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Team Rehabilitation in Inflammatory Arthritis Benefits Functional Outcomes Along With Improved Body Composition Associated With Improved Cardiorespiratory Fitness

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ABSTRACT. ***Objective.*** We investigated the effect of team rehabilitation in inflammatory arthritis (IA) on body composition and physical function. Further, we examined whether body composition and physical function are associated with disability and cardiorespiratory fitness (CRF).

Methods. The participants were 149 patients (74% women) with chronic arthritis, a mean age of 53 (SD 13) years, and mean disease duration of 21 (SD 13) years. They participated in a 4-week team rehabilitation program and were evaluated at prerehabilitation, and at 3 and 12 months postrehabilitation. Body composition was assessed by bioelectrical impedance analysis and CRF by the Åstrand 6-minute cycle test. ANCOVA with Bonferroni correction and linear mixed models were applied.

Results. After 3 and 12 months, there were significant reductions in waist circumference and measures of fat, adjusted for age, sex, and baseline measures. The prevalence of adiposity and central obesity decreased after 12 months. Hand grip strength and timed sit-to-stand (TST) improved together with reduction in Health Assessment Questionnaire (HAQ) and increased VO_2max after 3 and 12 months. HAQ reduction over time was associated with prerehabilitation measures of lean mass of legs, hand grip strength, TST, and physical activity, and changes in hand grip strength, physical activity, and sedentary time, but not with changes of body composition. VO_2max improvement over time was associated with prerehabilitation BMI, waist circumference, measures of fat and lean mass, changes in BMI, waist circumference, and measures of fat.

Conclusion. In patients with IA, 4-week team rehabilitation benefited body composition, level of physical functioning, activity, and CRF for up to 12 months. Measures of physical function and activity were linked to HAQ over time, whereas body composition was linked to CRF.

Key Indexing Terms: arthritis, cardiovascular, exercise therapy

Altered body composition is a frequent finding in inflammatory arthritis (IA)[1] and is associated with the 2 major outcomes of the disease: disability and cardiovascular (CV) morbidity.[2,3] Systemic inflammatory pathways in IA promote protein degradation, leading to loss of lean mass and concomitant increase in fat mass (FM).[4] The therapeutic advances of recent years have improved disease outcomes, but many patients with IA still experience functional disability and body composition alterations, favoring increased FM deposition that can further affect body function.[5] Nonpharmaceutical interventions are still necessary and exercise has several additional benefits for health outcomes such as improved functional level, cardiorespiratory fitness (CRF), and reduced CV risk.[6,7,8,9] Over the longer term, exercise is believed to reduce inflammation through beneficial effects on body composition.[10] Physical functional level, body composition, and CRF are associated with cardiometabolic health.[11,12] CRF is a stronger predictor of cardiometabolic risk than physical activity level.[11,13]

Rehabilitation incorporated into routine clinical care of IA can promote maintenance of physical activity and long-lasting improvement of quality of life.[10,14,15] When addressing the benefits of interventions in IA, the focus is primarily on disease activity and level of impairment of physical functioning according to the generic Health Assessment Questionnaire (HAQ).[16] Far less is known regarding the effects of interventions on body composition and CRF. Further, there are limited insights currently on which components of body composition

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contribute to functional impairment and CRF in arthritis, as well as which objective measures of physical function could explain these outcomes.

This study aimed to evaluate the effect of a team rehabilitation program in IA on body composition, measures of physical function, and CRF. We further hypothesized that components of body composition and physical tests could contribute differentially to these outcomes.

METHODS

Patients. The patients originated from the observational cohort of 161 consecutive patients with IA, for whom outpatient physiotherapy had been insufficient and who had a need for multidisciplinary rehabilitation according to their rheumatologist. After application, they participated in a team rehabilitation program for 4 weeks and were followed for 1 year, as previously described.[15] The team rehabilitation was offered at 2 rehabilitation establishments in Spain (Vintersol, Tenerife, and Centro Forestal Sueco, Marbella) with similar interventions and rehabilitation teams, comprising physicians, nurses, physiotherapists, and occupational therapists. The interventions were individualized depending on the baseline ability and functional limitations. The training was performed individually and in groups, with at least 3 scheduled activities each day, a minimum of 45 minutes each, 5 days per week, and consisted of dynamic and static exercises on land and in swimming pools. The intensity and length of each item varied because of the individually tailored program. Additionally, patients were given lectures on disease-specific themes and they were encouraged to participate in lifelong regular exercise.

