# Improved Physical Fitness Induced by Physiotherapist-led Exercise in Patients With Permanent Atrial Fibrillation Disappears and Health-related Quality of Life Is Impaired After Detraining – A 3 Months Follow-up

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**Research**

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# Abstract

**Background:** Atrial fibrillation negatively impact physical fitness and health-related quality of life in patients. We recently showed that physiotherapist-led exercise-based cardiac rehabilitation improves physical fitness in patients with permanent atrial fibrillation, however little is known about the effect of detraining after finishing an exercise period. The purpose of the study was to examine the impact of 3 months of detraining on physical fitness, physical activity level and health-related quality of life among patients with permanent atrial fibrillation, after ending a randomized comparison of physiotherapist-led exercise-based cardiac rehabilitation versus physical activity on prescription.

**Methods:** Prospective 3-month follow-up study after a randomized multi-centre study.

Of the 87 patients completing the intervention study, 80 (92%) participated in the detraining part (22 women; age 74 ± 5 years), 38 from the physiotherapist-led exercise-based cardiac rehabilitation group and 42 from the physical activity on prescription group. All patients were asked to refrain from organised exercise during the 3-months period of detraining. The primary outcome measure was maximal exercise capacity using an exercise tolerance test. Secondary outcomes measures were muscle function, physical activity level, and health-related quality of life using a muscle endurance tests, Short Form-36, and physical activity assessments (questionnaire and accelerometer), as in the intervention study. We used the Mann-Whitney *U*-test and $X^2$ test to analyse differences between the groups, and Cohen's *d* to determine the effect size. A mixed effect model analysis was used to identify predictors of change in physical fitness.

**Results:** Compared to the physical activity on prescription, physiotherapist-led exercise-based cardiac rehabilitation showed a significantly decreased exercise capacity (−9 ± 11 vs. −2 ± 12 W, $P < .0001$), reduction in shoulder flexion repetitions (−4 ± 8 vs. 2 ± 7 repetitions, $P = .001$), and reduced health-related quality of life in the Short Form-36 dimension Role Emotional (−13 ± 39 vs. 6 ± 27 points, $P = .006$).

**Conclusion:** In elderly patients with permanent atrial fibrillation detraining negatively impacted previously achieved improvements from physiotherapist-led exercise-based cardiac rehabilitation in physical fitness and reduce health-related quality of life. The importance of continued exercise is emphasized and should be part of the strategy.

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# Background

In elderly patients, atrial fibrillation (AF) has clinically significant negative impacts on physical fitness and health-related quality of life (HR-QoL) (1–4). Two recent meta-analyses (5, 6) conclude that cardiac rehabilitation in patients with AF can increase physical fitness and improve some aspects of HR-QoL(5). Accordingly, we recently demonstrated that 12 weeks of physiotherapist-led exercise-based cardiac rehabilitation (PT-X) improved physical fitness in elderly patients with permanent AF and several co-

morbidities, compared to physical activity on prescription (PAP) (7). The physical fitness improvements following PT-X were comparable to those achieved in patients with chronic heart failure, in whom such improvements were associated with decreased mortality and hospital admissions(8).

Although it appears that a period of PT-X improves physical fitness in patients with permanent AF, little is knowns about the long-term effects and what happens upon detraining. Detraining is defined as the cessation or reduction of training, or a decrease in physical fitness caused by training cessation or reduction(9). In the English literature, we have found no report addressing the impact of detraining in patients with permanent AF.

In the present study, our primary aim was to investigate the impact of 3 months detraining in terms of physical fitness, physical activity level, and HR-QoL among patients with permanent AF who had participated in a randomized study comparing PT-X and PAP(7). Our secondary aim was to identify predictors of outcome, measured as a change in physical fitness.

## Methods

We conducted a patient follow-up at 3 months after the cessation of an intervention comprising 12 weeks of either PT-X or PAP. The PT-X intervention involved central circulatory interval exercise and circuit training at two 60-min hospital-based sessions, along with two home-based exercise sessions per week. PAP comprised 40-min sessions of active walking four times per week, and the patients recorded home-based exercises and PAP in a diary. The PT-X and PAP interventions have previously been described in detail(7).

# Patiens

A total of 87 patients (24 women) who had completed the intervention part of the study (40 PT-X and 47 PAP)(7) were eligible to participate this detraining analysis. Participants completed a 3-month detraining period and follow-up assessment. The patients received both written and verbal information, and provided written informed consent to participate. The investigation conformed to the declaration of Helsinki, was approved by the Regional Ethics Committee of Gothenburg., and was retrospectively registred at ClinicalTrials.gov Identifier: NCT02493400.

# Protocol

During the 3-month detraining period, the patients were asked to avoid participation in any systematic exercise program that could improve physical fitness (aerobic capacity and muscular function). After the detraining period the patients in the PT-X group were motivated and supported to regain their exercise habits, and the PAP group were offered a period of PT-X.

