercise on sleep quality has been evaluated in RA.

The focus of our study was patient-based and for this reason, self-reported outcomes are relied upon and our patients did not undergo polysomnography testing. Although our numbers are small in both groups, they were adequate to demonstrate the difference that was present in the intervention arm of our study. We did not control for baseline differences of pain as this was not a primary outcome and is a fluctuant variable. This may have biased our results, although the groups were in all other ways comparable. Challenges for the future include the implementation of more longterm strategies for increasing physical activity in our patient population and reevaluating those who took part in our 12-week program to see whether it has had a lasting effect.

Fatigue, poor sleep, functional limitation, and chronic pain are common in RA. A 12-week exercise program can yield significant and clinically important improvements in fatigue and sleep quality. Exercise has long been encouraged in both health and chronic disease for its numerous health benefits. To our knowledge, this is the first time the effect of exercise on sleep and fatigue in RA has been explored. It gives us further reasons to encourage and specifically prescribe exercise in RA.

REFERENCES

1. Gabriel SE, Crowson CS, Kremers HM, Doran MF, Turesson C, O'Fallon WM, et al. Survival in rheumatoid arthritis: a population-based analysis of trends over 40 years. Arthritis Rheum 2003;48:54-58.
2. Abruzzo JL. Rheumatoid arthritis and mortality. Arthritis Rheum 1982;25:1020-3.
3. Bacon PA, Townend JN. Nails in the coffin: increasing evidence for the role of rheumatic disease in the cardiovascular mortality of rheumatoid arthritis. Arthritis Rheum 2001;44:2707-10.
4. Stebbings S, Herbison P, Doyle TC, Treharne GJ, Highton J. A comparison of fatigue correlates in rheumatoid arthritis and osteoarthritis: disparity in associations with disability, anxiety and sleep disturbance. Rheumatology 2010;49:361-7.
5. Abad VC, Sarinas PS, Guilleminault C. Sleep and rheumatologic disorders. Sleep Med Rev 2008;12:211-28.
6. Drewes AM, Nielsen KD, Hansen B, Taagholt SJ, Bjerregård K, Svendsen L. A longitudinal study of clinical symptoms and sleep parameters in rheumatoid arthritis. Rheumatology 2000;39:1287-9.
7. Drewes AM. Pain and sleep disturbances with special reference to fibromyalgia and rheumatoid arthritis. Rheumatology 1999;38:1035-8.
8. Wolfe F, Michaud K, Li T. Sleep disturbance in patients with rheumatoid arthritis: evaluation by medical outcomes study and visual analog sleep scales. J Rheumatol 2006;33:1942-51.
9. Taylor-Gjevre RM, Gjevre JA, Skomro R, Nair B. Restless legs syndrome in a rheumatoid arthritis patient cohort. J Clin Rheumatol 2009;15:12-15.
10. Nicassio PM, Ormseth SR, Kay M, Custodio M, Irwin MR, Olmstead R, et al. The contribution of pain and depression to self-reported sleep disturbance in patients with rheumatoid arthritis. Pain 2012;153:107-12.
11. Sutton DA, Moldofsky H, Badley EM. Insomnia and health problems in Canadians. Sleep 2001;24:665-70.
12. Ford DE, Kamerow DB. Epidemiologic study of sleep disturbances and psychiatric disorders. An opportunity for prevention? JAMA 1989;262:1479-84.
13. Power JD, Perruccio AV, Badley EM. Pain as a mediator of sleep problems in arthritis and other chronic conditions. Arthritis Rheum 2005;53:911-9.
14. Kripke DF, Garfinkel L, Wingard DL, Klauber MR, Marler MR. Mortality associated with sleep duration and insomnia. Arch Gen Psychiatry 2002;59:131-6.
15. Kapur VK, Redline S, Nieto FJ, Young TB, Newman AB, Henderson JA, et al. The relationship between chronically disrupted sleep and healthcare use. Sleep 2002;25:289-96.
16. Kripke DF, Langer RD, Kline LE. Hypnotics' association with mortality or cancer: a matched cohort study. BMJ Open 2012;2:e000850.
17. Kupfer DJ, Reynolds CF. Management of insomnia. N Engl J Med 1997;336:341-6.
18. Espie CA. ABC of sleep disorders. Practical management of insomnia: behavioural and cognitive techniques. BMJ 1993;306:509-11.
19. King AC, Pruitt LA, Woo S, Castro CM, Ahn DK, Vitiello MV, et al. Effects of moderate-intensity exercise on polysomnographic and subjective sleep quality in older adults with mild to moderate sleep complaints. J Gerontol A Biol Sci Med Sci 2008;63:997-1004.
20. Buman MP, Hekler EB, Bliwise DL, King AC. Moderators and mediators of exercise-induced objective sleep improvements in midlife and older adults with sleep complaints. Health Psychol 2011;30:579-87.
21. Kirwan JR, Boonen A, Harrison MJ, Hewlett SE, Wells GA, Singh JA, et al. OMERACT 10 Patient Perspective Virtual Campus: valuing health; measuring outcomes in rheumatoid arthritis fatigue, RA sleep, arthroplasty, and systemic sclerosis; and clinical significance of changes in health. J Rheumatol 2011;38:1728-34.
22. Ibn Yacoub Y, Amine B, Laatiris A, Wafki F, Znat F, Hajjaj-Hassouni N. Fatigue and severity of rheumatoid arthritis in Moroccan patients. Rheumatol Int 2011; 32:1901-7.
23. Cramp F, Hewlett S, Almeida C, Kirwan JR, Choy EH, Chalder T, et al. Non-pharmacological interventions for fatigue in rheumatoid arthritis. Cochrane Database Syst Rev 2013;8:CD008322.
24. Prevoo ML, van't Hof MA, Kuper HH, van Leeuwen MA, van de Putte LB, van Riel PL. Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. Arthritis Rheum 1995;38:44-8.
25. Fries JF, Spitz P, Kraines RG, Holman HR. Measurement of patient outcome in arthritis. Arthritis Rheum 1980;23:137-45.