The 149 patients included in this analysis were all those with arthritis, who were according to the current procedure allocated for team rehabilitation, and had available data on HAQ and CRF. There was no difference in key patient characteristics between patients who were included or excluded.

Rehabilitation in a warm climate is an established supplementary therapeutic option for patients with IA in Stockholm, Sweden, and is paid for by the healthcare system. Since assessments were carried out in accordance with usual care and the Swedish National Rheumatology Quality Register and as a part of recording outcomes of routine care, no formal approval from an ethics committee was requested. All patients signed informed consent for the rehabilitation follow-up and data monitoring in the Swedish National Rheumatology Quality Register.

Data collection. The patients completed assessments prerehabilitation, and at 3 and 12 months postrehabilitation. Information on diagnosis, disease characteristics, and comorbidities (hypertension, diabetes mellitus, chronic lung disease, CV disease, cerebrovascular disease, kidney disease, and osteoporosis) was extracted from the records. Smoking was defined as ever or never smoked.

Anthropometry and body composition assessments. BMI was calculated from weight/height^2 (kg/m^2). Obesity was defined as BMI values > 30 kg/m^2.[17] Waist circumference (cm) was measured in a standing position midway between the iliac crest and the lower rib margin. Central obesity was defined as waist circumference ≥ 94 cm in men and ≥ 80 cm in women.[18]

Bioelectrical impedance analysis was performed with the BC-418 8-contact electrode Segmental Body Composition Analyzer (Tanita Corp.) to measure total body composition and segmental parts including arms, legs, and the trunk area. The measurements were carried out according to the manufacturer's manual and performed by the same operator.

Fat-free mass (FFM), a proxy for muscle mass, and FM were expressed in kg; FM was also expressed as a percentage of total mass. Because FFM and FM are dependent on height, the FFM index (kg/m^2) and FM index (FMI; kg/m^2) were calculated. Complementary to the classical expression of obesity by BMI, adiposity based on relative excess of body fat was defined as FMI values > 90th percentile of the reference values of the European population of a given age and sex.[19]

Physical function assessments. Hand grip strength was measured with the electronic hand dynamometer Grippit (Grippit AB Detektor). The patient pressed the handle of the instrument for 10 seconds with each hand. Measurements of the peak and average values (in Nm) were performed in each hand alternating with a 2-minute break between measurements.[20]

The timed sit-to-stand (TST) test recorded the time in seconds needed to stand up from a sitting position and sit down on a standard chair (45 cm) 10 times as quickly as possible without using the hands and keeping both feet on the floor.[21]

Activity limitation and aerobic fitness. The Swedish version of the HAQ[22] was self-administered to measure the difficulty of coping with activities of daily living, such as dressing, walking, arising, reaching, eating grip, hygiene, and outside activity, scored from 0 to 3 (0 = able to perform without difficulty; 3 = unable to perform).

CRF was assessed by the submaximal Åstrand cycle ergometer test.[23] The whole-body maximal oxygen uptake (VO_2max; mL/kg/min) was estimated using the Åstrand-Rhyming nomogram based on age, sex, mechanical load, and mean heart rate at steady state, and classified into the fitness categories of low, moderate, average, good, and very good aerobic capacity.[24]

Physical activity. Physical activity level was measured by the self-reported International Physical Activity Questionnaire–Short Form (IPAQ-SF),[25] consisting of 7 questions about the time spent in vigorous- and moderate-intensity activities, walking, and sedentary activity during the past week. Total weekly overall physical activity was estimated by weighting time spent in each activity intensity with its estimated metabolic equivalent of task (MET; min/week). An IPAQ-SF score < 600 MET-min/week assigns to low-intensity activity, 600 to 1500 MET-min/week to moderate-, and > 1500 MET-min/week to vigorous-intensity physical activity.

The sedentary time (h/day) in a seated or reclining posture throughout the day, which refers to a low energy expenditure (i.e., a lack of moderate-to-vigorous physical activity), was self-reported.

Statistical methods. Descriptive statistics are reported as mean (SD) for continuous variables and percentages for categorical variables. ANCOVA was used to analyze the change in the measures from baseline to postrehabilitation follow-up. When assumption of sphericity was violated according to Mauchly's test of sphericity, Greenhouse–Geisser correction was applied. The covariates of age, sex, and baseline measures were included in the final models. Bonferroni correction of *P* values was applied for multiple comparisons. The Wilcoxon signed-rank test was used for pairwise comparisons of categorical values at follow-up.