# Tests

The testing procedures followed the same protocol as previously described in detail(7). The tests were performed after the detraining period by physiotherapists blinded to the randomisation. The primary outcome measure was maximum exercise capacity, assessed using a symptom-limited ergometer cycle test (Monark ergometer 839e; Monark, Varberg, Sweden) (10). The workload began at 25 W, and was increased by 25 W every 4.5 min until the patient's rated perceived exertion (RPE) was 17 (very heavy) on the Borg scale(11). At each workload, the patient's heart rate and blood pressure were measured.

The secondary outcome measures included HR-QoL, muscular endurance, and physical activity level. HR-QoL was measured using the Swedish version of the Short Form-36 Health Survey Questionnaire (SF-36) (12). The muscular endurance test involved unilateral isoinertial shoulder flexion in a sitting position with a dumbbell (2 kg for women, and 3 kg for men); bilateral isometric shoulder abduction in a sitting position with a dumbbell (1 kg for both women and men); and an unilateral isoinertial heel-lift with a straight knee, on a 10° tilted wedge, with shoes on(13).

Physical activity level was measured using an accelerometer (Actigraph® GT3x+; Actigraph, Pensacola, Florida, USA). Patients were instructed to wear the accelerometer throughout the whole day for 7 days, except when taking a shower or bath.(14) Accelerometer data were calculated using the algorithm validated by Choi et al(15). The accelerometer measured the patient's MET-minutes per week (MET level × minutes of activity × events per week), and one metabolic equivalent of tasks (1 MET) was equal to an oxygen uptake ($VO_2$) of 3.5 mL × $kg^{-1}$ × $min^{-1}$. Physical activity was also self-reported using the Swedish version of the Short Form International Physical Activity Questionnaire (IPAQ).(16) IPAQ categories were low (1), medium (2), and high (3) physical activity levels. For self-reported physical activity level during detraining, we also used the Saltin-Grimby's 6-grade physical activity level scale, which has been previously validated(17).

# Statistics

Statistical analyses were performed using the Statistical Package for Social Science (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0.; Armonk, NY, USA). Ratio and interval data are presented as mean (SD), ordinal data as median (range), and nominal data as absolute and relative numbers. The Mann-Whitney *U*-test and $X^2$ test were used to analyse differences between groups. Cohen's *d* was calculated to determine the effect size using the mean difference between groups and pooled standard deviation of the mean differences. A *d* value of ~ 0.2 indicated a small effect size, ~ 0.5 medium, and ~ 0.8 large.(18) Differences were considered statistically significant if $P$ was < .05.

We performed mixed effect model analysis to identify predictors of change in physical fitness. Independent variables were evaluated in a pairwise manner for possible collinearity, with Spearman's $r \geq 0.7$. For variable pairs having one categorical variable with few categories, we additionally checked for overlapping boxplots. When both variables were categorical with few categories, we checked cross tables for > 80% observations in diagonal, and cells with < 5 observations.

Three models were created, and each variable was checked in a stepwise manner and carried forward when $P < .20$. Model 1 included intervention, time, and intervention × time. Model 2 was model 1 with the addition of possible confounders: age, sex, and body mass index (BMI). Model 3 additionally included secondary explanatory variables for physical fitness at baseline, mean value for heel-lift with the left and right leg, SF-36 PF (physical function), IPAQ category, and moderate-to-vigorous physical activity measured by accelerometer. The final model 3 comprised the model 1 variable, significant model 2 variables (age and sex), and significant secondary explanatory variables (SF-36 PF and moderate-to-vigorous physical activity measured by accelerometer). Variables in models were considered statistically significant if $P < .05$.

# Results

Of the 87 patients who finished the main study, 80 (92%) completed the detraining period (22 women; 38 PT-X and 42 PAP). The remaining 7 patients (median age, 77 years; age range, 67–85 years; 2 PT-X and 5 PAP) withdrew their participation from the follow-up analysis. Of these 7 patients, 6 did not participate in follow-up due to medical causes or unwillingness, while one patient died within 3 months after the intervention due to causes unrelated to the intervention. All 80 patients who agreed to participate in the follow-up completed a detraining period according to the instructions and were included in the analysis. Figure 1 presents a flow-chart of the inclusion process.

Table 1 summarizes the patients' demographic data and clinical characteristics, and Table 2 the patient's pharmacological therapies. The two intervention groups remained well balanced for the detraining period. The only significant difference was a slightly higher left ventricular ejection fraction in the PAP group, but the level was normal in both groups (58% vs 54%. $P = .0014$). The groups did not significantly differ in terms of pharmacological therapy. Around 90% received some form of stroke prophylaxis (mainly oral anticoagulation), > 80% required heart rate regulation (mainly beta-blockers), and the majority used renin-angiotensin-inhibiting therapy.

We compared the data from the tests performed after the intervention period with those obtained after the 3-month detraining period.

