

ORIGINAL REPORT

A FOUR-WEEK TEAM-REHABILITATION PROGRAMME IN A WARM CLIMATE DECREASES DISABILITY AND IMPROVES HEALTH AND BODY FUNCTION FOR UP TO ONE YEAR: A PROSPECTIVE STUDY IN SWEDISH PATIENTS WITH INFLAMMATORY JOINT DISEASES

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Objective: In the era of biologics, we evaluated the short- and long-term effects of team-rehabilitation in a warm climate in patients with arthritis and an inadequate response to physiotherapy in Sweden.

Methods: A total of 161 patients with peripheral arthritis and spondyloarthritis, 63% treated with biologics, followed team-rehabilitation for a period of 4 weeks. The outcomes assessed pre- and post-rehabilitation and after 3 and 12 months covered the Health Assessment Questionnaire (HAQ), Bath Ankylosing Spondylitis Functional Index (BASFI), EuroQoL 5-Dimensions (EQ-5D), general health (VAS-GH), pain (VAS-pain) and the International Physical Activity Questionnaire.

Results: HAQ, VAS-GH and VAS-pain improved significantly from pre-rehabilitation to all follow-up time-points, and BASFI and EQ-5D up to 3 months. In patients treated with biologics, the results were similar. At 3 and 12 months the proportions of patients reporting improvement above the minimal clinically important difference were HAQ 62% and 35%, BASFI 73% and 61%, EQ-5D 47% and 39%, VAS-GH 68% and 52%, and VAS-pain 68% and 51%, respectively. Physical activity increased significantly from pre-rehabilitation to 12 months and this increase correlated with an improvement in EQ-5D ($r=0.20$, $p=0.040$).

Conclusion: Team-rehabilitation in a warm climate resulted in clinically meaningful improvements in body function, activities and well-being, and promoted physical activity for up to one year.

Key words: rehabilitation; patient outcome assessment; arthritis; team-rehabilitation; rheumatoid arthritis; spondyloarthritis; patient-reported outcomes; physical activity.

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INTRODUCTION

Inflammatory rheumatic joint diseases have long been associated with disability and poor health. However, the introduction

of early and aggressive treatment regimens, together with access to modern biologic agents, has diminished patients' disability, and health status has improved at a group level (1). The need for comprehensive team-rehabilitation, which has a long tradition in Europe, has therefore been questioned as a part of modern therapy.

In the 2000s a substantial proportion of the rheumatoid arthritis (RA) population still reports lower physical activity than is recommended for public health (2–4). This is a concern, as regular physical activity, besides having a positive impact on activity limitation and wellbeing, could also have benefits for reported overweight (5) and cardiovascular morbidity (6–8). Thus, exercise and physical therapy are essential components of treatment.

Comprehensive team-rehabilitation, aimed at improving physical and psychosocial functioning, may still play an important role in the care of patients with chronic inflammatory joint disorders. As team-rehabilitation is a complex intervention, it is difficult to perform controlled studies; hence, only a few randomized studies exist. To complement randomized controlled studies, observational studies have been requested to evaluate the effects of multidisciplinary rehabilitation programmes in patients with chronic inflammatory arthritis (9).

For many years, patients with inflammatory joint diseases in Sweden and Norway have been offered a 4-week team-rehabilitation in a sub-tropical climate, in the Mediterranean area with its warm and stable climatic conditions. Most of the earlier evaluations of effects of these rehabilitation programmes are from periods before the widespread use of biologics, and have heterogeneous study designs, interventions and outcomes; thus a concise description of the effects is not feasible (10–13). Furthermore, the long-term effects have not been studied, except for patients with fibromyalgia (14).

We questioned whether a structured holistic rehabilitation programme is still important for current patients and whether it benefits functional ability and quality of life. The aim of the present prospective 1-year study was to assess the short- and long-term efficacy of comprehensive team-rehabilitation in a warm climate provided to patients with inflammatory joint diseases. The primary endpoints were change in outcomes measuring activity and participation (International Classification of Functioning, Disability and Health). We also assessed whether the rehabilitation programme resulted in change in

body function and physical activity, and analysed the associations of reported responses and change in physical activity.

METHODS

Study design

This is an open longitudinal observational study, into which patients were recruited from the applicants by their physicians, mostly a rheumatologist, to 4-week team-rehabilitation in a sub-tropical climate and followed for 1 year.

Patients

Patients were eligible if they had a chronic inflammatory arthritis, such as RA, juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA) and spondyloarthritis (SpA) diagnosed by rheumatologist, were between 18 and 80 years of age, had a documented clear clinical need for team-rehabilitation and for whom outpatient physiotherapy was not sufficient. This decision was made by the patient together with the physician and, most often, also the physiotherapist. Exclusion criteria included severe handicap that made evaluation assessments impossible and difficulties in answering questionnaires in written Swedish. Overall, 167 consecutive outpatients were included from January 2012 until June 2013, of whom 161 were evaluated (Fig. 1).