Association between body composition, physical function, and activity, and the course of HAQ and CRF for 12 months postrehabilitation was determined with linear mixed models with 3 measurements of mean HAQ and CRF over time as response, and patient characteristic measures and time as explaining variables. The interaction term by time of assessment visit was included in the models to estimate rates of progression of the outcomes over time in association with the change of measures between prerecruitment and at 3 and 12 months. Multivariate models were adjusted for age, sex, and variables of patient characteristics with $P < 0.1$ in unadjusted analyses, and level of statistical significance was set at $\alpha < 0.05$.

RESULTS

The analysis included 149 patients, 74% women, with rheumatoid arthritis (RA), psoriatic arthritis, spondyloarthritis, and juvenile idiopathic arthritis, with a mean age of 53 (SD 13) years, a mean (SD) disease duration of 21 (SD 13) years, and a mean HAQ of 1.1 (SD 0.6). All patients followed their standard care antirheumatic treatment with synthetic and/or biologic disease-modifying antirheumatic drugs (DMARDs; Table 1).

Table 1. Characteristics of the 149 patients with chronic inflammatory arthritis at inclusion.

	n = 149
Diagnosis, n (%)	
RA	66 (44)
Psoriatic arthritis	31 (21)
Spondyloarthritis	30 (20)
Juvenile idiopathic arthritis	22 (15)
Age, yrs	53.4 (13.3)
Women, %	73.8
Disease duration, yrs	21.3 (13.4)
Seropositive[a], %	80.3
Smoking ever, %	47.0
Comorbidity, %	52.3
DAS28[b]	4.08 (1.31)
Current treatment, %	
Synthetic DMARD	51.0
Biologic DMARD	65.8
Glucocorticoids	21.8

Values are means (SD) and percentages, unless otherwise indicated. [a] Seropositive defined as RF- and/or ACPA-positive. [b] Within patients with RA. ACPA: anticitrullinated protein antibodies; DAS28: Disease Activity Score in 28 joints; DMARD: disease-modifying antirheumatic drug; RA: rheumatoid arthritis; RF: rheumatoid factor.

Measures over time of body composition, physical function, activity limitation, and CRF. There was a statistically significant reduction in waist circumference, FM, body fat, and FMI after 3 and 12 months, whereas the lean mass of total body, arms, and legs did not change significantly (Table 2). The frequency of obesity defined by BMI ≥ 30 kg/m^2 did not change significantly. However, the frequency of adiposity defined by excess body fat (FMI ≥ 90th of the reference values) decreased from 40% to 35% (P = 0.04), and the central obesity decreased from 70% to 61% (P = 0.01; Figure 1). Hand grip strength, TST, and physical activity assessed by IPAQ-SF improved after 3 and 12 months, together with a significant reduction in sedentary time after 3 months (Table 2).

During the study, HAQ and VO_2max improved significantly, adjusted for age, sex, and a baseline measure. Within the groups of CRF, the number of patients categorized as having a weak CRF decreased from 36% to 8%, whereas the number of patients having a good or very good CRF increased from 6% to 38% (P < 0.001) for overall change between the groups (Table 2).

Association of body composition and physical function with the outcome of HAQ and CRF over 1-year postrehabilitation. HAQ over time was higher in older patients, women, and in the presence of comorbidities. VO_2max over time was better in younger patients, never smokers, and those without comorbidities (Table 3).

Table 2. Measures over time of body composition, physical ability, and physical limitations.