# Physical fitness

Detraining led to a significantly greater reversal of physical fitness in the PT-X group compared to the PAP group in terms of maximum workload (− 9 vs 2 Watts; $P = .000014$), and muscle endurance in shoulder flexion in the left arm (− 4 vs 2 repetitions. $P = .00078$) (Fig. 2A, B and Table 3). The mixed effect model confirmed that physical fitness decreased after the detraining period in the PT-X group but not in the PAP group (Table 5). The same result was obtained after adjustments for confounders (age and sex), and for the secondary explanatory variables, including the SF-36 physical function (PF) and moderate-to-vigorous physical activity measured by accelerometer (Fig. 3, Tables 5 and 6).

# Physical activity

After detraining, the PAP group reported significantly higher energy expenditure compared to the PT-X group: 1863 kcal vs − 59 kcal ($P$ = .036); 3464 MET/min/week vs − 96 MET/min/week ($P$ = .040). However, these differences were not corroborated by accelerometer data. The two groups did not significantly differ in self-reported physical activity during the detraining period as measured by the Saltin-Grimby scale (Table 3).

# Health-related quality of life

Detraining led to a significantly greater reduction of HR-QoL in the PT-X group compared to the PAP group when measured using the SF-36 dimension Role Emotional (RE) (− 13 vs 6 points; $P$ = .0058) (Table 4).

## Discussion

The present results showed that 3-month detraining almost completely reversed the improvement in physical fitness (2 mL × $kg^{-1}$ × $min^{-1}$ measured as maximum work load) that had been achieved through 12 weeks of PT-X. Furthermore, the PT-X group exhibited impaired HR-QoL, with decreased scores on all SF-36 dimensions, a moderate decrease in Role Emotional (− 13 points), as well as clinically and socially significant decreases (− 5 to − 6 points) in Role Physical, Vitality, and Social Functioning. These findings indicate that both physical fitness and HR-QoL deteriorate if PT-X-induced improvements are not preserved. In the PAP group, detraining did not affect physical fitness, but had contrasting effects on Role Emotional (improved by 6 points) and Role Physical (deteriorated by − 5 points).

Several studies among patients with cardiovascular diseases other than AF show that patients have difficulty continuing exercise and maintaining a sufficient physical activity level after finishing exercise-based cardiac rehabilitation(19, 20). We previously found that elderly patients, with permanent AF and several co-morbidities, could achieve significant improvements in physical fitness. However, our present results demonstrated that these improvements disappeared after 3 months of detraining, with the additional cost of impaired HR-QoL. Although a 3-month period of PT-X improves physical fitness in older patients with permanent AF(7). and it has been shown that older adults require a longer time to retrain physical fitness lost after detraining(21), it is rare for patients with AF to have access PT-X(22, 23). How to best maintain improvement in physical fitness is an active field of research and development(6).

Previous investigations have shown that detraining causes central and peripheral alterations in athletes and recently trained healthy individuals(24–26). These alterations are multifactorial, and include a reduced $VO_{2max}$ due to reduced blood volume and higher heart rate response, which reduce stroke volume and affect cardiac output(26). The peripheral alterations include reduced muscular capillarisation and oxidative enzyme activities, and a decreased arterial-venous oxygen difference and reduced oxygen delivery to the cells, which affect mitochondrial ATP production(24). Our present findings also revealed significant loss of muscular endurance, in line with previously reported results of detraining in patients with and without cardio vascular disease(27–29). Our results were comparable to those of Volaklis et al (28) and Ratel et al(29), which revealed that detraining led to reversal of improvements of $VO_{2peak}$ and

muscular strength among patients with cardio vascular disease and in older adults(24, 25, 27–29). Our study showed that detraining had similar effects in patients with permanent AF.

Compared to after the intervention, patients in the PT-X group showed reduced HR-QoL after detraining, according to the scores on all dimensions of SF-36. In some dimensions, the post-detraining scores were lower than the scores before PT-X. In three of these dimensions, the SF-36 scores exhibited a reduction of at least 5 points, which is considered a clinically and socially relevant difference. Notably, the PT-X group showed a 13-point deterioration in the Role Emotional dimension, which is considered a moderate change(30), and which was significantly larger compared to the change seen in the PAP group.

Risom et al (6) found no evidence that PT-X improved HR-QoL. This was also our finding in our main study, in which the patients self-rated scores were similar to in the normative Swedish population of the same age range(31) Teixeira-Salmela et al (27) reported that HR-QoL increased with exercise training in the elderly population, and this increase persisted during detraining. They proposed that patients felt better about their physical abilities and, therefore, adopted a more active lifestyle. That situation differs from the situation in our present study, in which patients were asked to avoid structured exercise. Clearly, adherence to these instructions led to a reduction of HR-QoL in the PT-X group. Our results are congruent with the findings of an observational study, in which elderly individuals (> 65 years of age) participated in a detraining period after a period of structured exercise(32). The participants received instructions similar to those given in the present study, and the results revealed significant deterioration of all dimensions of the HR-QoL as measured by SF-36, as in our study(32). These findings clearly confirm that after cessation of PT-X, it is crucial to support patients to maintain their physical fitness and HR-QoL.

