

Physical activity and sedentary behavior in women with rheumatoid arthritis: a comparison of patients with low and high disease activity and healthy controls

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Objective: In rheumatoid arthritis (RA) patients, low levels of physical activity (PA) and high levels of sedentary behavior (SB) may play a role in enhancing cardiovascular risk. We do not know how long-term control of disease activity impacts upon daily PA levels and if treated patients attain PA levels seen in healthy controls. We therefore compared habitual levels of PA and SB between female RA patients with low disease activity achieved by anti-tumor necrosis factor (TNF) therapy, those with active arthritis (aRA) and non-RA controls.

Methods: We carried out a cross-sectional comparison of 40 RA patients on anti-TNF therapy for >2 years with DAS28<3.2 (tRA), 32 patients on conventional disease modifying anti-rheumatic drugs with DAS28>3.2 (aRA) and 34 healthy controls (C) with the groups matched for age and body mass index. PA was assessed using the ActiGraph accelerometer to determine step count and time spent in moderate-to-vigorous physical activity (MVPA), light activity and sedentary time.

Results: Daily step count was 72% higher in tRA and 40% higher in C in comparison to aRA ($p<0.01$). Sedentary time (as a proportion of wear time) was 10% less in tRA than aRA ($p=0.03$), while light activity time was 18% higher ($p=0.014$). Both RA groups had 40% lower MVPA time than C ($p=0.001$). Only half of either RA group fulfilled current WHO guidelines for PA compared with 82% of controls.

Conclusion: RA patients who had long-term disease suppression were more physically active with less SB compared to RA patients with active disease. They had similar light PA and SB to controls although lower MVPA. Behavioral change interventions are likely to be needed in order to restore moderate exercise, further reduce SB and to meet guidelines for daily PA.

Keywords: rheumatoid arthritis, physical activity, sedentary behavior, accelerometry

Introduction

In the general population, there is good evidence that sedentary behavior (SB; defined as time spent sitting) is hazardous to health.¹⁻⁴ SB has been associated with an increased risk of type 2 diabetes, cardiovascular disease, cancer and all-cause mortality, often independently of body mass index (BMI) and physical activity (PA).¹⁻⁴ Recent evidence has suggested that high levels of moderate-to-vigorous physical activity (MVPA), for example, at least 60–90 mins per day, may have a protective effect against the health consequences associated with high levels of sitting.⁵ However, these high levels of activity may not be achievable by the

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majority of the population given the current low levels of MVPA engagement.⁶ Experimental evidence has suggested that breaking up long periods of sitting with light and moderate intensity activity improves glucose and insulin levels and blood pressure in those at risk of chronic disease.^{7–9} Avoiding a sedentary lifestyle (characterized by prolonged periods of sitting) is likely to reduce the aforementioned health risks, and delay the onset of age-related functional limitation by reducing muscle and bone loss and preventing falls and fractures.¹⁰

Rheumatoid arthritis (RA) is characterized by joint swelling, muscle wasting, fatigue and elevated cardiovascular risk associated with cytokine-driven systemic inflammation.¹¹ Several controlled studies using accelerometry^{12–14} have shown reduced total PA in patients with RA compared to healthy controls although others have shown no difference.^{15–17} Nevertheless, the balance between SB, light PA and MVPA is likely to be most important and indeed Pioreschi et al¹² have reported that RA patients spend around 2 hrs more each day in sedentary activities than healthy controls. Such SB may persist due to inadequate control of inflammation, habit or psychological factors and lead to serious long-term consequences for the health of the individual. Basic research has suggested that SB induces a pro-inflammatory and potentially atherogenic state by cellular mechanisms including reduction in lipoprotein lipase activity leading to a rise in triglycerides and cholesterol.¹⁸ This may help to perpetuate RA and add to its comorbidities.¹⁹ RA patients who are physically active have better psychological wellbeing than those who are inactive,¹² exhibit fewer cardiovascular risk factors,^{16,20–23} fewer hospital admissions,²⁴ have higher bone mineral density (BMD) and reduced bone loss.²⁵

Anti-tumor necrosis factor (TNF) therapy has revolutionized the management of RA with rapid and sustained improvements in pain, function, quality of life²⁶ and workforce participation.²⁷ Improving locomotor, cardiovascular and psychological health is likely to depend upon not only control of inflammation but also restoring PA. We do not know however how long-term control of disease activity impacts upon habitual daily PA and SB levels and whether treated patients attain PA levels seen in healthy controls. The aim of this study was to assess habitual levels of PA and SB in women with RA who had experienced long-term low disease activity achieved by anti-TNF therapy compared to RA patients with active arthritis (aRA) and non-RA controls.