All patients signed informed consent for the rehabilitation follow-up, and the study was performed in compliance with the Declaration of Helsinki. Since assessments by the study protocol were carried out in accordance with usual care and the Swedish National Rheumatology Quality Register, no formal approval from the ethics committee was requested.

Intervention rehabilitation programme in a warm climate

The team-rehabilitation was offered at establishments used for rehabilitation purposes: Vintersol, Tenerife (54 patients), and Centro Forestal Sueco, Marbella (107 patients), with similar rehabilitation teams and interventions. These settings combined in-patient and day-patient care, with an emphasis on day-patient care. The patients had all-day access

to hotel services and also, when needed, to medical services. The patients had free time when they were not scheduled for the training programme. The rehabilitation team comprised physicians, nurses, physiotherapists and occupational therapists.

On arrival at the rehabilitation centre, each patient was provided with an individual rehabilitation plan based on individual physical functional (dis)ability and limitations. The rehabilitation programme aimed at reducing pain, improving muscular strength, joint mobility, endurance and aerobic capacity and thereby at decreasing functional limitations and improving general well-being. Training was performed individually and in groups, with at least 3 scheduled activities each day, with a minimum of 45 min each, 5 days a week, and consisted of dynamic and static exercise programmes on land and in temperature-controlled swimming pools. In addition, patients were given lectures focusing on disease-specific themes, self-management techniques, diet and advice related to general health, and they were encouraged to participate in lifelong regular exercise.

After returning to Sweden. After rehabilitation the patients were recommended to follow supervised activities along with individualized everyday activities, as indicated by the rehabilitation centre. During follow-up, medical treatment with disease-modifying anti-rheumatic drugs (DMARDs) was given and adjusted, if necessary, by the patient's physician.

Assessments

According to the study protocol, the patients were assessed 1–14 days before the intervention period (inclusion), at discharge from the rehabilitation centres (month 1), and 3 and 12 months post-rehabilitation (months 4 and 13).

Activity limitation. In patients with peripheral arthritis, the Swedish version of the Stanford Health Assessment Questionnaire (HAQ) (15) assessed the performance of activities of daily living, scored from 0 to 3 (0 = able to perform without difficulties and 3 = unable to perform). In patients with spondyloarthritis, the Swedish version of the Bath Ankylosing Spondylitis Functional Index (BASFI) on 10-cm visual analogue scales (VAS) (16) was used. To evaluate clinically meaningful improvement between inclusion and follow-up time-points, the minimal clinically important difference (MCID) was set at 0.22 for the change in the HAQ score (17) and 7 mm for the change in BASFI (18).

Health-related quality of life (HRQoL). Patient assessment of general health (well-being) was recorded on a 100-mm horizontal non-graded VAS (VAS-GH), where higher scores indicate worse health perception. The EuroQoL 5-domain (EQ-5D) health states profile was also assessed. The EQ-5D is a self-reported generic instrument consisting of 5 questions on mobility, self-care, pain, usual activities and psychological status, with a single value anchored at 1 (full health) and 0 (death) (19, 20). Thresholds of MCID were defined as a change ≥ 10 mm in VAS-GH and 0.05 in EQ-5D (21, 17).

Body function. Body function was measured using VAS-pain (a 100-mm VAS with anchors of no pain and severe pain), with thresholds of a MCID change of ≥ 10 mm (17).

Physical activity. Patients self-assessed their physical activity using the short version of the International Physical Activity Questionnaire (IPAQ) (22, 23) at inclusion and at 3 and 12-months post-rehabilitation. IPAQ estimates overall physical activity during the past week without separating aerobic physical activity from muscle strength training. IPAQ reports activities across leisure-time, work, domestic activities, and transport at each of 3 intensities: walking, moderate and vigorous. Total weekly physical activity is estimated by weighting time spent in each activity intensity with its estimated metabolic equivalent of task (MET) energy expenditure. The IPAQ score assigns < 600 MET-min/week to low intensity activity, $600 - < 1,500$ MET-min/week to moderate and $\geq 1,500$ MET-min/week to vigorous intensity physical activity.