Our results also showed that participating in PT-X was the most important factor for improved physical fitness, and that the detraining-induced decline in physical fitness in the PT-X group can partly explain the deterioration of physical scores on SF-36. However, the PT-X group participants also exhibited declines of scores related to mental well-being and social life(33). This may indicate the importance of PT-X participation for elderly patients with permanent AF. Although the intervention part of our study confirms a benefit of PT-X among elderly patients with permanent AF and co-morbidities, the overall evidence supporting PT-X is low(6). This extended study contributes additional knowledge, and corroborates that patients require support to preserve the improvements achieved through a period of PT-X.

### Methodological aspects and limitations

In this study, we investigated the impact of detraining among patients with permanent AF after a period of PT-X or PAP. Allowing patients to participate in detraining may be ethically questionable due to the high evidence of benefits from improved physical fitness. However, it is well known that it is difficult to maintain good exercise habits, and the need for support in lifestyle changes is an important issue. The present findings provide solid evidence supporting the need to continue exercising after a period of successful PT-X, and can thus serve to motivate patients to pursue this goal.

# Conclusions

Although PT-X improves physical fitness also in elderly patients with AF and concomitant diseases, a subsequent period of detraining has negative effects not only on physical fitness but also on HR-QoL. The importance of continued exercise after PT-X is emphasized and should be part of the strategy.

# List Of Abbreviations

AF: Atrial fibrillation; HR-QoL: Health-Related Quality of Life; IPAQ: Short Form International Physical Activity Questionnaire; MET: Metabolic equivalent of task; PAP: Physical Activity on Prescription; PT-X: Physiotherapist-led exercise-based cardiac rehabilitation; PF: The Short Form-36 physical function dimension; RPE: Rate of perceived exertion (Borg's scale 6-20); SF-36: The Short Form-36 Health Survey Questionnaire: $VO_{2peak:}$ Highest oxygen uptake achieved

# Declarations


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## Declarations

In compliance with the Declaration of Helsinki, the protocol was approved by the Regional Ethics Committee of Gothenburg with registration number DNR 074-13. ClinicalTrials.gov Identifier: NCT02493400. All participants signed informed consent.

## Availability of data and materials

The dataset used and/or analysed for this current study may be available from the corresponding author upon resenable request. However, this is not applied for in the ethical application and must so be done before data sharing.


## Founding

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## Declaration of Conflicting Interests

The authors declare that there is no conflict of interests

## Authors contribution

**Maria Borland, Lenart Bergfeldt, Åsa Cider, Lars Andersson** and **Lena Nordeman,** contributed to the conception and design of the work. **Maria Borland, Agneta Rosenkvist, Marika Jakobsson, Kristin Olsson, Adam Lundwall** contributed to the acquisition of the work, **Maria Borland, Lennart Bergfeldt, Åsa Cider and Lena Nordeman,** made the analysis and interpretation of the data. **Maria Borland, Lennart Bergfeldt, Åsa Cider and Lena Nordeman** drafted the manuscript, **Maria Borland, Lennart Bergfeldt, Åsa Cider Agneta Rosenkvist, Marika Jakobsson, Kristin Olsson, Adam Lundwall, Lars Andersson and Lena Nordeman,** critically revised the manuscript. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy

### Declaration of Competing Interests

The authors declare that there is no conflict of interests

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# Tables

**TABLE 1** Demographic data, left ventricular function, and co-morbidities at follow-up according to type of intervention

| | PT-X (n = 38) | PAP (n = 42) | *P* value |
|---|---|---|---|
| Male/female, n | 28/10 | 30/12 | .82 |
| Age, years | 75 (4) | 74 (6) | .47 |
| Weight, kg | 87 (14) | 84 (16) | .42 |
| Height, m | 1.76 (0.08) | 1.75 (0.09) | .92 |
| Body mass index, kg/$m^2$ | 28 (4) | 27 (4) | .52 |
| LV-EF, % | 54 (1) | 58 (5) | .0014 |
| ***Comorbidity*** | | | |
| Myocardial infarction | 1 (3%) | 2 (5%) | 1.0 |
| TIA | - | 3 (7%) | .24 |
| Stroke | 3 (8%) | 1 (2%) | .34 |
| Diabetes mellitus type 2 | 2 (3%) | 3 (7%) | 1.0 |
| Hypertension | 11 (29%) | 12 (29%) | .97 |
| Hyperlipidaemias | 4 (10%) | 1 (2%) | .18 |
| COPD | 1 (3%) | - | .47 |
| Asthma | 2 (5%) | 1 (2%) | .60 |
| Gout | 2 (5%) | 2 (4%) | 1.0 |
| Osteoarthritis | 2 (5%) | 8 (19%) | .063 |
| Psoriasis | 2 (5%) | 2 (4%) | 1.0 |
| Hypothyroidism | 1 (2%) | 1 (2%) | 1.0 |
| Rheumatoid arthritis | 1 (2%) | 2 (4%) | .62 |
| Spinal stenosis | 1 (2%) | - | .47 |
| Osteoporosis | 1 (2%) | - | .47 |
| ***Surgical Procedures*** | | | |
| Mitral valve replacement | 1 (2%) | - | .47 |
| Aortic valve replacement | - | 1 (2%) | 1.0 |
| CABG | - | 1 (2%) | 1.0 |

Data are presented as mean (SD) or n (%).
Abbreviations: PT-X, physiotherapist-led exercise-based cardiac rehabilitation; PAP, physical activity on

prescription; LV-EF, left ventricular ejection fraction; TIA, transient ischemic attack; COPD, chronic obstructive pulmonary disease; CABG, coronary aortic bypass grafting; SD, standard deviation.

