

Supplementary files for manuscript

Effect of high-intensity interval training in physiotherapy primary care for patients with inflammatory arthritis: The ExeHeart randomized controlled trial

Table a: Baseline characteristics for all study participants, exercise group and control group; supplementary data. Data are presented as mean (SD) unless otherwise indicated.

Baseline characteristics	All n=60	Exercise group n=30	Control group n=30
<i>Anthropometric measures</i> [§]			
Waist circumference, cm	93 (12)	91 (11)	95 (13)
Fat mass, kg ^b , median (IQR)	18.8 (13.5-26.7)	17 (13.6-23.4)	22.9 (13.5-27.6)
Fat-free mass ^b , kg	54.4 (11.8)	53.5 (12.6)	55 (11.2)
Fat mass, % body weight	26.4 (7.4)	25.6 (6.6)	27.3 (8.1)
Visceral fat indicator ^b , median (IQR)	7 (5-10)	7 (5-9)	8 (6-12)
<i>Inflammatory markers</i>			
CRP, mg/L, median (IQR)	1 (1-2)	1 (1-2)	2 (1-3)
ESR, mm, median (IQR)	9 (5-15)	7 (4-15)	10 (5-16)
<i>Clinical disease activity</i>			
DAS28 ^d , median (IQR)	2.4 (2.1-4.4)	2.4 (2.1-4.4)	2.8 (2.2-3.8)
DAPSA ^e , median (IQR)	8.5 (5-29)	8 (4-26)	10.5 (6-36)
ASDAS ^f , median (IQR)	1.9 (1.2-2.4)	2.0 (1.1-2.2)	1.7 (1.3-3.1)
<i>Clinical disease category</i>			
Remission, n (%)	22 (37)	12 (40)	10 (33)
Low, n (%)	17 (28)	6 (20)	11 (37)
Moderate, n (%)	14 (23)	9 (30)	5 (17)
High, n (%)	7 (12)	3 (10)	4 (13)
<i>Self-reported disease activity, 0-10, 10= worst</i>			
RAID ^d , median (IQR)	1.8 (1.0-3.6)	3.3 (1.8-4.4)	1.8 (0.4-3.2)
PsAID ^e , median (IQR)	1.0 (0.4-1.6)	0.9 (0.3-1.3)	1.2 (0.8-1.7)
BASDAI ^f , median (IQR)	2.3 (1.2-4.5)	3.4 (1.5-4.1)	2.2 (1.2-6.5)
BASFI ^f , 0-10, 10= impossible, median (IQR)	2 (1-2.8)	2.2 (0.9-2.6)	1.9 (1.2-3.2)
BAS-G ^f , 0-10, 10= very severe, median (IQR)	3.5 (1-4.5)	3.5 (1-4.5)	2.8 (1.5-6.5)
<i>EQ-5D-5L</i>			
Utility index (0-1), 1=best, median (IQR)	0.87 (0.82-0.94)	0.86 (0.81-0.94)	0.88 (0.83-0.94)
EQ-VAS (0-100), 100=best, median (IQR)	70 (50-80)	70 (60-80)	60 (40-85)
<i>CardioPulmonary Exercise Test</i>			
<i>Spirometry</i>			
Forced vital capacity, L	3.9 (1.0)	3.8 (1.0)	3.9 (1.0)
Forced expiratory volume, L	2.9 (0.7)	2.8 (0.7)	3.0 (0.8)
Peak expiratory flow, L/min, median (IQR)	7.50 (6.2-8.5)	6.7 (6.0-8.5)	7.3 (6.3-8.6)
Maximal voluntary ventilation, L/min, median (IQR)	115 (94-133)	115 (94-137)	115 (93-131)
<i>Ventilatory threshold 1</i>			
VO ₂ , mL/kg/min	17.5 (3.8)	17.9 (4.0)	17.2 (3.7)
Heart rate, beats/min	107 (11)	105 (10)	109 (12)
<i>Ventilatory threshold 2^a</i>			
VO ₂ , mL/kg/min, median (IQR)	25.6 (20.9-28.9)	27.3 (24.4-27.4)	23.9 (20.7-28.9)
Heart rate, beat/min	138 (15)	138 (15)	138 (14)
<i>VE/VO₂</i>			
at ventilatory threshold 1, median (IQR)	21 (20-23)	21 (20-23)	22 (20-23)
at ventilatory threshold 2, median (IQR) ^a	26 (23-27)	26 (23-27)	26 (25-27)
<i>VE/VCO₂</i>			
at ventilatory threshold 1, median (IQR)	29 (27-31)	29 (27-30)	30 (28-32)
at ventilatory threshold 2, median (IQR) ^a	28 (26-29)	28 (26-29)	28 (26-30)
VO _{2peak} over fat-free mass, mL/kg/min ^b	43.1 (7.0)	42.8 (6.2)	43.3 (7.7)
<i>Blood pressure and arterial stiffness</i>			
Systolic, mmHg	127 (13)	125 (12)	129 (14)
Diastolic, mmHg	83 (10)	82 (10)	85 (8)
Mean arterial pressure, mmHg	103 (10)	102 (10)	105 (10)
Pulse wave velocity, m/s	8.2 (1.0)	8.2 (1.1)	8.2 (1.0)
Augmentation index	22.1 (13.1)	21.3 (13.4)	22.8 (12.9)
<i>Lipids</i>			