Statistical analysis

The study outcomes considered HAQ, BASFI, EQ-5D and VAS-GH, VAS-pain and IPAQ: (i) changes from inclusion to post-rehabilitation

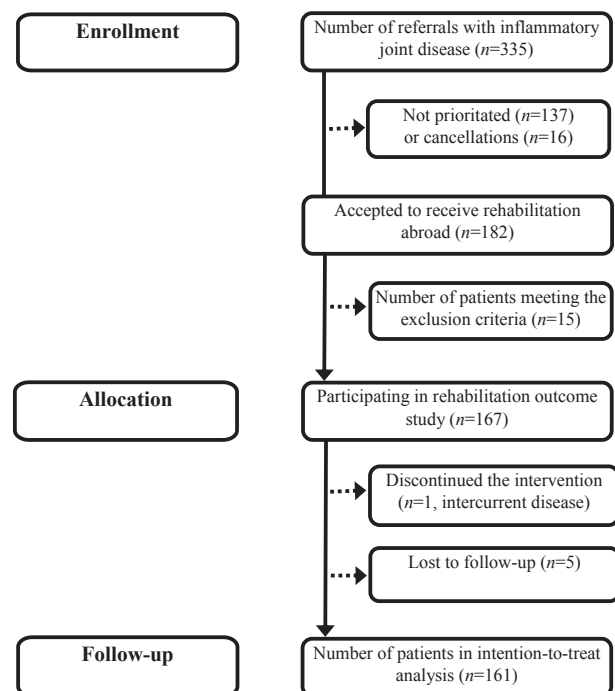


Fig. 1. Patient participation from referral to rehabilitation.

assessments; (ii) changes greater or equal to the MCID from baseline to 12 months. The outcomes were analysed for all allocated patients who started team-rehabilitation. Confirmatory analyses were performed, with the exclusion of patients who changed anti-rheumatic medication or occurred with clinically important events throughout the observation period and also in the subgroup of patients treated with biologics.

Proportions between the groups were compared by χ^2 test. One-way repeated measures analysis of variance (ANOVA) with Greenhouse-Geisser correction were applied to analyse the change in HAQ, BASFI, VAS-GH and VAS-pain over time. To assess differences between assessments, Bonferroni correction was used. As the EQ-5D and IPAQ scores markedly deviated from normality, the Friedman test was used to examine the changes over time. Thereafter, Wilcoxon signed-rank test with Bonferroni correction for planned contrasts was used to compare changes in patient-reported outcomes and proportions of the achieved improvements. Longitudinal analyses were run in complete datasets at all assessments ($n=107/124$ for HAQ, $n=28/37$ for BASFI, $n=142/161$ for EQ-5D and VAS pain, $n=150/161$ for VAS-GH).

Regression analyses were performed to examine whether demographic and disease-related factors influenced the outcomes. Spearman's rank-order correlations were used to evaluate the correlation between self-reported physical activity (IPAQ) and HAQ, BASFI, EQ-5D, VAS GH and pain at the study follow-ups and the correlation between changes in these measures during the observation period.

RESULTS

Patient baseline characteristics

Patients' characteristics are shown in Table I. There was a large variation in age and disease duration between the patients. Age

ranged from 21 to 77 years, and duration of arthritis ranged from 2 to 63 years. There was no difference in age and disease duration between patients admitted to Vintersol and to Centro Forestal Sueco. At inclusion, patients reported activity limitations and reduced quality of life. Approximately half of the patients had a comorbidity and 63% were treated with biologic DMARDs. During follow-up, 37% of the patients changed their DMARDs or experienced a clinically significant event (mostly infections and surgery).

Change in outcomes post-rehabilitation

HAQ. Over the study period, HAQ improved significantly in patients with RA, PsA and JIA, $F(2.72, 288.58)=47.22$, $p<0.001$, with 31% of the variance in HAQ explained by the time effect.

HAQ improved significantly from baseline to all follow-up time-points (all $p<0.001$) (Table II, Fig. 2A). As shown in Table II mean differences in HAQ exceeded MCID ≥ 0.22 points post-rehabilitation and after 3 months. Furthermore, the proportion of patients reporting improvements in HAQ from baseline \geq MCID was highest post-rehabilitation and after 3 months.

We further proceeded with regression analyses to investigate what factors influenced the change in HAQ from baseline to 12-months post-rehabilitation. In regression analyses this change in HAQ was associated with seropositivity, beta 0.19