**TABLE 2** Pharmacotherapy at start of the detraining period

| | PT-X (n = 38) | PAP (n = 42) | *P* value |
|---|---|---|---|
| Anticoagulants | 35 (92%) | 35 (83%) | .32 |
| Platelet inhibitors | 2 (5%) | 3 (7%) | 1.0 |
| Heart rate regulators * | 32 (84%) | 35 (83%) | .92 |
| Calcium channel antagonists † | 4 (11%) | 7 (17%) | .43 |
| ACE-I/ARB | 24 (63%) | 18 (43%) | .07 |
| Alpha-receptor antagonists | - | 1 (2%) | 1.0 |
| Diuretics | 9 (24%) | 10 (24%) | .99 |
| Nitrates | 3 (8%) | 2 (5%) | .66 |
| Potassium supplement | 2 (5%) | 2 (5%) | 1.0 |
| Oral antidiabetics | 2 (5%) | 1 (2%) | .60 |
| Lipid modulators | 17 (45%) | 15 (36%) | .41 |
| Thyroid hormone | 3 (8%) | 4 (10%) | 1.0 |
| COPD medication | 3 (8%) | - | .10 |

Data are presented as n (%).

Abbreviations: PT-X, physiotherapist-led exercise-based cardiac rehabilitation; PAP, physical activity on prescription; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II-receptor antagonist; COPD, chronic obstructive pulmonary disease.

*Beta-blockers, the calcium channel antagonists verapamil, diltiazem, and digoxin.

†Calcium antagonists, except verapamil and diltiazem.

**TABLE 3** Comparisons of physical fitness and physical activity between after the intervention (PT-X or PAP) and after 3-month detraining

| | After intervention | | | After 3-month detraining | | | |
|---|---|---|---|---|---|---|---|
| | PT-X | PAP | *P* value | PT-X | PAP | *P* value | C's *d* |
| Exercise Tolerance Test, primary end-point | | | | | | | |
| Maximum workload, W | 103 (27) | 86 (27) | **<.0001** | **−9 (11)** | **2 (12)** | **<.0001** | **0.98** |
| Exercise Tolerance Test, secondary end-points | | | | | | | |
| HR at rest, bpm | 79 (16) | 72 (11) | .93 | −2 (14) | 1 (11) | .33 | 0.29 |
| SBP at rest, mmHg | 139 (20) | 135 (14) | .13 | −2 (18) | 3 (15) | .16 | 0.35 |
| DBP at rest, mmHg | 77 (11) | 76 (10) | .13 | 1 (12) | 1 (9) | .89 | 0.010 |
| Exercise time, s | 1123 (290) | 951 (298) | **<.0001** | **−102 (129)** | **24 (136)** | **<.0001** | **0.97** |
| HR at RPE 17, bpm | 140 (28) | 133 (30) | .20 | −1 (20) | −1 (18) | .96 | 0.00027 |
| Max SBP, mmHg | 172 (28) | 172 (23) | .065 | −7 (25) | −4 (19) | .65 | 0.12 |
| Shoulder abduction, s | 85 (43) | 85 (38) | **.010** | −7 (40) | 3 (29) | .65 | 0.28 |
| Heel lift right, reps | 15 (11) | 10 (8) | **.045** | −2 (8) | 1 (6) | .16 | 0.42 |
| Heel lift left, reps | 14 (8) | 11 (7) | **<.001** | −2 (7) | 0 (5) | .13 | 0.47 |
| Physical Activity, secondary end-points | | | | | | | |
| IPAQ, Kcal | 3555 (4208) | 3778 (3985) | .64 | **−59 (3476)** | **1863 (4486)** | **.036** | **0.48** |
| IPAQ MET, min/week | 2517 (3126) | 2715 (2636) | .80 | **−96 (3667)** | **1320 (3060)** | **.040** | **0.42** |
| IPAQ Category | 2 (1-3) | 2 (1-3) | .84 | 0 (1-3) | 0 (1-3) | .27 | 0.14 |
| Accelerometer, Kcal | 1924 (1093) | 2366 (1886) | **.038** | 132 (726) | 120 (912) | .85 | 0.015 |
| Accelerometer MPA, min | 129 (96) | 192 (134) | .069 | 18 (80) | 2 (100) | .46 | 0.18 |
| Accelerometer | 134 | 194 | .069 | 17 (84) | −4 | .59 | 0.17 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| MVPA, min | (103) | (135) | | | | (100) | | |
| Accelerometer step counts, n | 29671 (15,676) | 38288 (16,806) | .017 | | 2997 (13,754) | 1641 (13,161) | .75 | 0.10 |
| Saltin-Grimby scale | | | | | 3 (1-6) | 4 (1-6) | .51 | |

Data are presented as mean (SD).