Total cholesterol, mmol/L	4.8 (1.2)	4.9 (1.4)	4.6 (1.1)
HDL-c, mmol/L	1.7 (0.3)	1.7 (0.5)	1.6 (0.5)
LDL-c, mmol/L	2.6 (1.2)	2.7 (1.3)	2.5 (1.1)
Triglycerides, mmol/L	1.4 (0.7)	1.3 (0.6)	1.4 (0.8)
SCORE2 ^g , median (IQR)	4 (3-6)	4 (3-5)	4.5 (3-7)

^a $n=58$. ^b $n=59$. ^c $n=57$, values ≥ 20 omitted. ^d patients with RA, $n=27$. ^e patients with PsA, $n=14$. ^f patients with SpA, $n=19$. ^g calculated in patients free from statins and blood pressure medication, $n=23$. ASDAS: Ankylosing Spondylitis Disease Activity Score, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis Functional Index, BAS-G: Bath Ankylosing Spondylitis Patient Global Score, CRP: C-reactive protein, CVD: Cardiovascular disease, DAS28: Disease Activity Score Calculator for RA, DAPSA: Disease Activity Index for Psoriatic Arthritis, ESR: erythrocyte sedimentation rate, HDL: high-density lipoprotein, HR: heart rate, LDL: low-density lipoprotein, PsAID: Psoriatic Arthritis Impact of Disease, RAID: Rheumatoid Arthritis Impact of Disease, SCORE2: Systemic COronary Risk Estimation 2, VCO₂: volume of carbon dioxide, V_E: minute ventilation, VO₂: volume of oxygen

Table b: Efficacy results in outcome from baseline to 3-month follow-up. Values are presented as mean (SD) unless otherwise indicated. Significant differences signaled by *