Table I. Patients' characteristics by arthritis groups

	RA <i>n</i> =67	PsoA <i>n</i> =34	JIA <i>n</i> =23	SpA <i>n</i> =37	All <i>n</i> =161
Age, years, mean (SD)	57.7 (11.7)	48.7 (10.4)	41.5 (15.3)	56.5 (11.3)	53.2 (13.2)
Females, %	82.1	79.4	82.6	45.9	73.3
Disease duration, mean (SD) years	17.6 (16.0)	14.9 (9.1)	32.2 (28.0)	27.2 (13.1)	21.4 (13.5)
RF-pos, %	58.2	11.8	8.7	–	36.3
ACPA-pos, %	73.4	6.1	17.4	–	44.2
Smoking ever, %	50.7	47.1	21.7	59.5	47.8
Comorbidity, %	58.2	44.1	39.1	51.4	50.9
DAS28, mean (SD)	4.19 (1.37)	4.30 (1.12)	4.17 (1.35)	–	4.21 (1.30)
HAQ (0–3), mean (SD)	1.21 (0.59)	0.97 (0.48)	1.13 (0.49)	–	1.13 (0.55)
BASDAI (0–10), mean (SD)	–	–	–	5.13 (2.21)	–
BASFI (0–10), mean (SD)	–	–	–	4.14 (3.80)	–
EQ-5D, median (IQR)	0.66 (0.55–0.73)	0.62 (0.30–0.69)	0.62 (0.52–0.69)	0.71 (0.52–0.79)	0.66 (0.52–0.73)
General health (VAS 0–100), mean (SD)	50.8 (20.6)	60.0 (19.0)	55.0 (23.3)	51.4 (23.0)	53.3 (21.3)
Pain (VAS 0–100), mean (SD)	49.2 (22.0)	55.6 (24.1)	57.6 (22.0)	48.5 (23.3)	51.6 (22.8)
Treatments					
Synthetic DMARDs, %	67.2	44.1	47.8	21.6	49.1
Biologic DMARDs, %	67.2	70.6	73.9	43.2	63.4
Glucocorticoids, %	32.8	12.5	21.7	2.9	20.1
Physical activity by IPAQ					
MET-min/week, median (IQR)	990 (504–1,893)	1,216 (516–2,585)	1,386 (812–2,589)	2,064 (754–3,567)	1,253 (587–2,583)
Low activity (<600 MET-min/week), %	35.3	25.0	17.6	17.2	26.4
Moderate activity (600 – <1,500 MET-min/week), %	33.3	28.6	47.1	24.1	32.0
Vigorous activity ($\geq 1,500$ MET-min/week), %	31.4	46.4	35.3	58.6	41.6
Therapy change or intercurrent event during follow-up, %	37.3	41.2	47.8	27.0	37.3

RA: rheumatoid arthritis; PsoA: psoriatic arthritis; JIA: juvenile idiopathic arthritis; SpA: spondyloarthritis; RF: rheumatoid factor; ACPA: anti-citrullinated protein antibody; DAS28: Disease Activity Score on 28 joints; HAQ: Health Assessment Questionnaire; BASDAI: Bath Ankylosing Spondylitis Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; EQ-5D: EuroQoL 5-Dimensions Questionnaire; VAS: visual analogue scale, DMARD: disease-modifying anti-rheumatic drug; IPAQ: International Physical Activity Questionnaire; MET: metabolic equivalent of task; IQR: interquartile range.

Table II. Outcomes from inclusion to the end of the rehabilitation period, and 3 and 12 months thereafter

	At inclusion	End of rehabilitation	After 3 months	After 12 months
		<i>p</i>	<i>p</i>	<i>p</i>
^a HAQ (0–3 scale)	1.13 (0.55)	0.74 (0.48)	0.87 (0.55)	1.00 (0.53)
Mean reduction	–	0.36 (0.20–0.52)	0.27 (0.17–0.37)	0.15 (0.06–0.25)
Improvement ≥MCID	–	66%	62%	35%
^b BASFI (0–10 scale)	4.14 (2.57)	2.34 (1.83)	2.97 (2.03)	3.70 (2.27)
Mean reduction	–	1.55 (0.4–2.71)	0.83 (–0.06–1.72)	0.20 (–0.93–1.33)
Improvement ≥MCID	–	75%	73%	61%
EQ-5D (–0.59–1)	0.66 (0.52–0.73)	0.76 (0.69–0.80)	0.73 (0.62–0.80)	0.69 (0.54–0.76)
Improvement ≥MCID	–	70%	47%	39%
VAS general health (0–100)	53.3 (21.3)	18.5 (13.6)	33.4 (21.6)	41.5 (23.9)
Mean reduction	–	34.4 (29.6–39.0)	19.9 (15.1–24.7)	12.4 (7.4–17.4)
Improvement ≥MCID	–	87%	68%	52%
VAS pain (0–100 scale)	51.6 (22.8)	18.5 (15.9)	31.4 (21.69)	39.4 (24.6)
Mean reduction	–	33.4 (28.1–38.7)	21.0 (15.8–26.1)	12.4 (6.6–18.1)
Improvement ≥MCID	–	84%	68%	51%
IPAQ	1,253 (587–2,583)	–	2,375 (1,152–4,136)	2,026 (1,064–3,592)
IPAQ by categories	–	–	<0.001	<0.001
Low activity (<600 MET-min/week)	26%	–	10%	13%
Moderate activity(600–<1,500)	32%	–	21%	26%
Vigorous activity (≥1,500)	42%	–	69%	61%

Values are means (SD) and mean differences (95% CI: confidence interval for difference), medians (IQR) or percentages, *p*-value for difference from baseline. HAQ: Health Assessment Questionnaire (^ameasured in patients with rheumatoid arthritis, psoriatic arthritis and juvenile idiopathic arthritis); BASFI: Bath Ankylosing Spondylitis Functional Index (^bmeasured in patients with spondyloarthritis); EQ-5D: EuroQoL 5-Dimensions Questionnaire; VAS: visual analogue scale; IPAQ: International Physical Activity Questionnaire; MET: metabolic equivalent of task; MCID: minimal clinically important difference, defined as improvement in HAQ ≥0.22, BASFI ≥0.7, EQ5D ≥0.05 utility values, VAS scores ≥10.