Abbreviations: C's *d,* Cohen's d; PT-X, physiotherapist-led exercise-based cardiac rehabilitation; PAP, physical activity on prescription; bpm, beats per minute; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; Reps, repetitions; IPAQ, International Physical Activity Questionnaire; Kcal, kilocalorie; MET, metabolic equivalent; MPA, moderate physical activity; MVPA, moderate-to-vigorous physical activity.

**TABLE 4** Differences in health-related quality of life between after the intervention (PT-X or PAP) and after 3-month detraining

| SF-36 dimension | After intervention | | *P* value | After 3-month detraining | | *P* value | C's *d* |
|---|---|---|---|---|---|---|---|
| | PT-X | PAP | | PT-X | PAP | | |
| PF | 74 (18) | 73 (18) | .13 | −3 (10) | 0 (15) | .16 | 0.25 |
| RP | 73 (37) | 68 (39) | .24 | −6 (36) | −5 (40) | .96 | 0.039 |
| BP | 74 (23) | 76 (23) | .79 | −3 (20) | 1 (21) | .35 | 0.23 |
| GH | 65 (18) | 70 (17) | .50 | −2 (12) | −3 (13) | .76 | 0.033 |
| VT | 64 (21) | 69 (19) | .42 | −5 (14) | 0 (11) | .18 | 0.36 |
| SF | 89 (19) | 89 (21) | .98 | −5 (21) | 1 (23) | .28 | 0.27 |
| RE | 83 (33) | 79 (31) | .19 | **−13 (39)** | **6 (27)** | **<.01** | **0.58** |
| MH | 81 (19) | 87 (15) | .62 | −4 (15) | −1 (10) | .14 | 0.23 |
| PCS | 44 (9) | 44 (9) | .19 | −1 (7) | −1 (8) | .85 | <0.01 |
| MCS | 51 (11) | 54 (9) | .83 | −3 (12) | 0 (6) | .06 | 0.44 |

Data are presented as points, mean (SD).
Abbreviations: C's *d,* Cohen's d; SF-36, Short form-36; PT-X, physiotherapist-led exercise-based cardiac rehabilitation; PAP, physical activity on prescription; BP, bodily pain; GH, general health; MH, mental health; PF, physical function; RE, role emotional; RP, role physical; SF, social functioning; VT, vitality; MCS, Mental Component Score; PCS, Physical Component Score.

**TABLE 5** Mixed effects models for each of the two outcomes, PT-X with respect to PAP, with adjustment for possible confounders

| | Model 1 | Model 2 | Model 3 |
|---|---|---|---|
| | *P* value | *P* value | *P* value |
| **Intercept** | **<.001** | **<.001** | **<.001** |
| **Primary variables:** | | | |
| Intervention (PT-X vs PAP) | .15 | .08 | **.02** |
| Time | **<.001** | **<.001** | **<.001** |
| Intervention × Time | **<.001** | **<.001** | **<.001** |
| **Potential confounders** | | | |
| Age, years | | **<.001** | **.001** |
| Sex | | **<.001** | **<.001** |
| BMI, kg/m$^2$ | | - | - |
| **Other explanatory variables:** | | | |
| Heel-lift of right and left leg, mean, *n* | | | - |
| SF-36 PF, points | | | **<.001** |
| IPAQ, category | | | - |
| Accelerometer (time in moderate-to-vigorous range) | | | **.007** |

In all models, time is used as a categorical variable to allow for non-linear relationships.

Model 1: intervention, time, and intervention × time.
Model 2: model 1 plus possible confounders: age, sex, and body mass index.
Model 3: model 2 plus adjustment for other explanatory factors.
Abbreviations: PT-X, physiotherapist-led exercise-based cardiac rehabilitation; PAP, physical activity on prescription; BMI, body mass index; SF-36, Short form-36; PF, physical function; IPAQ, International Physical Activity Questionnaire.

**TABLE 6** Estimates of exercise capacity in Watts for the two intervention groups (PT-X and PAP) over the three time-points, using model-based mean (LS mean) and 95% confidence interval (CI)

| | | Baseline | After intervention | After 3-month detraining |
|---|---|---|---|---|
| | | LS mean (CI) | LS mean (CI) | LS mean (CI) |
| **Model 1** | PT-X | 87 (78.7-94.5) | 103 (95.0-110.6) | 94 (85.7-102.0) |
| Intervention, time, intervention × time | PAP | 88 (80.1-95.3) | 85 (77.4-92.2) | 87 (79.5-95.1) |
| **Model 2** | PT-X | 80 (73.6-86.4) | 96 (89.8-102.2) | 87 (80.5-93.8) |
| Model 1 plus adjustment for age and sex | PAP | 82 (75.9-87.9) | 79 (73.1-84.7) | 81 (75.2-87.7) |
| **Model 3** | PT-X | 82 (76.9-87.6) | 98 (93.0-103.7) | 90 (83.7-95.3) |
| Model 2 plus adjustment for secondary variables (SF-36 PF, accelerometer) | PAP | 84 (78.6-88.7) | 80 (75.6-85.5) | 83 (77.6-88.5) |
| Abbreviations: PT-X, physiotherapist-led exercise-based cardiac rehabilitation; PAP, physical activity on prescription. | | | | |