	At Inclusion	At 3 Months	At 12 Months	P	P^1	P^2
BMI, kg/m^2	26.99 (26.99–26.99)	26.70 (26.43–26.97)	26.61 (26.17–27.06)	0.20	0.12	0.30
Waist circumference, cm	92.52 (92.52–92.52)	89.38 (88.56–90.21)	88.84 (87.59–90.08)	0.001	< 0.001	< 0.001
Fat mass, kg	26.66 (26.66–26.66)	25.54 (24.94–26.15)	25.23 (24.32–26.14)	0.58	0.001	0.007
Body fat, %	34.04 (34.04–34.04)	32.95 (32.40–33.50)	32.77 (31.98–33.56)	0.61	< 0.001	0.006
Fat mass index, kg/m^2	9.49 (9.49–9.49)	9.09 (8.86–9.31)	8.96 (8.63–9.30)	0.74	0.002	0.007
Lean mass (fat-free mass), kg	49.90 (49.90–49.90)	49.94 (49.52–50.36)	50.0 (49.49–50.43)	0.02	0.90	0.90
Fat-free mass index, kg/m^2	17.51 (17.51–17.51)	17.50 (17.36–17.64)	17.45 (17.31–17.60)	0.10	0.90	0.90
Arms, lean mass, kg	5.31 (5.31–5.31)	5.38 (5.28–5.48)	5.37 (5.28–5.47)	0.002	0.632	0.63
Legs, lean mass, kg	16.70 (16.70–16.70)	16.64 (16.44–16.85)	16.60 (16.44–16.77)	0.10	0.90	0.72
Grip strength (right and left, mean), Nm	164.6 (164.6–164.6)	220.2 (205.7–234.6)	211.5 (196.5–226.5)	0.01	< 0.001	< 0.001
Grip strength max, Nm	204.4 (204.4–204.4)	253.4 (233.9–272.9)	246.8 (227.4–266.2)	0.40	< 0.001	< 0.001
Timed sit-to-stand test, sec	26.98 (26.98–26.98)	18.89 (17.74–20.03)	19.84 (18.49–21.19)	0.01	< 0.001	< 0.001
HAQ	1.08 (1.08–1.08)	0.84 (0.77–0.90)	0.96 (0.90–1.02)	0.02	< 0.001	0.001
CRF (VO_2max), mL/kg/min	27.50 (27.50–27.50)	32.70 (30.75–34.64)	34.87 (33.03–36.72)	0.001	< 0.001	< 0.001
Weak CRF, %	36	12	8	< 0.001		
Moderate CRF, %	34	33	27			
Average CRF, %	24	24	27			
Good CRF, %	4	19	16			
Very good CRF, %	2	12	22			
Physical activity volume, MET-min/week, %	1915 (1915–1915)	3564 (2957–4171)	3349 (2685–4012)	0.29	< 0.001	< 0.001
Low activity (< 600)	26	10	13	< 0.001		
Moderate activity (600 to < 1500)	32	21	26			
Vigorous activity (> 1500)	42	69	61			
Sedentary time, h/d	6.21 (6.21–6.21)	5.32 (4.76–5.88)	5.66 (5.07–6.24)	0.003	0.007	0.19

Presented are estimated means (95% CI) with adjustment for age, sex, and the inclusion measure. P value of overall within-subject variations, and P values of pairwise comparisons of within-subject effects between inclusion and 3 months[1], and between inclusion and 12 months[2], with Bonferroni adjustment. CRF: cardiorespiratory fitness; HAQ: Health Assessment Questionnaire; MET: metabolic equivalent of task; VO_2max: maximal oxygen uptake.

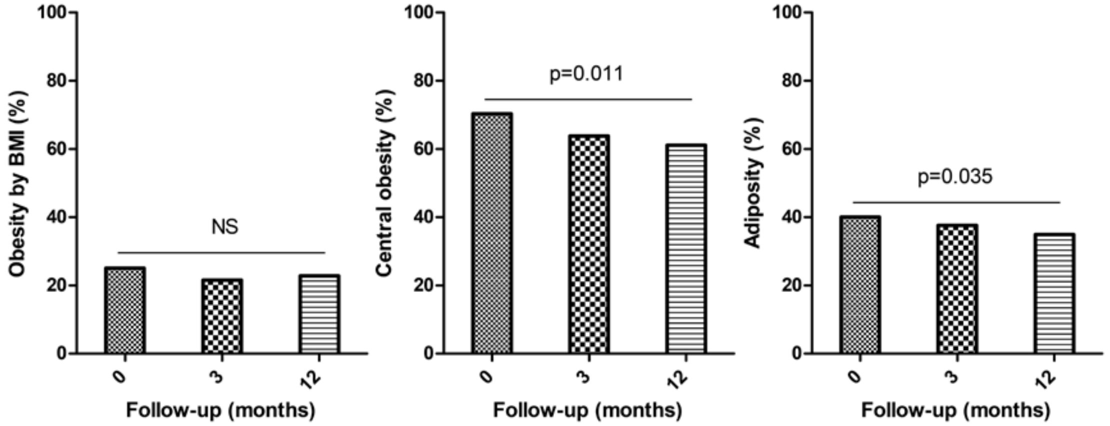

Figure 1. Frequency of obesity by BMI, central obesity, and adiposity according to FMI in patients with chronic inflammatory arthritis prerehabilitation and at 3 to 12 months' follow-up. Obesity if BMI ≥ 30 kg/m^2; central obesity if waist circumference ≥ 94 cm in men or ≥ 80 cm in women; and adiposity if FMI > 90th percentile of the reference population. Statistical significance was determined using Wilcoxon signed-rank test for pairwise comparisons. FMI: fat mass index.