Patients and methods

Study protocol

This cross-sectional study measured PA and SB levels in three groups of patients: RA patients on their first anti-TNF drug for >2 years with consistently low disease activity (tRA), RA patients with moderate to high disease activity on conventional disease modifying anti-rheumatic drug (cDMARD) therapy who had never had a biologic drug (aRA) and non-RA controls (C). Anti-TNF patients were selected as the participants of this study as these individuals had documented high RA disease activity in the past and had regular subsequent measurements recorded confirming low disease activity. A 2-year minimum time period on anti-TNF was considered appropriate based on the clinical observation that at least one year was required for an individual to adjust physically and mentally to a low disease activity state. The aRA group was chosen as a comparator as these patients would have been similar in terms of RA disease activity and treatment to the tRA group before they were established on biologic therapy. High disease activity patients were selected for the aRA group where possible, particularly those undergoing assessment with a view to biologic therapy. The study was limited to women in order to maintain consistency. The sample size for this study was based on information quoted in the paper by Roubenoff et al.¹⁴ In order to detect an effect size in activity energy expenditure as reported by these authors of $1,264 \pm 992$ kJ/day in patients versus $2,280 \pm 1,469$ kJ/day in controls with a power of 90% at 95% significance level would require 32 participants per group. Forty patients per group were planned to allow for dropouts and inadequate data recording (20%) yielding a target sample size of 120 participants in total. At the time of planning our study, there were no other relevant accelerometry papers.

Participants

Women 18 years or above, resident in the catchment areas of the Royal Derby Hospital and local community hospitals were eligible for the study. Potential participants were identified from the Departmental anti-TNF database and from the health records of patients attending the clinic. Exclusion criteria were pregnancy or breastfeeding within the previous 12 months, oral corticosteroid therapy, insulin-dependent diabetes, structural damage to a lower limb joint or joint replacement, use of a walking aid or any significant disorder which might influence the result of the trial or the person's ability to participate in the trial. tRA patients were recruited if

their 3 monthly DAS28 scores were consistently ≤ 3.2 for 2 years or more and at study entry. aRA had a DAS score > 3.2 on entry to the study. Controls were recruited by advertisement among hospital staff and through the local newspaper. They were volunteers who considered themselves to be healthy and had no restrictions on PA. Exclusion criteria similar to other participants were applied. No remuneration other than for parking charges was provided. Anti-TNF patients were recruited first of all and participants in the other two groups were selected so as to match the group means for age and BMI.

Assessments

RA clinical assessment

Rheumatoid disease activity was measured using the DAS28 score with tender and swollen joint counts (TJC, SJC), patient global health VAS and erythrocyte sedimentation rate. Low Rheumatoid disease activity was defined as $\text{DAS28} \leq 3.2$ and moderate to high disease activity as $\text{DAS28} > 3.2$.²⁸ The Health Assessment Questionnaire (HAQ) was used as a standard measure of functional disability.

Anthropometry

Height, body mass and waist circumference were recorded, and a GE Lunar Prodigy dual-energy X-ray absorptiometry scanner was used to measure fat mass and BMD.

Questionnaires

The SF-36 v2 questionnaires were completed at the end of the 7-day monitoring period. Participants were questioned regarding alcohol consumption, current and previous smoking.

Accelerometry

Participants wore an ActiGraph GT3X + accelerometer (ActiGraph, Pensacola, FL, USA) throughout waking hours (taken off at bedtime) for seven consecutive days, except during water-based activities, on an elasticated belt on the waist above the mid-line of the right thigh. The device was initialized at a frequency of 30 Hz and downloaded using ActiLife software version 6.9.0. The low-frequency extension filter was selected during the download process, and data were downloaded into 60-s epochs. Accelerometer data were considered valid if there were > 600 mins of monitoring per day (excluding continuous strings of zero counts for 60 mins or longer) recorded on at least three weekdays and one weekend day.²⁹ The widely used < 100 counts/min (cpm) cut-point was employed to estimate sedentary time (ie, estimated time spent sitting)³⁰ while the Freedson cut-points (applied to the

vertical axis) were used to estimate time spent in light intensity activity (100–1,951 cpm) (such as slow walking) and MVPA (such as brisk walking or jogging/running) ($\geq 1,952$ cpm).³¹ Information on daily step counts was also retrieved from the device. Mean times spent per day in SB, light intensity activity and MVPA, along with the proportion of time spent per day in each behavior (accounting for accelerometer wear time) were calculated for each participant over the 7-day monitoring period.

Statistical analysis

Analysis was performed using SPSS for Windows version 23 (IBM Corporation, Armonk, NY, USA) Data were checked and distributions assessed using Kolmogorov–Smirnov tests and visual inspection of histograms and Q–Q plots. Means and SDs (or median and inter-quartile ranges) were calculated. For normally distributed data, comparisons between groups were conducted using ANOVA with Bonferroni *post hoc* tests. Variables that were not normally distributed were compared between groups using independent samples Kruskal–Wallis test or Mann–Whitney *U*-test as appropriate. Categorical variables were compared using chi-squared tests. One-way ANOVAs compared mean daily step counts across the three study groups. The proportions of daily accelerometer wear time spent sedentary, in light activity and in MVPA were compared between groups to control for differences in accelerometer wear time. Body composition variables (fat mass and waist circumference) as well as BMD at the spine and hip were analyzed using one-way ANOVAs to test for differences between the three groups. The ANOVAs were repeated using % fat as a covariate in view of the reported association of BMI and fat mass with PA, particularly MVPA.³² Statistical significance was set at $p < 0.05$ for all analyses.