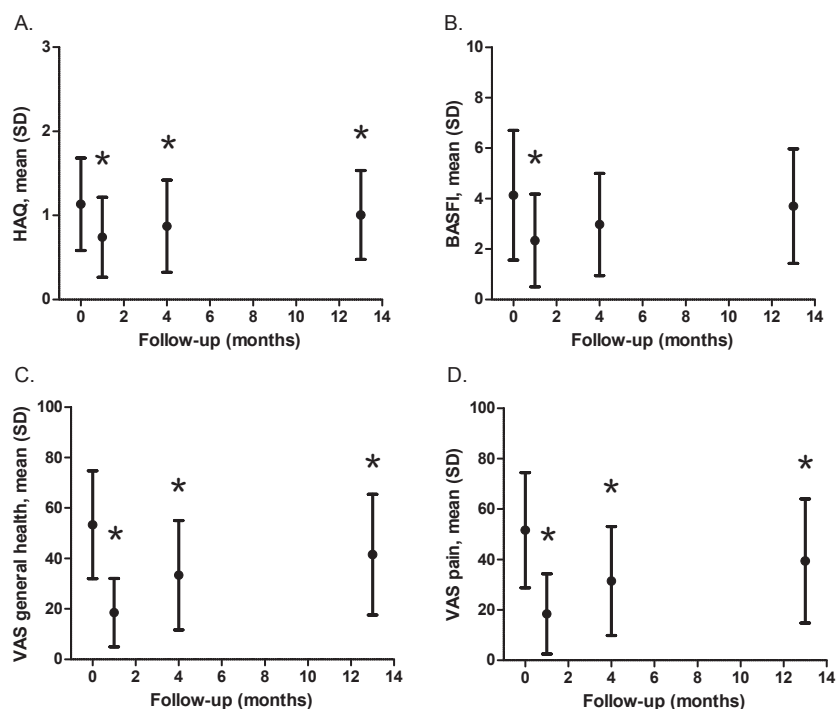


Fig. 2. Patient-reported measures at inclusion (0), end of the rehabilitation period (1 month), 3 and 12 months after rehabilitation (4 and 12 months after inclusion) presented as means (SD) for (A) Health Assessment Questionnaire (HAQ) in patients with rheumatoid arthritis, psoriatic arthritis and juvenile idiopathic arthritis; (B) Bath Ankylosing Spondylitis Functional Index (BASFI) in patients with spondyloarthritis; (C) visual analogue scale (VAS) general health and (D) VAS pain in all patients. *The mean difference from baseline is significant at the 0.05 level.

(95% confidence interval (95% CI) 0.02–0.28), $p=0.038$, but not demographic and other disease variables.

BASFI. BASFI changed statistically significantly over the observation period in the patients with SpA, $F(2.75, 74.11)=7.65$, $p<0.001$, where 22% of the variance in BASFI was explained by the time effect.

BASFI improved from baseline to post-rehabilitation and to 3-month assessments. At 12-month follow-up, BASFI regressed to the baseline level (Table II, Fig. 2B). The proportion of patients reporting BASFI improvements ≥MCID (7 mm) from baseline to follow-up is shown in Table II.

Improvement in BASFI over 12 months was inversely associated with age and body mass index (BMI), betas -0.47 (95% CI -0.14 to -0.02), $p=0.006$, and -0.37 (-0.32 to -0.01), $p=0.035$.

EQ-5D. At baseline, most patients showed an impaired status of HRQoL compared with the general population (>0.8). Medians (IQR) and distribution of EQ-5D at the study time-points are shown

in Table II and Fig. 3. There was a statistically significant change in EQ-5D over the observation period, $\chi^2(3)=124.79$, $p<0.001$.

Significant improvements in EQ-5D from baseline was evident post-rehabilitation ($z=-9.152$, $p<0.001$) and at 3-months after rehabilitation ($z=-5.136$, $p<0.001$), but was not sustained at 12-month ($z=-2.167$, $p=0.030$, significance level $p<0.017$ for Bonferroni correction).

A substantial proportion of patients reported clinically relevant improvements from baseline greater than or equal to the MCID in EQ-5D ≥ 0.05 points to discharge from the rehabilitation centre and at 3-months post-rehabilitation (Table II).