Table 3. Association of patient characteristics at inclusion with HAQ and CRF over 1-year postrehabilitation.

	HAQ				CRF			
	Unadjusted Models β Coefficient (95% CI)	*P*	Multivariate Models β Coefficient (95% CI)	*P*	Unadjusted Models β Coefficient (95% CI)	*P*	Multivariate Models β Coefficient (95% CI)	*P*
Age	0.009 (0.003–0.016)	0.007	0.007 (0.001–0.014)	0.049	−0.210 (−0.307 to −0.114)	< 0.001	−0.165 (−0.271 to −0.060)	0.002
Sex (men vs women)	−0.257 (−0.453 to −0.062)	0.01	−0.262 (0.454 to −0.070)	0.008	1.728 (−1.250 to 4.705)	0.25	–	
Smoking (ever vs never)	−0.130 (−0.305 to 0.045)	0.15	–		−3.934 (−6.509 to −1.370)	0.003	−2.370 (−5.017 to 0.276)	0.08
Comorbidity	0.239 (0.067–0.411)	0.007	0.186 (0.001–0.372)	0.048	−4.224 (−6.776 to −1.671)	0.001	−2.484 (−5.184 to 0.216)	0.07
Disease duration	0.004 (−0.003 to 0.010)	0.27	–		−0.077 (−0.179 to 0.024)	0.14	–	–
GC use	0.201 (−0.019 to 0.420)	0.07	0.138 (−0.074 to 0.350)	0.20	−0.504 (−3.855 to 2.846)	0.77	–	–
DAS28[a]	0.109 (0.033–0.184)	0.005	0.071 (−0.003 to 0.145)	0.06	0.327 (−0.780 to 1.433)	0.56	–	–

Presented results of β coefficients with 95% CI are based on mixed linear regression models. Multivariate models were adjusted for age, sex, comorbidity, and GC use for the outcome of HAQ; and for age, sex, comorbidity, and smoking for the outcome of CRF. [a] Within patients with rheumatoid arthritis. CRF: cardiorespiratory fitness; DAS28: Disease Activity Score in 28 joints; GC: glucocorticoid; HAQ: Health Assessment Questionnaire.

The course of HAQ postrehabilitation. The association between body composition, physical function, and the course of HAQ and CRF throughout the study are presented in Table 4.

Higher HAQ over 1 year in unadjusted models was associated with prerehabilitation measures of lower lean body mass, FFM index, lean mass of arms and legs, higher body fat, lower hand grip strength, longer TST, and lower IPAQ-SF. In multivariate analyses adjusted for age, sex, comorbidities, and use of glucocorticoids, the association between HAQ and prerehabilitation measures of lean mass of legs, hand grip strength, TST, and IPAQ-SF was confirmed.

When analyzing the effect of changes in body composition and physical function throughout the observation period on the outcome of HAQ, HAQ progression was independently associated with change in hand grip strength and IPAQ-SF after 12 months and change in sedentary time after 3 months, but not with changes in measures of body composition and CRF.

The course of CRF postrehabilitation. Better VO_2max over time was associated with prerehabilitation measures of lower BMI, waist circumference, FM and body fat, FMI, higher lean mass, FFM, lean mass of arms and legs, and independent of age, sex, comorbidity, and smoking.

As to the effect of changes in body composition during the study, a higher rate of VO_2max progression was independently associated with change after 3 and/or 12 months and a higher reduction in BMI, waist circumference, FM, body fat, and FMI, as well as with improvement in hand grip strength after 3 months. There were no significant associations between VO_2max and changes in TST and IPAQ-SF.

DISCUSSION

In this study we observed favorable changes in measures of body composition, improved levels of physical function and physical activity, and increased CRF after a 4-week team rehabilitation. These benefits were measurable and were maintained through the observation period of 1 year. Different aspects of body composition and physical function were associated with levels of disability measured by HAQ and with CRF. The level of HAQ was mostly associated with prerehabilitation measures

Table 4. Association of body composition and physical ability with HAQ and CRF over 1-year postrehabilitation.