	Exercise group			Control group			Estimated mean group difference (95% CI) ^a	p values	
	n	Baseline	3 months	n	Baseline	3 months			
Primary outcome (no imputations)									
VO _{2peak} , ml/kg/min	27	30.4 (5.9)	32.9 (6.4)	28	30.1 (7.9)	30.3 (7.5)	55 [^]	2.4 (0.8- 3.9)	<0.01*
Primary outcome (per protocol)									
VO _{2peak} , ml/kg/min	19	29.5 (6.2)	32.4 (6.7)	20	30.3 (8.1)	30.1 (8.1)	39	3.2 (1.7-4.8)	0.000*
VO _{2peak} , L/min	19	2.2 (0.7)	2.4 (0.7)	20	2.4 (0.6)	2.4 (0.6)	39	0.2 (0.1-0.3)	0.002*
Secondary outcomes (no imputations)									
VO _{2peak} , L/min	27	2.3 (0.76)	2.5 (0.73)	28	2.4 (0.62)	2.4 (0.62)	55 [^]	0.13 (0.03- 0.23)	0.01*
Change in VO _{2peak} ≥3.5 ml/kg/min, yes, n (%)	27	na	9 (33)	28	na	4 (14)	55		0.10 ^c
Resting heart rate beat/min§	28	64 (9)	61 (7)	29	73 (11)	69 (11)	57	-3 (-7- 1)	0.11
<i>Body composition</i>									
Waist circumference, cm	28	91 (12)	90 (13)	29	95 (13)	95 (13) 22.8	7	-1.0 (-2.6- 0.5)	0.19
Fat mass, kg	28	19.3 (7.6)	18.9 (7.7)	28	22.6 (8.7)	(8.8)	56	-0.7 (-1.7-0.4) ^d	0.21
Fatmass, % body weight	28	25.1 (6.6)	24.6 (7.4)	28	27.8 (7.9)	27.9 (7.8)	56	-0.6 (-1.6-0.4)	0.22
Visceral fat indicator	28	7.9 (4.0)	7.8 (3.9)	28	8.7 (3.7)	8.9 (3.9)	56	-0.2 (-0.7-0.2) ^d	0.31
<i>Blood pressure and arterial stiffness</i>									
Mean arterial pressure, mm Hg	28	101 (10)	103 (13)	29	105 (10)	104 (9)	57	1 (-3-5)	0.60
Pulse wave velocity, m/s	25	8.3 (1.1) 20.0	8.3 (1.0)	28	8.2 (1.0)	8.2 (1.1)	53	0.0 (-0.2-0.2) ^d	0.80
Augmentation index	25	(13.3)	24.4 (18)	25	23.2 (13.1)	21.9 (13.1)	53	3.5 (-5.3-12.3)	0.43
SCORE2 median (IQR) §	10	3 (2-6)	3.5 (2-5)	9	4 (3-6)	5 (3-6)	19		0.93 ^b
Presence of increased CVD, n (%)	28	23 (82)	23 (82)	30	25 (83)	27 (90)	58		0.34 ^c
RAID, 0-10, 10=worst, median (IQR) [□]	10	3.3 (1.8-4.4)	2.9 (1.8-3.9)	15	1.8 (0.4-3.2)	1.8 (0.7-2.9)	25		0.82 ^b
PsAID, 0-10, 10=worst, median (IQR) [#]	6	0.9 (0.3-1.0)	0.7 (0-1.3)	5	1.5 (0.8-1.7)	1.3 (0.6-1.6)	11		0.52 ^b
BASDAI, 0-10, 10=severe, median (IQR) [£]	10	2.7 (1.5-4.0)	2.4 (1.4-4.4)	8	2.2 (1.2-6.5)	2.2 (0.8-6.3)	18		0.42 ^b
BASFI, 0-10, 10=impossible, median (IQR) [£]	9	2.2 (0.9-2.5)	1.6 (0.6-1.9)	8	1.9 (1.2-3.2)	1.9 (1.0-2.3)	17		0.44 ^b
BAS-G, 0-10, 10= very severe, median (IQR) [£]	10	3.0 (1.0-4.0)	2.8 (1.5-4)	8	2.8 (1.5-6.5)	4.5 (1.5-5.5)	18		0.64 ^b
EuroQol-5D-5L utility index, 0-1, 1= best health state	28	0.86 (0.11)	0.87 (0.10)	29	0.85 (0.11)	0.86 (0.11)	57	0.01 (-0.03-0.0) ^d	0.58
EuroQol-5D-5L, VAS 0-100, 100= best imaginable health)	28	65 (18)	75 (17)	29	61 (21)	63 (20)	57	11 (1-20) ^d	0.02*
<i>Self-reported change in CRF, n (%)</i>									
Much better			10 (34)			1 (3)			
Somewhat better			17 (59)			5 (17)			
Unchanged			1 (3)			22 (73)			
Somewhat worse			1 (3)			2 (3)			
Much worse	29	na	0 (0)	30	na	0 (0)	59		<0.001 ^{c*}
<i>Exercise beliefs and self-efficacy (sub-domains)</i>									
Self-efficacy, 1-20, 20=best	29	16.4 (2.4)	16.9 (2.6)	30	15.9 (3.3)	15.5 (3.4)	59	1.1 (-0.2-2.4)	0.09
Barriers to exercise, 1-15, 15=best	28	12.8 (1.7)	12.4 (1.6)	29	11.7 (1.9)	11.4 (2.5)	57	0.2 (-0.7-1.1)	0.67
Benefits of exercise, 1-25, 25=best	28	21.9 (2.3)	21.2 (2.8)	26	20.7 (3.0)	20.7 (3.1)	54	-0.4 (-1.7-0.9)	0.51
Impact of exercise on IJD, 1-40, 40=best	28	31.2 (3.4)	31.4 (3.4)	28	29.8 (3.6)	29.9 (3.0)	56	0.7 (-0.7-2.2)	0.31

[^]Primary analysis without multiple imputation, § All patients, including patient with change in betablocker from baseline (n=1) § calculated in patients free from statins and blood pressure medication at baseline and 3-months. ^aAnalysed with ANCOVA with gender, group, age at baseline and baseline value as covariates.