# Figures

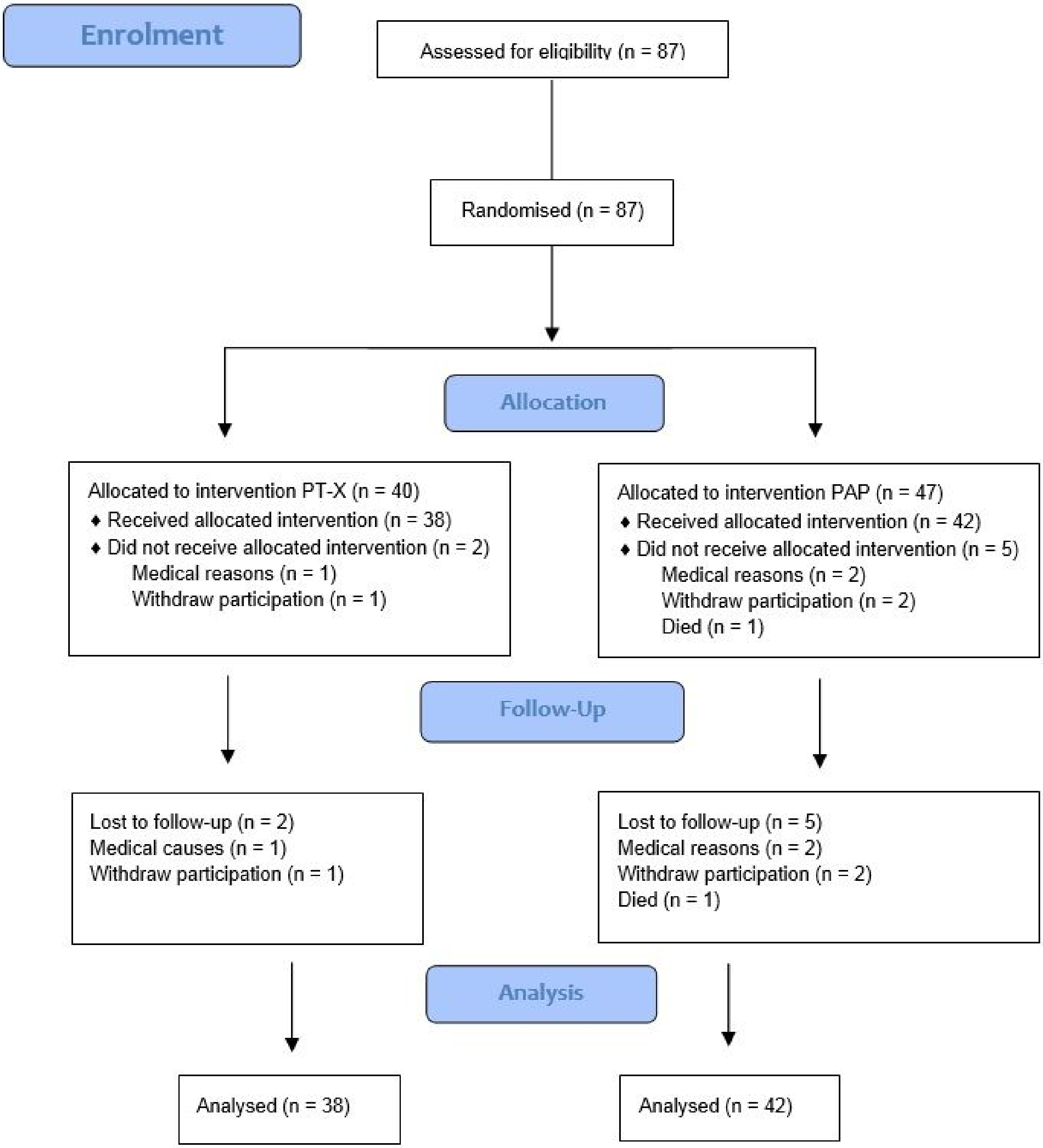
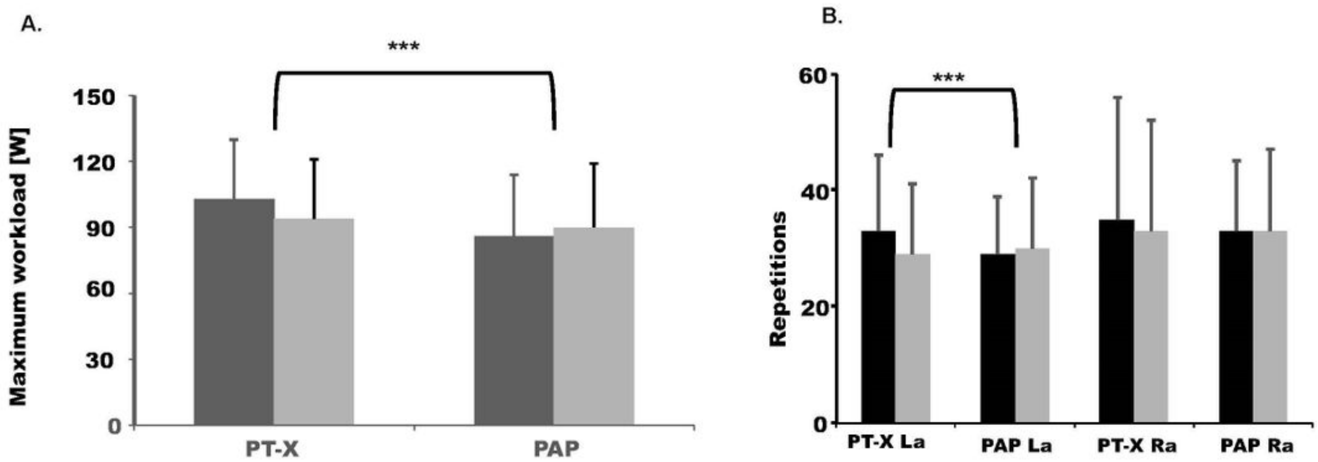