	HAQ				CRF			
	Unadjusted Models β Coefficient (95% CI)	P	Multivariate Models β Coefficient (95% CI)	P	Unadjusted Models β Coefficient (95% CI)	P	Multivariate Models β Coefficient (95% CI)	P
BMI	0.007 (−0.010 to 0.024)	0.397	–		−0.817 (−1.040 to −0.593)	< 0.001	−0.734 (−0.956 to −0.511)	< 0.001
Change 0–12	NS				0.342 (0.074–0.610)	0.01	0.338 (0.071 to 0.606)	0.01
Waist circumference	−0.002 (−0.009 to 0.005)	0.592	–		−0.229 (−0.313 to −0.145)	< 0.001	−0.225 (−0.321 to −0.129)	< 0.001
Change 0–12	NS				0.183 (0.057–0.308)	0.005	0.179 (0.054 to 0.304)	0.006
Fat mass	0.003 (−0.007 to 0.012)	0.583	–		−0.356 (−0.465 to −0.247)	< 0.001	−0.372 (−0.484 to −0.261)	< 0.001
Change 0–3	NS				0.327 (0.039–0.616)	0.03	0.323 (0.034 to 0.611)	0.03
Change 0–12	NS				0.284 (0.127–0.442)	0.001	0.285 (0.128 to 0.443)	0.001
Body fat, %	0.012 (0.001–0.023)	0.039	0.001 (−0.013 to 0.014)	0.922	−0.331 (−0.467 to −0.195)	< 0.001	−0.555 (−0.717 to −0.393)	< 0.001
Change 0–12	−0.001 (−0.009 to 0.008)	0.943	–		0.307 (0.091–0.522)	0.006	0.307 (0.092 to 0.522)	0.006
Fat mass index	0.012 (−0.014 to 0.039)	0.346	–		−0.906 (−1.213 to −0.599)	< 0.001	−1.042 (−1.368 to −0.716)	< 0.001
Change 0–3	NS				0.849 (0.068–1.639)	0.03	0.833 (0.053 to 1.613)	0.04
Change 0–12	NS				0.759 (0.323–1.195)	0.001	0.761 (0.325 to 1.196)	0.001
Lean mass	−0.015 (−0.025 to −0.006)	0.002	−0.014 (−0.029 to 0.001)	0.062	0.132 (0.001–0.263)	0.048	0.276 (0.078 to 0.476)	0.007
Fat-free mass index	−0.051 (−0.091 to −0.011)	0.012	−0.034 (−0.086 to 0.018)	0.193	0.707 (0.173–1.240)	0.01	0.991 (0.311 to 1.672)	0.005
Arms, lean mass	−0.096 (−0.162 to −0.032)	0.004	−0.086 (−0.187 to 0.014)	0.091	0.969 (−0.073 to 1.866)	0.03	1.804 (0.437 to 3.171)	0.01
Legs, lean mass	−0.047 (−0.074 to −0.020)	0.001	−0.042 (−0.084 to −0.001)	0.047	0.394 (0.014–0.773)	0.04	0.888 (0.324 to 1.451)	0.002
Grip strength, mean, per 10 Nm	−0.016 (−0.026 to −0.007)	0.001	−0.021 (−0.034 to −0.009)	0.001	0.005 (−0.013 to 0.022)	0.60	–	
Change 3–0	NS		–		0.178 (0.009–0.348)	0.04	0.177 (0.008 to 0.346)	0.04
Change 12–0	−0.007 (−0.013 to 0)	0.05	−0.009 (−0.016 to −0.003)	0.008	0.098 (−0.059 to 0.255)	0.22	–	
Grip strength, max, per 10 Nm	−0.016 (−0.028 to −0.003)	0.01	−0.013 (−0.027 to 0.001)	0.07	0.018 (−0.212 to 0.248)	0.88	–	
Change 3–0	−0.013 (−0.025 to 0)	0.049	−0.012 (−0.025 to 0)	0.05	0.322 (−0.044 to 0.689)	0.08	0.339 (−0.027 to 0.705)	0.07
Change 12–0	−0.012 (−0.023 to −0.001)	0.04	−0.012 (−0.023 to −0.001)	0.04	0.343 (−0.037 to 0.724)	0.08	0.345 (−0.034 to 0.724)	0.07
Timed sit-to-stand test	0.016 (0.010 to 0.022)	< 0.001	0.013 (0.006–0.020)	< 0.001	−0.148 (−0.251 to −0.044)	0.005	−0.099 (−0.201 to 0.004)	0.06
HAQ	N/A		N/A		−0.625 (−3.056 to 1.806)	0.61	–	
CRF	−0.008 (−0.020 to 0.004)	0.21	–		N/A		N/A	
Physical activity volume per 100 MET-min/week	−0.007 (−0.011 to −0.003)	0.001	−0.005 (−0.009 to −0.001)	0.008	0.009 (−0.050 to 0.068)	0.77	–	
Change 12–0	−0.001 (−0.002 to −0.001)	0.02	−0.001 (−0.002 to −0.001)	0.03	NS			
Sedentary time	0.016 (−0.019 to 0.052)	0.37	–		0.071 (−0.449 to 0.591)	0.79	–	
Change 0–3	−0.016 (−0.027 to −0.004)	0.008	−0.016 (−0.027 to −0.004)	0.009	−0.068 (−0.418 to 0.281)	0.70	–	