^bAnalysed with Wilcoxon rank sum. ^cAnalysed with Chi-square test. ^dBootstrap CI with 10000 replications. [□]patients with RA, [#]patients with PsA, [£]patients with SpA. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis Functional Index, BAS-G: Bath Ankylosing Spondylitis Patient Global Score, CRF: Cardiorespiratory fitness, CVD: Cardiovascular disease, IJD: Inflammatory joint disease, PsAID: Psoriatic Arthritis Impact of Disease, RAID: Rheumatoid Arthritis Impact of Disease, SCORE2: Systemic COronary Risk Estimation 2, VO_{2peak}: Peak oxygen uptake

Table c: Efficacy results in outcome from baseline to 6-month follow-up. Values are presented as mean (SD) unless otherwise indicated. Significant differences signaled by *

	Exercise group			Control group			Estimated mean group difference (95% CI) ^a	p values	
	n	Baseline	3 months	n	Baseline	3 months			
Primary outcome (no imputations)									
VO _{2peak} , ml/kg/min	27	30.4 (5.9)	33.2 (7.4)	28	30.4 (8.0)	30.7 (7.8)	55 [^]	2.6 (0.8- 4.4)	<0.01*
Secondary outcomes (no imputations)									
VO _{2peak} , L/min	27	2.3 (0.8)	2.5 (0.7)	28	2.4 (0.6)	2.4 (0.6)	55 [^]	0.14 (0.0- 0.2)	0.01*
Change in VO _{2peak} ≥3.5 ml/kg/min, yes, n (%)	27	na	9 (33)	28	na	3 (11)	55		0.04 ^c
Resting heart rate beat/min [§]	28	64 (9)	63 (8)	30	72 (12)	67 (8)	58	-0 (-4- 4)	0.90
<i>Body composition</i>									
Waist circumference, cm	28	91 (12)	91 (13)	30	95 (13)	95 (12)	58	-0.1 (-2.6-1.6)	0.65
Fat mass, kg	28	19.3 (7.6)	19.4 (8.2)	29	22.3 (8.8)	22.3 (8.8)	57	0.1 (-1.2-1.3) ^d	0.89
Fatmass, % body weight	28	25.1 (6.6)	25.1 (7.3)	29	27.3 (8.1)	27.3 (7.9)	57	0.1 (-1.1-1.3)	0.89
Visceral fat indicator	28	7.9 (4.0)	7.9 (4.1)	29	8.7 (3.7)	8.7 (3.5)	57	-0.0 (-0.5-0.5) ^d	0.96
<i>Blood pressure and arterial stiffness</i>									
Mean arterial pressure, mm Hg	28	101 (10)	103 (11)	30	105 (10)	102 (10)	58	3 (-1-8) ^d	0.15
Pulse wave velocity, m/s	27	8.2 (1.1)	8.3 (1.1)	27	8.1 (1.0)	8.1 (1.2)	54	0.2 (-0.1-0.4) ^d	0.19
Augmentation index	27	20.0 (13.3)	17.1 (12.4)	27	22.8 (13.1)	18.4 (12.6)	54	-0.9 (-7.7-6.0)	0.80
SCORE2 median (IQR) [§]	11	3 (2-6)	3 (2-6)	9	4 (3-6)	4 (2-5)	20		0.15 ^b
Presence of increased CVD, n (%)	28	23 (82)	22 (79)	30	25 (83)	25 (83)	58		0.60 ^c
RAID, 0-10, 10=worst, median (IQR) [⊖]	8	3.5 (2.4-4.5)	3.5 (1.3-5.2)	15	1.8 (0.4-3.2)	1.7 (0.5-3.4)	23		0.95 ^b
PsAID, 0-10, 10=worst, median (IQR) [#]	7	0.8 (0.3-1.0)	0.5 (0.2-1.6)	6	1.2 (0.8-1.7)	1.6 (1.0-3.3)	13		0.43 ^b
BASDAI, 0-10, 10=severe, median (IQR) [£]	10	2.7 (1.5-4.0)	2.4 (1.4-4.4)	8	2.2 (1.2-6.5)	2.2 (0.8-6.3)	18		0.31 ^b
BASFI, 0-10, 10=impossible, median (IQR) [£]	10	1.8 (0.9-2.5)	1.5 (0.7-2.1)	8	1.9 (1.2-3.2)	1.6 (1.2-3.1)	18		0.40 ^b
BAS-G, 0-10, 10= very severe, median (IQR) [£]	10	3.0 (1.0-4.0)	2.0 (1.0-3.5)	8	2.8 (1.5-6.5)	3.5 (2.0-6.0)	18		0.20 ^b
EuroQol-5D-5L utility index, 0-1, 1= best health state	28	0.86 (0.11)	0.85 (0.15)	30	0.85 (0.11)	0.86 (0.09)	58	-0.1 (-0.01-0.0) ^d	0.56
EuroQol-5D-5L, VAS 0-100, 100= best imaginable health)	28	65 (18)	74 (17)	29	61 (22)	68 (15)	58	5 (2-12)	0.18
Self-reported change in CRF, n (%)									
Much better			10 (36)			0 (0)			
Somewhat better			14 (50)			7 (23)			
Unchanged			2 (7)			14 (47)			
Somewhat worse			4 (4)			9 (30)			
Much worse	28	na	1 (4)	30	na	0 (0)	58		<0.001 ^{c*}
<i>Exercise beliefs and self-efficacy (sub-domains)</i>									
Self-efficacy, 1-20, 20= best	27	16.1 (2.3)	16.7 (2.8)	29	16.0 (3.3)	16.6 (3.2)	56	-0.0 (-1.3-1.3)	0.98
Barriers to exercise, 1-15, 15= best	27	12.7 (1.7)	12.5 (1.7)	29	11.8 (2.0)	11.6 (2.4)	56	0.1 (-0.8-1.0)	0.87
Benefits of exercise, 1-25, 25= best	28	21.9 (2.3)	21.4 (2.4)	30	21.0 (3.1)	20.2 (4.0)	58	0.4 (-0.8-1.6) ^d	0.51
Impact of exercise on IJD, 1-40, 40=best	28	31.0 (3.4)	32.4 (3.0)	29	30.4 (3.8)	29.7 (3.8)	57	2.3 (0.9-3.8)	<0.01