The data indicated an inverse association between improvement in EQ-5D from baseline to 12 months and the presence of comorbidity at inclusion, beta -0.21 (-0.21 to -0.03), $p=0.010$. The EQ-5D change was not influenced by demographic and other disease-related factors (all $p>0.05$). Thus, improvement in EQ-5D from inclusion to 12-months post-rehabilitation was lower in patients with comorbidity than in those without. At baseline, EQ-5D did not differ between patients who had comorbidities or those who did not, corresponding medians (IQR) 0.62 ($0.52-0.73$) and 0.69 ($0.52-0.73$), $p=0.13$. The distribution of EQ-5D across the scale range was also similar (data not shown). The patients with comorbidity were older than those without, means (SD) 58.8 (10.0) years and 47.4 (13.7), $p<0.001$, and had a longer mean (SD) disease duration, 24.2 (15.0) and 18.5 (11.2), $p=0.008$.

VAS general health and pain. The team-rehabilitation also resulted in significant change in VAS-GH and VAS-pain over the study period: respectively, $F(2.91, 433.91)=135.31$ and $F(2.84, 400.28)=109.43$, both $p<0.001$, time effect explained 48% of the variance in VAS-GH and 44% in VAS-pain.

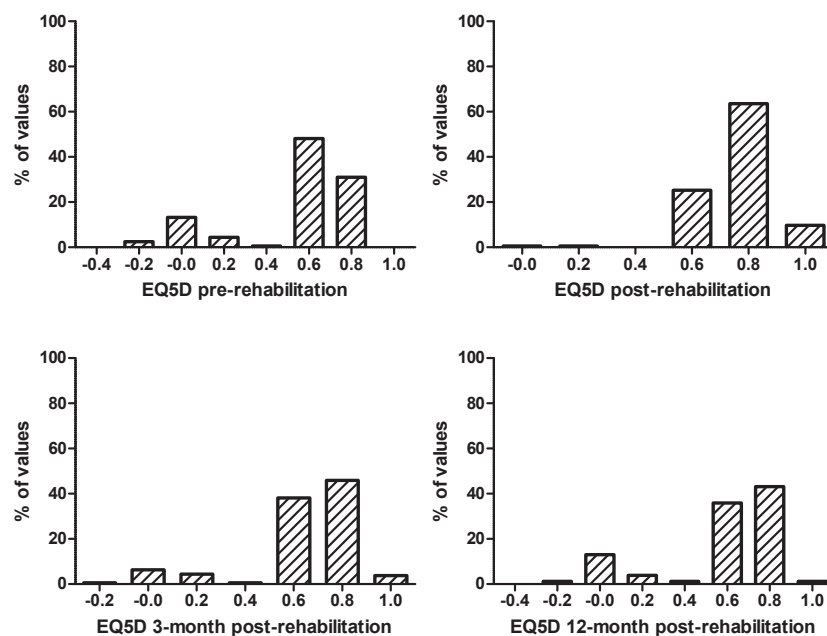


Fig. 3. EuroQoL 5-Dimensions (EQ-5D) frequency distribution at baseline (pre-rehabilitation) and post-rehabilitation assessments.

Statistically and clinically significant improvements in the VAS scores, MCID ≥ 10 mm, were reported from baseline to all assessments (Fig. 2C and D, Table II). Individually most of the patients reported improvement \geq MCID at post-rehabilitation assessments (Table II).

No demographic or disease-related variables were found to associate with the improvement in the VAS scores throughout the study.

IPAQ. The patient-reported physical activity during the week prior to baseline evaluation is shown in Table I. Approximately one-third of the patients with RA had low physical activity, one-third moderate and one-third high physical activity, measured in MET-min/week. The mean values for all patient groups corresponded to moderate or high physical activity.

The level of physical activity improved significantly between baseline and 1-year follow-up, $\chi^2(2)=43.42$, $p<0.001$, the medians (IQR) of IPAQ at post-rehabilitation assessments are shown in Table II. Differences in the IPAQ score were statistically significant for comparisons between baseline and 3 months ($z=-6.151$, $p<0.001$), and baseline and 12 months ($z=-4.027$, $p<0.001$).

Relationship between physical activity and patient-reported outcomes

We further questioned whether the level of physical activity was associated with patient-reported outcomes. As shown in Table III, the level of IPAQ at baseline correlated inversely with HAQ at inclusion, and 3 and 12-month assessments. Furthermore, IPAQ at baseline also correlated with EQ-5D at baseline and at 3-months, as well as with VAS scores at 3-months.

A higher level of IPAQ at 12-months correlated with a larger reduction in HAQ from baseline to 12-months, improved VAS-GH and improved VAS-pain.

Improved IPAQ from baseline to 12-months showed a trend-wise correlation with a total improvement in HAQ, a greater increase in EQ-5D over the study period, and improved VAS-pain, as well as a greater reduction in BASFI between post-rehabilitation and 12-months, $r=0.45$, $p=0.042$.

Confirmatory analyses and subgroup analyses

Across all measured outcomes (with the exception of BASFI), the results were similar in the confirmatory analyses in the patients without therapy change or unexpected events throughout the observation period, all $p<0.001$.