Presented are associations between baseline measures and their changes between prerecruitment and at 3 and 12 months. Results are β coefficients (95% CI) and are based on mixed linear regression models. Multivariate models were adjusted for age, sex, comorbidity, and glucocorticoid use for the outcome of HAQ, and for age, sex, comorbidity, and smoking for the outcome of cardiorespiratory fitness. CRF: cardiorespiratory fitness; HAQ: Health Assessment Questionnaire; MET: Metabolic Equivalent of Task; N/A: not applicable; NS: nonsignificant.

and changes in muscle strength and physical activity, but not with body composition, whereas CRF was associated with prerehabilitation measures and changes in body composition, primarily measures of body fat.

The implications of the observations are several-fold. First, the results provide further support for the beneficial effects of physical exercise in IA, over and above the effects on physical functioning and HAQ.[8] We observed improved body composition with decreased waist circumference, measures of body fat, adiposity, and central obesity and improved CRF. These beneficial changes were maintained at the 12-month follow-up, indicating that the effect of rehabilitation could be maintained even with less training effort after rehabilitation. Our patients had rather long disease duration and > 60% of the patients were treated with biologics, emphasizing a need for rehabilitation even in times of modern pharmacological treatment. As expected, the improvements in HAQ and CRF were dependent on age, sex, and presence of comorbidities.

Second, our observations indicate that measures of body composition are related more to CRF than to HAQ. Whereas monitoring HAQ as an important outcome measure in IA is well recognized, assessments of CRF and body composition are not included in the core set evaluation of health-related function. Higher HAQ is predictive of mortality, especially due to CV disease, in aging and in arthritis.[12,26,27] Low CRF has also been reported to associate with all-cause and disease-specific mortality, and CV mortality and morbidity.[28] CRF is not only a potentially stronger predictor of mortality than established risk factors such as smoking, hypertension, high cholesterol, and type 2 diabetes mellitus, but its addition to traditional risk factors significantly improves the reclassification of risk for adverse outcomes.[13] Reducing CV risk factors through improved

CRF could be of great importance as a supplement to advances in treatments of arthritis.

A surprising finding was that after the 4-week rehabilitation, patients improved their VO_2max at a group level by 26%. The increase in VO_2max was higher than earlier reported after high-intensity training in chronic arthritis.[9,29,30] The prerecruitment VO_2max in our patients was lower than that in 2 cohorts of Swedish adults (mean 27.5 vs 33–36 mL O_2/min/kg),[31] indicating recruitment of patients with a sedentary lifestyle. Although most of the patients (70%) had low aerobic capacity prerecruitment, 65% of patients reached at least normal aerobic capacity after 1 year. Previous studies have indicated that only 2 to 4 minutes of high-intensity training performed 3 times per week might be adequate to improve VO_2max by 10% and reduce total body fat after 10 to 12 weeks.[32,33] The longstanding effect following team-based rehabilitation has previously been reported in patients with IA, and implies that, in addition to the short-term benefits, the benefits of exercise intervention could be maintained when patients have changed to a more physically active lifestyle.[14]

The observed reductions in FM, body fat, and FMI were more pronounced than reduction in BMI. Importantly, despite only 25% of patients in this study being classified as obese with BMI ≥ 30 kg/m^2, as many as 70% of patients had central obesity and 40% had adiposity with FMI values > 90th percentile of the reference population. This confirms the shortcomings of BMI definitions to detect an altered body composition characteristic for patients with RA.[34] The observation of association between higher VO_2max over time and fat reduction is in line with earlier reports on the inverse association between these measures.[9,30,35] Improvement of CRF and reductions in central obesity and adiposity highlight the need for physical activity in patients with arthritis.