26. Fries JF, Spitz PW, Young DY. The dimensions of health outcomes: the health assessment questionnaire, disability and pain scales. J Rheumatol 1982;9:789-93.

27. Chalder T, Berelowitz G, Pawlikowska T, Watts L, Wessely S, Wright D, et al. Development of a fatigue scale. J Psychosom Res 1993;37:147-53.

28. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 1989;28:193-213.

29. Krupp LB, Coyle PK, Doscher C, Miller A, Cross AH, Jandorf L, et al. Fatigue therapy in multiple sclerosis: results of a double-blind, randomized, parallel trial of amantadine, pemoline, and placebo. Neurology 1995;45:1956-61.

30. Goligher EC, Pouchot J, Brant R, Kherani RB, Aviña-Zubieta JA, Lacaille D, et al. Minimal clinically important difference for 7 measures of fatigue in patients with systemic lupus erythematosus. J Rheumatol 2008;35:635-42.

31. Buysse DJ, Reynolds CF, Monk TH, Hoch CC, Yeager AL, Kupfer DJ. Quantification of subjective sleep quality in healthy elderly men and women using the Pittsburgh Sleep Quality Index (PSQI). Sleep 1991;14:331-8.

32. Berger AM, Kuhn BR, Farr LA, Von Essen SG, Chamberlain J, Lynch JC, et al. One-year outcomes of a behavioral therapy intervention trial on sleep quality and cancer-related fatigue. J Clin Oncol 2009;27:6033-40.

33. Berger AM, Lockhart K, Agrawal S. Variability of patterns of fatigue and quality of life over time based on different breast cancer adjuvant chemotherapy regimens. Oncol Nurs Forum 2009; 36:563-70.

34. Inoue Y, Kuroda K, Hirata K, Uchimura N, Kagimura T, Shimizu T. Long-term open-label study of pramipexole in patients with primary restless legs syndrome. J Neurol Sci 2010;294:62-6.

35. Johnson DA, Orr WC, Crawley JA, Traxler B, McCullough J, Brown KA, et al. Effect of esomeprazole on nighttime heartburn and sleep quality in patients with GERD: a randomized, placebo-controlled trial. Am J Gastroenterol 2005;100:1914-22.

36. Skomro RP, Gjevre J, Reid J, McNab B, Ghosh S, Stiles M, et al. Outcomes of home-based diagnosis and treatment of obstructive sleep apnea. Chest 2010;138:257-63.