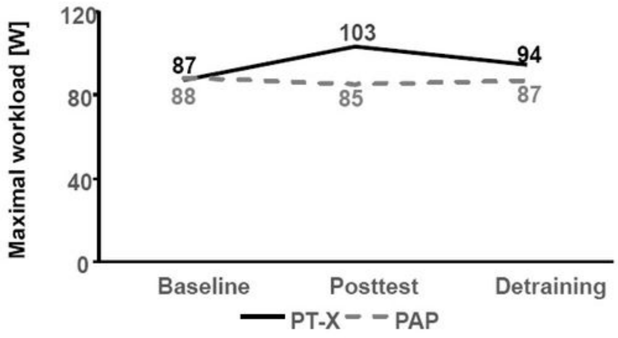

**Figure 1**

Flow-chart of the inclusion process.

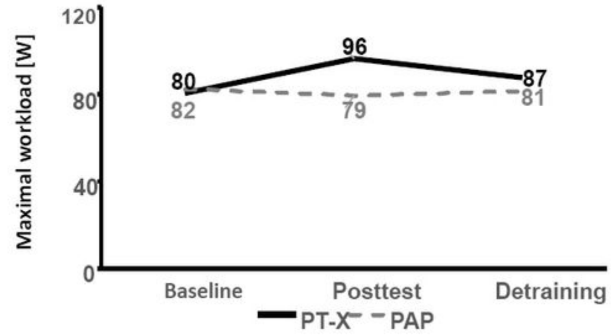



## Figure 2

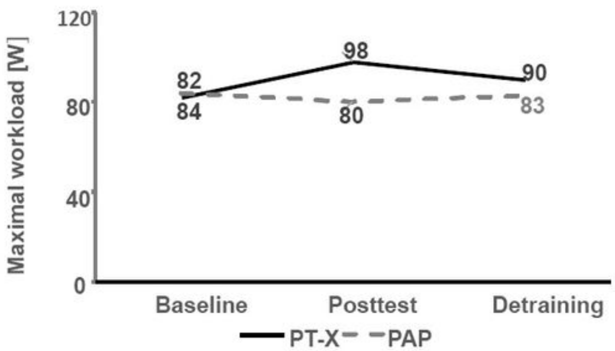
Physical fitness after intervention (black bars) and after 3-month detraining (grey bars). P values are for between-group comparisons of differences between after the intervention and after the 3-month detraining. Data are presented as mean (SD) and Cohen's d (C's d). (A) Bicycle ergometer test: −9 vs. 2 W for PT-X vs. PAP, P = .000014; C's d: +.98. (B) Shoulder flexion left arm: −4 vs. 2 repetition for PT-X vs. PAP, P = .00078; C's d +.080. Abbreviations: PT-X, physiotherapist-led exercise-based cardiac rehabilitation; PAP, physical activity on prescription; La, left arm; Ra, right arm; W, Watt.




Model 1. Intervention (PT-X, PAP) * time




Model 2. Intervention (PT-X, PAP)* Time and confounders (age and sex).




Model 3. Model 2. Intervention (PT-X, PAP) * Time, confounders (age and sex) and second explanatory variables (SF-36 PF and Moderate – Vigorous physical activity measured by accelerometer.

## Figure 3

Pattern of change over time and difference between PT-X and PAP. Black line indicates PT-X, grey dashed line indicates PAP. (A) Model 3: Intervention (PT-X, PAP) × Time, with adjustment for confounders (age and sex) and secondary explanatory variables (SF-36 PF and moderate-to-vigorous physical activity measured by accelerometer). Abbreviations: PT-X, physiotherapist-led exercise-based cardiac rehabilitation; PAP, physical activity on prescription.