Results

Participants

The three groups were similar in age, ethnicity, height, body mass, BMI and BMD although fat mass and waist circumference were greater in aRA than C (Table 1). Prevalence of current smoking or alcohol consumption did not differ between groups although a lower proportion of controls had a history of smoking. Among RA patients, measurements of functional disability (HAQ) and rheumatoid disease activity (DAS28, TJC, SJC and VAS) were significantly higher in aRA than tRA as expected by the selection criteria (Table 1). RA disease duration was significantly greater in tRA than aRA; 34% aRA patients were taking more than one cDMARD. In

Table 1 Characteristics of tRA, aRA and control (C) groups

Variable	tRA (n=40)	aRA (n=32)	C (n=34)	p
Age (years)	59.0±10.4	60.4±10.6	60.8±10.5	0.748
Height (cm)	163.2±7.1	163.7±6.9	162.1±6.0	0.606
Body mass (kg)	68.6±13.1	74.4±16.7	66.3±10.4	0.054
BMI (kg m ⁻²)	25.7±4.5	27.7±5.6	25.1±3.2	0.072
Waist circumference (cm)	86.3±12.5	91.5±10.5 ^c	83.6±8.9 ^c	0.019
% Fat	38.0±7.3	40.9±6.9 ^c	37.7±6.3 ^c	0.041
Left femoral neck BMD (T-score)	-0.8±1.1	-1.0±1.0	-0.6±0.9	0.317
L2-4 BMD (T-score)	-0.1±1.7	-0.2±0.3	-0.4±1.4	0.725
Ethnicity [§]				
White British	35 (88%)	31 (97%)	31 (91%)	0.210
Asian Chinese	0 (0%)	0 (0%)	1 (3%)	
Asian Indian	1 (3%)	0 (0%)	2 (6%)	
Black Caribbean	0 (0%)	1 (3%)	0 (0%)	
Mixed	2 (5%)	0 (0%)	0 (0%)	
Other	2 (5%)	0 (0%)	0 (0%)	
History of smoking [§]	19 (48%)	19 (59%)	9 (26%)	0.024
Current smoking [§]	2 (5%)	2 (6%)	1 (3%)	0.813
Alcohol consumption [§]				
≥4 times/week	6 (15%)	4 (13%)	8 (24%)	0.691
2-3 times/week	6 (15%)	7 (22%)	9 (26%)	
2-4 times/month	15 (38%)	8 (25%)	7 (17%)	
Monthly or less	8 (20%)	6 (19%)	4 (12%)	
Never	5 (13%)	7 (22%)	6 (18%)	
Duration of RA (years)	15.8±9.2 ^a	9.6±9.6 ^a	–	0.006
TJC*	1 (0-2) ^a	13 (9-22) ^a	–	<0.001
SJC*	0 (0-2) ^a	8 (7-12) ^a	–	<0.001
ESR*	11 (6-22)	13 (7-24)	–	0.202
VAS*	12 (10-20) ^a	50 (20-78) ^a	–	<0.001
DAS28	2.7 (0.9) ^a	5.3 (1.2) ^a	–	<0.001
HAQ summary score	0.7±0.6 ^a	1.2±0.6 ^{a c}	0.1±0.1 ^c	<0.001
Treatment				
Anti-TNF				
Etanercept	37 (93%)	–		
Adalimumab	2 (5%)	–		
Infliximab	1(2%)	–		
cDMARD				
Methotrexate	21 (53%)	20 (63%)		
Sulfasalazine	4 (10%)	6 (19%)		
Hydroxychloroquine	1 (3%)	16 (50%)		
Leflunomide	–	6 (19%)		
D-Penicillamine	–	2 (6%)		

Notes: Figures are presented as mean ± SD unless otherwise indicated; *Median (inter-quartile range), or [§]Number (%). According to Bonferroni post hoc tests: ^atRA significantly different from aRA, ^btRA significantly different from the control group, ^caRA significantly different from the control group. The p-values shown in bold are statistically significant, p<0.05.

Abbreviations: aRA, rheumatoid arthritis patients with active arthritis; BMD, bone mineral density; BMI, body mass index; cDMARD, conventional disease modifying anti-rheumatic drug; ESR, erythrocyte sedimentation rate; HAQ, Health Assessment Questionnaire; RA, rheumatoid arthritis; SJC, swollen joint count; TJC, tender joint count; TNF, tumour necrosis factor; tRA, rheumatoid arthritis patients on anti-TNF therapy.

tRA, 37 patients were taking Etanercept, two Adalimumab and one Infliximab and 60% were also taking a cDMARD.

Accelerometry

All but two participants provided ActiGraph data, collected over a mean of 6.6 days. Total daily wear time for the whole sample was 854±71 mins/day. ActiGraph wear time differed marginally between the three groups (Table 2); therefore, the proportions of time spent in each behavior (sedentary, light activity and MVPA) were used in the primary analyses. Significant differences were observed between groups in the proportions of time spent sedentary, in light activity, and MVPA (Table 2). Post-hoc comparisons revealed that tRA spent a 10% lower proportion of time sedentary ($p=0.03$) and an 18% higher proportion of time in light intensity PA ($p=0.014$) in comparison to aRA. No significant differences were observed between the controls and either aRA or tRA in the proportions of time spent sedentary and in light activity. Both tRA and aRA had 40% lower MVPA time in comparison to controls (both $p=0.002$). No significant differences in the proportion of time spent in MVPA were observed between the two RA groups. Mean daily step counts differed significantly

between groups (Table 2), with tRA accumulating 72% more daily steps and Controls 40% more steps in comparison to aRA ($p<0.001$). No significant differences in daily steps were observed between tRA and controls. Findings were not affected when results for three patients in the tRA group taking a biologic other than Etanercept were excluded. Adjustment of the results for the difference in % fat between the groups resulted in no material change in the level of significance (Table 3).