Also, in the subgroup of patients treated with biologics, the results were similar to those achieved in the whole study population. Thus, in this subgroup, the change over time in HAQ was $F(2.63, 197.34)=24.46$, $p<0.001$; in EQ-5D $\chi^2(3)=80.69$, $p<0.001$; VAS-GH $F(2.92$,

Table III. Correlations between International Physical Activity Questionnaire (IPAQ), change (Δ) in IPAQ between inclusion and 12 months after rehabilitation and patient-reported measures, presented as Spearman R coefficients (p -values)

	Time-points	IPAQ 0 months	IPAQ 12 months	IPAQ Δ 12-0
^a HAQ	Baseline	-0.282 $p=0.006$	0 NS	0.122 NS
	3	-0.351 $p<0.001$	-0.167 $p=0.092$	0.066 NS
	12	-0.268 $p=0.009$	-0.149 NS	-0.008 NS
	Δ 0-12	-0.098 NS	0.200 $p=0.045$	0.190 $p=0.086$
^b BASFI	Baseline	-0.279 NS	-0.104 NS	-0.205 NS
	3	-0.260 NS	-0.215 NS	-0.221 NS
	12	-0.06 NS	-0.267 NS	-0.346 $p=0.090$
	Δ 0-12	-0.276 NS	0.247 NS	0.219 NS
EQ-5D	Baseline	0.205 $p=0.022$	0.123 NS	-0.040 NS
	3	0.260 $p=0.004$	0.156 $p=0.076$	-0.034 NS
	12	0.123 NS	0.168 $p=0.057$	0.137 NS
	Δ 12-0	-0.154 $p=0.094$	-0.015 NS	0.199 $p=0.040$
VAS general health	Baseline	-0.076 NS	0.058 NS	0.046 NS
	3	-0.264 $p=0.003$	-0.12 NS	0.120 NS
	12	-0.153 $p=0.093$	-0.148 $p=0.090$	-0.108 NS
	Δ 0-12	0.144 NS	0.216 $p=0.013$	0.155 NS
VAS pain	Baseline	-0.088 NS	0.046 NS	0.066 NS
	3	-0.215 $p=0.016$	-0.104 NS	0.061 NS
	12	-0.148 NS	-0.147 $p=0.092$	-0.146 NS
	Δ 0-12	0.115 NS	0.172 $p=0.050$	0.183 $p=0.059$

p -values in bold are significant.

HAQ: Health Assessment Questionnaire (^ameasured in patients with rheumatoid arthritis, psoriatic arthritis and juvenile idiopathic arthritis); BASFI: Bath Ankylosing Spondylitis Functional Index (^bmeasured in patients with spondyloarthritis); EQ-5D: EuroQoL 5-Dimensions questionnaire; VAS: visual analogue scale.

283.05)=87.92, $p<0.001$, VAS-pain $F(2.94, 271.16)=65.70$, $p<0.001$ and IPAQ $\chi^2(2)=31.79$, $p<0.001$. There were too few cases for subgroup analyses for the BASFI outcome.

DISCUSSION

This study provides evidence for the efficacy of a 4-week comprehensive team-rehabilitation in a warm climate offered to patients with inflammatory joint diseases, who, at inclusion,

experienced activity limitations and reduced quality of life despite current therapeutic management and physiotherapy in Sweden. Rehabilitation in a warm climate resulted in improved patient-oriented outcomes on HAQ, BASFI, EQ-5D, VAS general health and pain. The benefit of intervention was evident post-rehabilitation and was maintained in most patients for up to 1-year follow-up. The health advantages of the rehabilitation programme were combined with increased health-enhancing physical activity.

The patients' judgement of response to intervention is of great importance, and has been considered objective in randomized placebo-controlled studies (24). The high frequency of patients who experienced clinically meaningful improvements in HAQ and in BASFI after the rehabilitation programme in the current study is impressive, as impaired physical function is considered to be partly irreversible in long-standing disease, and responsiveness in HAQ score has been shown to be inversely associated with mean disease duration in RA (25).

The improvements in HAQ, VAS general health and pain post-rehabilitation were notably comparable with those reported in recent randomized clinical trials of biologicals in RA. Thus, the mean changes in HAQ from baseline to 6-12 months in these trials were from 0.25 to 0.60, and percentage of MCID in HAQ from 31% to 64% (26-29). Likewise, improvements in VAS-pain reported in the trials were from 12 to 38 mm, with percentage of MCID in pain 31-37%, and improvement in VAS-general health approximately 14 mm with MCID improvement in 41-46% of the patients (26, 27, 30). Importantly, the gained effects in the current study were confirmed in the subgroup of patients treated with biologics, and the results were not affected by changes in medical treatments, as confirmatory analyses on patients without changed medication or unexpected clinical events yielded stable results across the outcomes.