While body fat decreased, measures of lean mass were unchanged during follow-up, in contrast with some reports of training,[36,37,38] but in line with another report.[39] The low muscle mass in our patients had likely been present for a long time and could not be restored by exercise. Neither DMARDs nor anti–tumor necrosis factor (TNF)-α therapy has been effective in increasing muscle mass,[40,41,42] even though inflammatory cytokines lead to wasting of lean mass.[43]

In patients with established RA, significant muscle loss has been observed in approximately 67%,[4] but is rarely diagnosed because of coincident increase in FM (i.e., rheumatoid cachexia).[44] In our study, lean mass and measures of muscle strength at baseline were inversely associated with the HAQ scores. This is in line with the reported negative association between appendicular lean mass and HAQ scores in a previous study.[2] However, in that study muscle strength was not assessed, which is why it could not be determined if the inverse association was dependent on low muscle strength.

There is no obvious explanation for the mechanisms by which muscle strength can increase without change in volume of lean mass, as observed here. One possibility might be reduction of accumulation of intramuscular fat, which has been observed in patients with arthritis and has been associated with poor physical function.[45,46,47] Fat accumulation inside and around the muscle could interfere with normal muscle metabolic and contractile functions.[48] In patients with RA, intramuscular fat accumulation associates with low lean mass, greater total and visceral adiposity, and greater disability, which supports a causal relationship between muscle density and physical function.[49] The increase in muscle strength observed in our patients could partially depend on the reduction of intramuscular fat due to reduced adiposity.

Interestingly, the IPAQ-SF was inversely associated with HAQ over time, but not with CRF. This seemingly contrasting result could have several explanations. The reported increase in physical activity was probably not sufficient for improvement of CRF. Further, the IPAQ-SF may overestimate activity levels, and may underestimate deficits in objectively measured physical function. Yet, the patients reported an increase of physical activity volume and reduction in sedentary time, which were inversely associated with a reduction in HAQ over 1 year.

It has been long debated whether "fitness" or "fatness" is the most important determinant of health status. If the same factors that promote body fat are related to CRF, this common origin would be reflected in the association between these measures and in their concurrent association with health outcomes. Indeed, our findings suggest a relationship between CRF and body fat stores. Thus, interventions reducing excess FM could improve CRF. Since excess FM and central obesity in arthritis are thought to be driven by inflammation, it would be anticipated that control of disease activity would benefit body composition and physical function. However, tight control of disease activity and anti–TNF-α therapy have been unsuccessful in reversing muscle loss in early and established RA.[41,42] The findings of this study are thus of importance because they support the need for physical activity even in patients responsive to pharmacological therapy.[50]

The health economic effect of team rehabilitation has not yet been clearly defined, mainly due to its complex interventions, and should be studied further. Cost effectiveness of the short-term, high-intensity program such as a warm climate comprehensive rehabilitation stimulating continued regular exercise, would be more likely preferable from the societal perspective than the long-term exercise classes.

Strengths of this study are the standardized assessments, objective outcome measures, and patient-reported outcomes and extension of observation for 12 months. We recognize the limitation of such a small sample size, which may have precluded detection of some effects. Although statistically significant effects were found for several outcomes, the effect size was moderate; hence, the clinical relevance should be interpreted with caution. The presence of comorbidities was not simplified as an index because each comorbidity could affect the studied outcomes.

We recognize the lack of a control group, but a study with equivalent experimental and control groups was not feasible. The rehabilitation abroad presented here was paid for by the healthcare system in Sweden and is offered to the patients who have insufficient results with usual outpatient physiotherapy in Sweden. In our opinion, it would be unethical to randomize some of these patients to a nonrehabilitation group. Systematic bias would have been introduced when using historical or nonrandomized concurrent controls. However, the lack of randomization facilitated recruitment of a large group of patients, thus increasing the generalizability of the results.

The principal disadvantage of the observational design is the potential bias from unmeasured confounding, which has been counteracted through the enrollment of consecutive eligible patients in this study and prospective detailed data collection with sufficiently long follow-up to estimate temporal changes. To minimize the possibility that the observed effects may reflect a contemporaneous phenomenon (i.e., regression to the mean), the baseline measures and changes over time with postintervention comparisons were considered in the analyses. However, it should be kept in mind that patients willing to participate in a rehabilitation program abroad might be more motivated with regard to physical activity and exercise, as well as more prone to lifestyle changes than nonparticipants. It is important to note that the results do not comment on each specific arthritis disease state.

In conclusion, team rehabilitation in patients with IA decreases activity limitations, mainly associated with an increase in muscle strength and physical activity. Team rehabilitation also increases CRF, associated with a reduction in measures of fat and adiposity. These effects could potentially lead to reduced cardiometabolic risk. Measures of CRF and elements of body composition could be valuable in studies of outcomes in IA.

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