Patient-reported outcome

The SF-36 physical health score differed significantly between the groups with C>tRA>aRA.

Discussion

Our study has documented that patients on long-term anti-TNF therapy have higher levels of overall PA (as estimated by steps/day) when compared to those with aRA as well as similar levels to healthy controls. This is mirrored by the HAQ scores which reflect mainly low intensity daily PAs and personal care showing that a stable period of prolonged low RA disease activity allows the rheumatoid patient to achieve a degree of normality with regards their overall PA behavior.

Table 2 Physical activity and questionnaire data for tRA, aRA and control (C) groups

ActiGraph data	tRA(n=40)	aRA (n=31)	C (n=33)	p
Step count (steps/day)	12808 ± 6005 ^a	7452 ± 3788 ^{ac}	10446 ± 4120 ^c	<0.001
Wear time (min/d)	862 ± 64	831 ± 78	870 ± 69	0.065
% sedentary	56.3 ± 10.8 ^a	62.6 ± 10.9 ^a	58.4 ± 7.2	0.030#
% light	40.8 ± 9.6 ^a	34.5 ± 1.0 ^a	36.8 ± 6.9	0.014
% MVPA	2.9 ± 2.2 ^b	2.9 ± 2.2 ^c	4.8 ± 2.8 ^{bc}	0.002
WHO exercise guidelines fulfilled (%)	50.0%	48.4%	81.8%	0.007**
SF36 mental health (0–100)*	50.6 ± 9.5 ^a	44.7 ± 12.2 ^{ac}	54.0 ± 5.5 ^c	0.001
SF36 physical (0–100)*	44.0 ± 9.0 ^{ab}	35.9 ± 11.1 ^{ac}	55.4 ± 5.5 ^{bc}	<0.001

Notes: Figures are presented as mean ±SD unless indicated otherwise. SF-36: *The lower the score the worse the health. According to Bonferroni post hoc tests: ^atRA significantly different from aRA, ^btRA significantly different from the control group, ^caRA significantly different from the control group. **p value from Chi-squared test. #p value for aRA v C = 0.09.

Abbreviations: aRA, rheumatoid arthritis patients with active arthritis; MVPA, moderate to vigorous physical activity; tRA, rheumatoid arthritis patients on anti-TNF therapy.

Table 3 Physical activity data adjusted for % body fat

Adjusted ActiGraph data	tRA (n=38)	aRA (n=30)	Control group (n=33)	p
% sedentary	55.6 (1.6) ^a	62.1 (1.8) ^a	58.6 (1.7)	0.030
% light	41.4 (1.4) ^a	34.9 (1.6) ^a	36.7 (1.6)	0.009
% MVPA	3.0 (0.4) ^b	3.0 (0.4) ^c	4.7 (0.4) ^{b,c}	0.006

Notes: Data are presented as mean (standard error). According to Bonferroni post hoc tests: ^atRA significantly different from aRA, ^btRA significantly different from the control group, ^caRA significantly different from the control group. The p-values shown in bold are statistically significant, $p<0.05$.

Abbreviations: aRA, rheumatoid arthritis patients with active arthritis; MVPA, moderate to vigorous physical activity; tRA, rheumatoid arthritis patients on anti-TNF therapy.

Step count is an important indicator of general health: in RA patients, for example, step count is highly correlated to aerobic capacity, a standard assessment of cardiorespiratory fitness.³³ Similarly, in the general population evidence demonstrates a linear association between step counts and a range of morbidity and mortality outcomes, as well as with markers of health status including inflammation, adiposity, insulin sensitivity and high-density lipoprotein-cholesterol in adults.^{34–36} Regardless of an individual's baseline value, even modest increases in daily step counts should, therefore, yield clinically meaningful health benefits for RA patients.

A further finding of our study is that low disease activity patients (tRA) were less sedentary than the aRA group with similar SB to the controls. In comparison to the aRA group lower % sedentary time was also associated with a higher % time in light activity. This suggests that long-term suppression of RA disease activity may result in the “rebalancing” of SB and light-intensity activity. These results are in accord with the one previous study looking at SB in relation to RA disease activity: Pioreschi et al³⁷ studied 18 drug-naive RA patients at baseline and after 3 months of DMARD therapy finding that improvements in RA disease activity were associated with a fall in sedentary time and an increase in time spent in light PA. The findings may have major implications for the cardiovascular health of RA patients: a study by Fenton et al³⁸ comparing cardiovascular risk factors with PA revealed significant positive associations between sedentary time and 10-year CVD risk, with the reverse true for light PA participation. Associations were independent of MVPA engagement. Khoja et al²¹ also found that the associations between accelerometer-measured PA and cardiovascular disease markers in RA patients were either equivalent or stronger at very light and light intensities, as compared to moderate intensity.