Earlier studies of comprehensive team-rehabilitation were mostly performed ahead of modern therapeutic strategies with access to treatment with biologic agents. In the 2000s, one study of comprehensive team-based out-patient rehabilitation in patients with peripheral arthritis and with similar patient characteristics to those in the present study, performed during 18 weekdays in Sweden, resulted in HAQ improvement after the intervention, but this improvement, contrary to our findings, was not maintained after 4 and 12 months (31). Because of the differences in anti-rheumatic treatments, interventions at the rehabilitation centres and the large variety of outcome measures, comparison of the present data with those in earlier studies of rehabilitation in a warm climate are hardly possible.

In our study we observed a higher HAQ improvement in the group of seropositive patients than in seronegative patients. It is, however, important to point out that improvement in function in the seronegative patients was also present. It has been disputed whether the difference in therapy responses and clinical outcome in seropositive and seronegative patients truly exists (32).

When we accounted for the baseline HAQ level in the analysis, the effect of seropositivity for the HAQ improvement was not confirmed (beta 0.11, $p=0.22$), which suggests a similar effect of rehabilitation intervention on the HAQ

score at a similar baseline level of the HAQ in seropositive and seronegative patients.

The efficacy of intervention was highest post-rehabilitation and regressed somewhat between the 3- and 12-month assessments. Loss of functional gains following training is suggested to be inevitable once training ceases, especially in the older population (33). In the younger patients with spondyloarthritis and a shorter disease duration than in our study, sustained improved BASFI has still been present over 12 months after team-rehabilitation (31). However, our data suggest that most patients can maintain the benefits of the rehabilitation programme through improved intensity of their physical activity.

To our knowledge EQ-5D has not previously been studied as a long-term outcome measure of team-rehabilitation in arthritis, although improvements in HRQoL measured with other instruments have been reported (31, 34). The improvement in EQ-5D in our study was hampered in the presence of comorbidity, which is consistent with the reports of lower quality of life in patients with comorbidity than those without (35, 36). Some residual EQ-5D cannot be changed, due to damage, but we believe that even minimum improvement in individual patients may lead to individual items responses not considered relevant for patients at a group level.

An integral part of the rehabilitation programme was the promotion of physical activity in the patients. At inclusion, the patients as a group fulfilled the World Health Organization's (WHO's) recommendation of a minimum of 150 min per week of moderate to intensive physical activity, but, individually, nearly 30% did not reach this recommendation. The proportionally high physical activity at inclusion into the study may have been influenced by inclusion requirements of active participation in routine outpatient physiotherapy (37). Still, we observed significantly increased intensity of physical activity throughout the study. Such long-lasting increase in regular physical activity is considered to be of great benefit for well-being status.

The increased physical activity at 12 months was correlated with a decrease in HAQ, BASFI and pain and an increase in EQ-5D. Neither correlation nor association establishes causality. Since exercise may reduce disease activity in inflammatory rheumatic conditions (38), increased physical activity may result in a reduction in activity limitations and increased HRQoL. On the other hand, improved function due to team-rehabilitation may prerequisite to increased physical activity.

The present patient population is representative of patients with established arthritis seen in secondary rheumatology care with access to modern treatments and ambulatory physiotherapy. The drop-out rate was very low and could have been explained by the requirement for a 4-week active participation in the rehabilitation programme abroad. The high sample size and consistent results across the outcome measures probably support the conclusions of the study.

Due to the complexity of the comprehensive rehabilitation programme, it is difficult to attribute demonstrated improvements to a particular component of the programme. Furthermore, it is possible that both change in the patient's environment and the subtropical climate itself could have contributed to health benefits.

In experimental studies, ultraviolet radiation acts as an immunosuppressant (39) and exposure to ultraviolet-B depresses disease activity in RA (40); both effects may facilitate physical activity.

The strengths of the study are its prospective design and structured assessments of the outcomes. A limitation of the study is the lack of a control group. Randomized study design with a control group not assigned for rehabilitation might have enhanced the effects of the rehabilitation reported here, since function worsens after stopping exercise. In our opinion, it would be inappropriate to randomize applicants in need of comprehensive rehabilitation to a no-rehabilitation group. To randomize a control group to multidisciplinary rehabilitation in Stockholm that could correspond to the rehabilitation in a warm climate was not possible, as such rehabilitation is unavailable. Due to the multiple health professionals involved it should be a resource-demanding task and would be much more expensive than the presented rehabilitation in a warm climate. Furthermore, in 2 earlier randomized studies a large number of patients dropped out, indicating the difficulty of performing randomized controlled trials in this area (11, 12).

In conclusion, this study documented the efficacy of comprehensive team-rehabilitation in a warm climate for multiple components of body function, activities and quality of life in Swedish patients with arthritis who have activity limitations. This study extends earlier reports with the findings of important clinically meaningful improvement up to 12 months in the whole study population and in the patients treated with biologics. The rehabilitation programme further promoted long-lasting health-related physical activity. The study supports the view that comprehensive rehabilitation programmes in a warm climate could be an integral part of management patients with arthritis in the Nordic countries.

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