37. Cakirbay H, Bilici M, Kavakçi O, Cebi A, Güler M, Tan U. Sleep quality and immune functions in rheumatoid arthritis patients with and without major depression. Int J Neurosci 2004;114:245-56.

38. Sechrist KR, Walker SN, Pender NJ. Development and psychometric evaluation of the exercise benefits/barriers scale. Res Nurs Health 1987;10:357-65.

39. Garber CE, Blissmer B, Deschenes MR, Franklin BA, Lamonte MJ, Lee IM, et al. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. Med Sci Sports Exerc 2011;43:1334-59.

40. American College of Sports Medicine, Durstine JL, Moore G, Painter P, Roberts S. ACSM's exercise management for persons with chronic diseases and disabilities. 3rd ed. Leeds: Human Kinetics; 2009.

41. Repping-Wuts H, Fransen J, van Achterberg T, Bleijenberg G, van Riel P. Persistent severe fatigue in patients with rheumatoid arthritis. J Clin Nurs 2007;16:377-83.

42. Wolfe F, Hawley DJ, Wilson K. The prevalence and meaning of fatigue in rheumatic disease. J Rheumatol 1996;23:1407-17.

43. Pollard LC, Choy EH, Gonzalez J, Khoshaba B, Scott DL. Fatigue in rheumatoid arthritis reflects pain, not disease activity. Rheumatology 2006;45:885-9.

44. Campbell RC, Batley M, Hammond A, Ibrahim F, Kingsley G, Scott DL. The impact of disease activity, pain, disability and treatments on fatigue in established rheumatoid arthritis. Clin Rheumatol 2012; 31:717-22.

45. Thyberg I, Dahlström O, Thyberg M. Factors related to fatigue in women and men with early rheumatoid arthritis: the Swedish TIRA study. J Rehabil Med 2009;41:904-12.

46. Repping-Wuts H, Uitterhoeve R, van Riel P, van Achterberg T. Fatigue as experienced by patients with rheumatoid arthritis (RA): a qualitative study. Int J Nurs Stud 2008;45:995-1002.

47. Chauffier K, Salliot C, Berenbaum F, Sellam J. Effect of biotherapies on fatigue in rheumatoid arthritis: a systematic review of the literature and meta-analysis. Rheumatology 2012;51:60-8.

48. Menefee LA, Cohen MJ, Anderson WR, Doghramji K, Frank ED, Lee H. Sleep disturbance and nonmalignant chronic pain: a comprehensive review of the literature. Pain Med 2000;1:156-72.

49. Bigatti SM, Hernandez AM, Cronan TA, Rand KL. Sleep disturbances in fibromyalgia syndrome: relationship to pain and depression. Arthritis Rheum 2008;59:961-7.

50. Li Y, Zhang S, Zhu J, Du X, Huang F. Sleep disturbances are associated with increased pain, disease activity, depression, and anxiety in ankylosing spondylitis: a case-control study. Arthritis Res Ther 2012;14:R215.

51. King AC, Baumann K, O'Sullivan P, Wilcox S, Castro C. Effects of moderate-intensity exercise on physiological, behavioral, and emotional responses to family caregiving: a randomized controlled trial. J Gerontol A Biol Sci Med Sci 2002;57:M26-36.

52. King AC, Oman RF, Brassington GS, Bliwise DL, Haskell WL. Moderate-intensity exercise and self-rated quality of sleep in older adults. A randomized controlled trial. JAMA 1997;277:32-7.

53. Irwin MR, Olmstead R, Motivala SJ. Improving sleep quality in older adults with moderate sleep complaints: A randomized controlled trial of Tai Chi Chih. Sleep 2008;31:1001-8.

54. Santos RV, Tufik S, De Mello MT. Exercise, sleep and cytokines: is there a relation? Sleep Med Rev 2007;11:231-9.

55. Driver HS, Taylor SR. Exercise and sleep. Sleep Med Rev 2000;4:387-402.

56. Baillet A, Vaillant M, Guinot M, Juvin R, Gaudin P. Efficacy of resistance exercises in rheumatoid arthritis: meta-analysis of randomized controlled trials. Rheumatology 2012;51:519-27.

57. Palmefors H, DuttaRoy S, Rundqvist B, Börjesson M. The effect of physical activity or exercise on key biomarkers in atherosclerosis — A systematic review. Atherosclerosis 2014;235:150-61.