An unexpected finding from the current study was the lack of difference in % sedentary time between those with aRA and controls. The expectation was that SB would be higher in the aRA group although the results do not support this: aRA patients were sedentary for a mean of 63% of the wear time in comparison to 58% for controls ($p=0.09$). It could be that a difference that was too small to detect with the sample size in this study. Nevertheless, similar results have been reported in other cross-sectional studies comparing SB in RA to healthy controls^{15,39} although Pioreschi et al¹² found a higher sedentary time in RA. The lack of difference between the RA group and controls in one study was thought to be due to a “ceiling effect” with a high level of SB of 91% accelerometer wear time in both groups.¹⁵ The interpretation of SB is therefore

complex as there may be different causes. In RA, pain, stiffness and fatigue are likely to be important whereas healthy controls may paradoxically have a higher sitting time through greater work participation. A recent study of office workers drawn from the same geographical area to the present study found that they were sedentary for 68% of wear time on work days and 60% non-work days.⁴⁰ The issue of employment was not explored in the current study. It is clear however that there are high levels of SB among RA patients as well as in the general population. RA patients are already susceptible to obesity, muscle wasting, osteoporosis, cardiovascular disease, depression and fatigue as a result of chronic systemic inflammation, perhaps partly mediated through increased SB. Reduction in SB is arguably even more urgent in this section of the population requiring both pharmacological and non-pharmacological approaches to management. Thomsen et al,⁴¹ for example, have recently shown that a 16-week individually tailored, theory-based behavioral intervention with motivational counseling and SMS reminders reduced daily sitting time by an average of 2 hrs as well as total cholesterol in sedentary patients with RA.

MVPA may be difficult for some people with RA to achieve and maintain. Our study demonstrated that RA patients with good disease control on long-term anti-TNF therapy continue to exhibit a deficit in MVPA compared to healthy controls with a level of MVPA similar to patients with active RA. Nevertheless, even for controls, MVPA accounted for only 5% of accelerometer wear time. These results are supported by the data from the SF-36 physical component score in which most questions are concerned with MVPA rather than light activity. Previous accelerometry studies also show a reduction in MVPA in RA patients compared to healthy individuals^{13,16} although Huffman et al¹⁵ in their extremely sedentary population found no difference to controls. Guidelines for PA⁴² recommend at least 150 mins moderate PA or 75 mins of vigorous activity per week in adults. Of our population, 82% of the controls, 48% aRA and 50% tRA fulfilled the criteria. It is well documented that exercise interventions are effective in promoting cardiovascular health in RA.^{43,44} There is a need for PA and exercise programmes that support RA patients in overcoming barriers in order to sustain this important health behavior.⁴⁵

Our study has a number of strengths and limitations. Comparing RA patients experiencing long-term disease suppression (tRA) with healthy controls and patients with aRA has allowed us to highlight the achievements and deficiencies of our current management in relation to restoring an

individual's PA. Nevertheless, as this is a cross-sectional study the conclusions should ideally be supported by prospective data. We are therefore unable to attribute the observed differences between the RA groups directly to the beneficial effects of sustained low rheumatoid disease activity. Indeed, we are also unable to say for certain whether the observed effects were due to low disease activity or anti-TNF per se. Nevertheless, improvement in patient-reported PA outcomes similar to those achieved by anti-TNF are also seen following disease suppression with other drugs,⁴⁶ suggesting that the observed effects on PA in this study are due to disease suppression rather than being drug specific. Our choice of cDMARD patients as a comparison group was a pragmatic one as such patients are common. The alternative choice of "anti-TNF failure" patients might have allowed us to distinguish between the effects of low disease activity and anti-TNF but there are far fewer such patients in our clinic and they are rapidly escalated to alternative biologic therapy. Additionally such a group is not free from possible channeling bias: for example, "anti-TNF failure" patients have a higher rate of smoking and obesity.⁴⁷ Our choice of a 2-year minimum time frame for the anti-TNF therapy has been subsequently supported by the results of follow-up studies showing maximum improvement in DAS28 and HAQ at about one year with no significant change up to 5 years.⁴⁸ Because of the inclusion and exclusion criteria, the results may not be generalizable to the whole RA population. The study was limited to women for the sake of consistency so some of the conclusions may not apply to men. There is some evidence, for example, that men in the general population engage in more MVPA than women.⁴⁹ It was not possible to BMI match the tRA with the aRA groups closely because of the higher BMI of patients meeting the aRA criteria attending our clinics although controlling for fat mass did not substantially change the results (Table 3). The shorter disease duration in aRA in comparison to tRA reflects the increasing tendency over the past few years to manage patients more aggressively and escalate to biologic treatment early in the disease course. The relatively small sample size limited our ability to detect differences between groups. The three groups contained a wide age spectrum (between 30 and 77 years) which might be viewed as a limitation of the study. Population studies show that levels of total and light PA are stable during midlife (ages 31–59) but decline subsequently whereas MVPA levels fall gradually from about age 50 years.⁵⁰ Nevertheless, the groups were closely matched for mean age and age distribution (Table 1), allowing for valid comparison. Additionally, the patients we recruited were all

in good health, apart from RA, potentially minimizing the age drop-off in PA seen in unselected populations. While the ActiGraph accelerometer has been widely used as an objective measure of SB, this waist-worn device is not capable of distinguishing between standing and sitting/lying postures. Therefore, some periods of standing still may have been misclassified as SB. Further research exploring SB in RA patients should use inclinometers to strengthen the measurement of sedentary time.³⁰

Conclusion

We have demonstrated that RA patients with low rheumatoid disease activity due to long-term anti-TNF therapy are more physically active and have lower SB compared with RA patients with active disease. Anti-TNF treated patients are similar to healthy controls in terms of total PA, SB, disability and fat mass although have a persisting deficit in MVPA. Although new biologic therapies have been successful in restoring RA patients to a more normal existence, we need to design behavioral change interventions in order to optimize our management of patients with RA. Moderate exercise should be encouraged where possible, but it also appears that reducing SB and encouraging light PA is an effective strategy in promoting cardiovascular and musculoskeletal health in RA.