[^]Primary analysis without multiple imputation, [§] All patients, including patient with change in betablocker from baseline (n=1) [§] calculated in patients free from statins and blood pressure medication at baseline and 6-months. ^aAnalysed with ANCOVA with gender, group, age at baseline and baseline value as covariates.

^bAnalysed with Wilcoxon rank sum. ^cAnalysed with Chi-square test. ^dBootstrap CI with 50 iterations. [⊖]patients with RA, [#]patients with PsA, [£]patients with SpA. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis Functional Index, BAS-G: Bath Ankylosing Spondylitis Patient Global Score, CRF: Cardiorespiratory fitness, CVD: Cardiovascular disease, IJD: Inflammatory joint disease, PsAID: Psoriatic Arthritis Impact of Disease, RAID: Rheumatoid Arthritis Impact of Disease, SCORE2: Systemic COronary Risk Estimation 2, VO_{2peak}: Peak oxygen uptake

Table d: SARS-CoV-2 incidence for the exercise group and control group.

Variable	Exercise group (n=26)	Control group (n=28)	p-values ^a
SARS-CoV-2 infection from baseline to 3 months, n (%)	9 (35)	9 (32)	0.85
	Exercise group (n=27)	Control group (n=30)	
SARS-CoV-2 infection from 3 months to 6 months, n (%)	6 (22)	8 (27)	0.70

^aAnalysed with Chi-square test. Missing data omitted from analyses.

Table e: Exercise habits, reported retrospectively at 6-month follow-up. Significant differences signaled by *

Variable	Exercise group (n=28)	Control group (n=30)	p-values ^a
Regular exercise past 3 months (≥ 1 /week), yes, n (%)	20 (71)	19 (63)	0.18
Exercise frequency (sessions pr. week)			
1-2 sessions/week, n (%)	8 (29)	11 (37)	
3-4 sessions/week, n (%)	10 (25)	8 (27)	
5 or more sessions/week, n (%)	2 (7)	0 (0)	0.26
Exercise mode			
Aerobic exercise, n (%)	18 (64)	8 (27)	0.004*
Strength exercise, n (%)	11 (29)	11 (37)	0.84
Mobility exercise, n (%)	10 (43)	6 (20)	0.18
Other mode of exercise, n (%)	0 (0)	5 (6)	0.02*

^aAnalysed with Chi-square test. Loss to follow-up omitted (n=2, HIIT group)