Ethics approval and informed consent

Approval was granted by the Southern Derbyshire Ethics Committee (12/EM/0433, RD-5103-001-12) and all patients and controls signed a written consent form. The procedures followed in the study were in accordance with the ethical standards of the responsible committee on human experimentation and with the Declaration of Helsinki.

Abbreviations

Anti-TNF drugs, Biopharmaceuticals given by regular injection which block the action of TNF; aRA, RA patients on conventional DMARDs with high disease activity (DAS>3.2); BMD, Bone mineral density; BMI, Body mass index; C, non-rheumatoid arthritis healthy controls; cDMARD, conventional disease modifying anti-rheumatic drug; DAS28/DAS score, a measure of the severity of rheumatoid arthritis using clinical and laboratory data, specifically the numbers of tender and swollen joints from a set of 28, the patient's global health score (0-10) and the erythrocyte sedimentation rate or CRP; HAQ, Health Assessment

Questionnaire; MVPA, moderate-to-vigorous physical activity; PA, physical activity; Q-Q plot, Quantile-quantile probability plot; RA, Rheumatoid arthritis; SB, sedentary behavior; SF-36, 36 item Short Form questionnaire to measure physical and mental health; SJC, Swollen joint count; SPSS, Statistical Package for the Social Sciences; TJC, Tender joint count; TNF, Tumour necrosis factor alpha which is produced in excess in RA causing inflammation, pain and damage to the bones and joints; tRA, Rheumatoid arthritis patients on anti-TNF therapy with low disease activity (DAS<3.2); VAS, 10 cm visual analogue scale.

Data sharing statement

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

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Author contributions

GS, AB, KB-W and SC made substantial contributions to conception and design of the study. TB and AB were responsible for data collection. All authors contributed to data analysis, drafting and revising the article, gave final approval to the version to be published and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Wilmot EG, Edwardson CL, Achana FA, et al. Sedentary time in adults and the association with diabetes, cardiovascular disease and death: systematic review and meta-analysis. *Diabetologia*. 2012;55:2895–2905. doi:10.1007/s00125-012-2677-z
2. de Rezende LFM, Rey-López JP, Matsudo VKR, et al. Sedentary behavior and health outcomes among older adults: a systematic review. *BMC Public Health*. 2014;14:33. doi:10.1186/1471-2458-14-333
3. Shen D, Mao W, Liu T, et al. Sedentary behavior and incident cancer: a meta-analysis of prospective studies. *PLoS One*. 2014;9:e105709. doi:10.1371/journal.pone.0105709
4. Biswas A, Oh PI, Faulkner GE, et al. Sedentary time and its association with risk for disease incidence, mortality, and hospitalization in adults: a systematic review and meta-analysis. *Ann Intern Med*. 2015;162:123–132. doi:10.7326/M14-1651
5. Ekelund U, Steene-Johannessen J, Brown WJ, et al. Does physical activity attenuate, or even eliminate, the detrimental association of sitting time with mortality? A harmonised meta-analysis of data from more than 1 million men and women. *Lancet*. 2016;388:1302. doi:10.1016/S0140-6736(16)30370-1
6. Hallal PC, Andersen LB, Bull FC, Guthold R, Haskell W, Ekelund U, for the Lancet Physical Activity Series Working Group. Global physical activity levels: surveillance progress, pitfalls, and prospects. *Lancet*. 2012;380:247–257. doi:10.1016/S0140-6736(12)60646-1
7. Henson J, Davies MJ, Bodicoat DH, et al. Breaking up prolonged sitting with standing or walking attenuates the postprandial metabolic response in postmenopausal women: a randomized acute study. *Diabetes Care*. 2016;39:130–138. doi:10.2337/dc15-1240
8. Thorp AA, Kingwell BA, Sethi P, Hammond L, Owen N, Dunstan DW. Alternating bouts of sitting and standing attenuate postprandial glucose responses. *Med Sci Sports Exerc*. 2014;46:2053–2061. doi:10.1249/MSS.0000000000000337
9. Larsen RN, Kingwell BA, Sethi P, Cerin E, Owen N, Dunstan DW. Breaking up prolonged sitting reduces resting blood pressure in overweight/obese adults. *Nutr Metab Cardiovasc Dis*. 2014;24:976–982. doi:10.1016/j.numecd.2014.04.011
10. Proctor DN, Melton LJ, Khosla S, Crowson CS, O'Connor MK, Riggs BL. Relative influence of physical activity, muscle mass and strength on bone density. *Osteoporos Int*. 2000;11:944–952.
11. Kitas GD, Gabriel SE. Cardiovascular disease in rheumatoid arthritis: state of the art and future perspectives. *Ann Rheum Dis*. 2010;70:8–14. doi:10.1136/ard.2010.142133
12. Pioreschi A, Hodkinson B, Avidon I, Tikly M, McVeigh JA. The clinical utility of accelerometry in patients with rheumatoid arthritis. *Rheumatology*. 2013;52:1721–1727. doi:10.1093/rheumatology/ket216
13. Paul L, Rafferty D, Marshall-McKenna R, et al. Oxygen cost of walking, physical activity, and sedentary behaviours in rheumatoid arthritis. *Scand J Rheumatol*. 2014;43:28–34. doi:10.3109/03009742.2013.802009
14. Roubenoff R, Walsmith J, Lundgren N, Snyderman L, Dolnikowski GJ, Roberts S. Low physical activity reduces total energy expenditure in women with rheumatoid arthritis: implications for dietary intake recommendations. *Am J Clin Nutr*. 2002;76:774–779. doi:10.1093/ajcn/76.4.774
15. Huffman KM, Pieper CF, Hall KS, St Clair EW, Kraus WE. Self-efficacy for exercise, more than disease-related factors, is associated with objectively assessed exercise time and sedentary behaviour in rheumatoid arthritis. *Scand J Rheumatol*. 2015;44:106–110. doi:10.3109/03009742.2014.931456
16. Hernández-Hernández V, Ferraz-Amaro I, Díaz-González F. Influence of disease activity on the physical activity of rheumatoid arthritis patients. *Rheumatology*. 2014;53:722–731. doi:10.1093/rheumatology/ket422
17. Abouassi H, Tune KN, Gilmore B, et al. Adipose depots, not disease-related factors, account for skeletal muscle insulin sensitivity in established and treated rheumatoid arthritis. *J Rheumatol*. 2014;41:1974–1979. doi:10.3899/jrheum.140224
18. Hamilton MT, Hamilton DG, Zderic TW. Role of low energy expenditure and sitting in obesity, metabolic syndrome and type 2 diabetes and cardiovascular disease. *Diabetes*. 2007;56:2655–2667. doi:10.2337/db07-0882
19. Fenton SAM, Kitas GD. Rheumatoid arthritis: sedentary behaviour in RA – a new research agenda. *Nat Rev Rheumatol*. 2016;12:698–700. doi:10.1038/nrrheum.2016.179
20. Metsios GS, Stavropoulos-Kalinoglou A, Panoulas VF, et al. Association of physical inactivity with increased cardiovascular risk in patients with rheumatoid arthritis. *Eur J Cardiovasc Prev Rehabil*. 2009;16:188–194. doi:10.1097/HJR.0b013e3283271ceb
21. Khoja SS, Almeida GJ, Chester Wasko M, Terhorst L, Piva SR. Association of light-intensity physical activity with lower cardiovascular disease risk burden in rheumatoid arthritis. *Arthritis Care Res*. 2016;68:424–431. doi:10.1002/acr.22711

22. Elkan A-C, Hakansson N, Frostegard J, et al. Low level of physical activity in women with rheumatoid arthritis is associated with cardiovascular risk factors but not with body fat mass – a cross sectional study. *BMC Musculoskelet Disord.* 2011;12:13. doi:10.1186/1471-2474-12-181
23. Sokka T, Häkkinen A, Kautiainen H, et al. Physical inactivity in patients with rheumatoid arthritis: data from twenty-one countries in a cross-sectional, international study. *Arthritis Rheum.* 2008;59:42–51. doi:10.1002/art.23255
24. Metsios GS, Stavropoulos-Kalinoglou A, Treharne GJ, et al. Disease activity and low physical activity associate with number of hospital admissions and length of hospitalisation in patients with rheumatoid arthritis. *Arthritis Res Ther.* 2011;13:R108. doi:10.1186/ar3390
25. Tourinho TF, Capp E, Brenol JC, Stein A. Physical activity prevents bone loss in premenopausal women with rheumatoid arthritis: a cohort study. *Rheumatol Int.* 2008;28:1001–1007. doi:10.1007/s00296-008-0554-3
26. Kievit W, Fransen J, Adang EMM, et al. Long-term effectiveness and safety of TNF-blocking agents in daily clinical practice: results from the Dutch rheumatoid arthritis monitoring register. *Rheumatology.* 2011;50:196–203. doi:10.1093/rheumatology/keq325
27. Augustsson J, Neovius M, Cullinane-Carli C, Eksborg S, van Vollenhoven RF. Patients with rheumatoid arthritis treated with tumour necrosis factor antagonists increase their participation in the workforce: potential for significant long-term indirect cost gains (data from a population-based registry). *Ann Rheum Dis.* 2010;69:126–131. doi:10.1136/ard.2009.108035
28. van Gestel AM, Haagsma CJ, van Riel PL. Validation of rheumatoid arthritis improvement criteria that include simplified joint counts. *Arthritis Rheum.* 1998;41:1845–1850. doi:10.1002/1529-0131(199810)41:10<1845::AID-ART17>3.0.CO;2-K
29. Matthews CE, Ainsworth BE, Thompson RW, Bassett DR. Sources of variance in daily physical activity levels as measured by an accelerometer. *Med Sci Sports Exerc.* 2002;34:1376–1381.
30. Atkin AJ, Gorely T, Clemes SA, et al. Methods of measurement in epidemiology: sedentary behaviour. *Int J Epidemiol.* 2012;41:1460–1471. doi:10.1093/ije/dys118
31. Freedson PS, Melanson E, Sirard J. Calibration of the computer science and applications, Inc. accelerometer. *Med Sci Sports Exerc.* 1998;30:777–781.
32. Berntzen B, Jukarainen S, Kataja M, et al. Physical activity, cardiorespiratory fitness, and metabolic outcomes in monozygotic twin pairs discordant for body mass index. *Scand J Med Sci Sports.* 2018;28:1048–1055. doi:10.1111/sms.12975
33. Yu C, Rouse PC, Veldhuijzen Van Zanten JJCS, et al. Subjective and objective levels of physical activity and their association with cardiorespiratory fitness in rheumatoid arthritis patients. *Arthritis Res Ther.* 2015;17:59. doi:10.1186/s13075-015-0584-7
34. Ewald B, Attia J, McElduff P. How many steps are enough? Dose-response curves for pedometer steps and multiple health markers in a community-based sample of older Australians. *J Phys Act Heal.* 2014;11:509–518. doi:10.1123/jpah.2012-0091
35. Thomson JL, Landry AS, Zoellner JM, et al. Several steps/day indicators predict changes in anthropometric outcomes: HUB city steps. *BMC Public Health.* 2012;12:983. doi:10.1186/1471-2458-12-983
36. Dwyer T, Ponsonby A-L, Ukoumunne OC, et al. Association of change in daily step count over five years with insulin sensitivity and adiposity: population based cohort study. *BMJ.* 2011;342:c7249. doi:10.1136/bmj.c7249
37. Pioreschi A, Hodkinson B, Tikly M, Mcveigh JA. Changes in physical activity measured by accelerometry following initiation of dmard therapy in rheumatoid arthritis. *Rheumatology.* 2014;53:923–926. doi:10.1093/rheumatology/ket457
38. Fenton SAM, Veldhuijzen van Zanten JJCS, Kitas GD, et al. Sedentary behaviour is associated with increased long-term cardiovascular risk in patients with rheumatoid arthritis independently of moderate-to-vigorous physical activity. *BMC Musculoskelet Disord.* 2017;18:131. doi:10.1186/s12891-017-1624-z
39. Legge A, Blanchard C, Hanly J. Physical activity and sedentary behavior in patients with systemic lupus erythematosus and rheumatoid arthritis. *Open Access Rheumatol.* 2017;9:191–200. doi:10.2147/OARRR.S148376
40. Clemes SA, O'Connell SE, Edwardson CL. Office workers' objectively measured sedentary behavior and physical activity during and outside working hours. *J Occup Environ Med.* 2014;56:298–303. doi:10.1097/JOM.0000000000000101
41. Thomsen T, Aadahl M, Beyer N, et al. The efficacy of motivational counselling and SMS reminders on daily sitting time in patients with rheumatoid arthritis: a randomised controlled trial. *Ann Rheum Dis.* 2017;76:1603–1606. doi:10.1136/annrheumdis-2016-210953
42. World Health Organization. *Global Recommendations on Physical Activity for Health.* Geneva, Switzerland: WHO Press; 2010.
43. Metsios GS, Stavropoulos-Kalinoglou A, Kitas GD. The role of exercise in the management of rheumatoid arthritis. *Expert Rev Clin Immunol.* 2015;11(10):1121–1130. doi:10.1586/17446-66X.2015.1067606
44. Verhoeven F, Tordi N, Prati C, Demougeot C, Mouglin F, Wendling D. Physical activity in patients with rheumatoid arthritis. *Joint Bone Spine.* 2016;83(3):265–270. doi:10.1016/j.jbspin.2015.10.002
45. Veldhuijzen van Zanten JJ, Rouse PC, Hale ED, et al. Perceived barriers, facilitators and benefits for regular physical activity and exercise in patients with rheumatoid arthritis: a review of the literature. *Sports Med.* 2015;45:1401–1412. doi:10.1007/s40279-015-0363-2
46. Li T, Wells G, Westhovens R, Emery P, Becker JC, Tugwell P. Improvements in participation in usual daily activities in patients with rheumatoid arthritis treated with abatacept. *Value Health.* 2011;14(2):361–370. doi:10.1016/j.jval.2010.10.008
47. Kiely PD. Biologic efficacy optimization – a step towards personalized medicine. *Rheumatology.* 2016;55:780–788. doi:10.1093/rheumatology/kev356
48. Keystone E, Landewé R, van Vollenhoven R, et al. Long-term safety and efficacy of certolizumab pegol in combination with methotrexate in the treatment of rheumatoid arthritis: 5-year results from the RAPID 1 trial and open-label extension. *Ann Rheum Dis.* 2014;73:2094–2100. doi:10.1136/annrheumdis-2014-205310
49. The Health and Social Care Information Centre. *Health Survey for England 2008 – Physical Activity and Fitness – Summary of Key Findings.* Craig R, Mindell J, Hirani V, editors. Leeds: The Health and Social Care Information Centre; 2009.
50. Varma VR, Dey D, Leroux A, et al. Re-evaluating the effect of age on physical activity over the lifespan. *Prev Med.* 2017;101:102–108. doi:10.1016/j.ypmed.2017.05.030

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