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**Effect of patient education and physical training on quality of life and physical exercise capacity in patients with paroxysmal or persistent atrial fibrillation**

*A randomized study*

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## EFFECT OF PATIENT EDUCATION AND PHYSICAL TRAINING ON QUALITY OF LIFE AND PHYSICAL EXERCISE CAPACITY IN PATIENTS WITH PAROXYSMAL OR PERSISTENT ATRIAL FIBRILLATION: A RANDOMIZED STUDY

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**Objective:** To examine the effect of a rehabilitation programme on quality of life and physical capacity in patients with atrial fibrillation. **Methods:** Patients with paroxysmal or persistent atrial fibrillation were randomized to either a 12-week rehabilitation programme with education and physical training (intervention group) or standard care (control group). At baseline, after 3, 6 and 12 months participants completed 5 different quality of life questionnaires (Quality of Life in patients with Atrial Fibrillation (AF-QoL-18), Atrial Fibrillation Effect on Quality of Life (AFEQT), Patient Health Questionnaire (PHQ-9), Generalised Anxiety Disorder Assessment (GAD-7) and EuroQol 5D (EQ-5D)), and physical exercise tests. Differences in mean scores between groups were analysed by repeated measures analysis of variance (ANOVA).

**Results:** Fifty-eight patients (age range 43–78 years, 31% female) were included. In the intervention group the AF-QoL-18 score increased from baseline (48.4 (standard deviation (SD) 22.8)) to 6 months (68.0 (SD 15.2)) compared with the control group (baseline 51.6 (SD 22.3), 6 months 59.2 (SD 27.3)). After 12 months, there was no difference. Similar patterns were found for the other questionnaires. Maximum exercise capacity improved in the intervention group from baseline (176 W (SD 48)) to 6 months (190 W (SD 55)). There was no change in the control group.

**Conclusion:** Education and physical training may have a short-term (but no long-term) beneficial effect on quality of life and physical exercise capacity in patients with atrial fibrillation.

**Key words:** atrial fibrillation; rehabilitation; quality of life; physical exercise; education.

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Cardiac rehabilitation takes a cross-functional approach to the aftercare of patients, including individually designed treatment plans, patient information and education plans, physical exercise, dietary guidance, psychosocial

### LAY ABSTRACT

Atrial fibrillation is the most common cardiac arrhythmia and the number of atrial fibrillation patients is growing worldwide. In addition to an increase in risk of stroke and heart failure patients with atrial fibrillation also experience decrease in fitness and quality of life. In our study 58 atrial fibrillation patients draw lots to participate or not in a rehabilitation program with education and exercise training in addition to usual treatment. We measured fitness by a bicycle test at the beginning of the study and after 3 and 6 months, moreover participants filled out questionnaires on quality of life at the beginning of the study and after 3, 6 and 12 months. We found that our rehabilitation program may have a short term (but no long term) effect on quality of life and fitness in atrial fibrillation patients.

support, optimization of medical treatment, risk factor control, and individual maintenance of treatment goals.

There is strong evidence that rehabilitation has a beneficial effect on quality of life (QoL) in patients with coronary heart disease (CHD) (1). However, patients with atrial fibrillation (AF) are seldom and not systematically offered rehabilitation.

Previous studies have demonstrated that patients with AF lack knowledge regarding the natural history of AF, consequences, treatment and how to manage a change in QoL caused by AF (2).

In addition, the relationship between physical exercise and AF has been disputed. Among 64,561 patients, Qureshi et al. found an inverse relationship between cardiorespiratory fitness and incident AF, especially in obese subjects who underwent exercise treadmill testing (3). In 825 obese patients with AF, Pathak et al. demonstrated a lower burden of AF in patients who lost weight and improved their cardiorespiratory fitness (4, 5). Pathak et al. also demonstrated a beneficial effect of aggressive risk factor management on the long-term success of AF ablation (6). Randomized studies on patients with primarily permanent AF have demonstrated beneficial effects of physical exercise on physical capacity, AF symptoms and QoL (7–11).

The prevalence of AF is increasing (12), therefore, it is important to investigate whether a rehabilitation

programme can improve QoL and physical exercise capacity in patients with AF and, potentially, prevent readmissions.

### Objective

The aim of this study was to investigate whether a rehabilitation programme with group education, physical exercise, optimization of medical treatment and monitoring of lifestyle changes can improve QoL and physical exercise capacity in patients with AF.

## METHODS

### Design

Clinical randomized controlled trial. ClinicalTrials.gov (record N-20120002).

### Patients

Patients with paroxysmal or persistent AF admitted to the Department of Cardiology, Aalborg University Hospital between 6 June 2012 and 4 April 2013 were consecutively invited to participate in the study. All patients received treatment according to the current guidelines. Patients who provided informed consent to participate were randomized to either specialized cardiac rehabilitation or standard follow-up. The rehabilitation programme consisted of groups of 10 patients.

At the primary admission, all patients underwent echocardiography and blood samples were taken.

**Inclusion criteria.** Patients  $\geq 18$  years of age, hospitalized at the Department of Cardiology, Aalborg University Hospital, with a diagnosis of paroxysmal or persistent AF documented by an electrocardiogram (ECG) or  $> 30$  s of AF recorded by long-term monitoring. All participants received oral and written information prior to providing written informed consent.

**Exclusion criteria.** Patients who qualified for cardiac rehabilitation due to other cardiac conditions (congestive heart failure or CHD) were excluded. If AF was caused by a reversible condition patients were also excluded.

Heart failure (New York Heart Association (NYHA) class III–IV or Left Ventricular Ejection Fraction (LVEF)  $< 40\%$ ) or valvular heart disease and patients admitted for radiofrequency ablation were also excluded. Patients considered too ill, physically or mentally, to participate in rehabilitation by the treating physicians were excluded.

### Randomization

Randomization was electronically, randomizing the participants into 2 groups of 20 participants at a time.

### Rehabilitation

The rehabilitation programme included education, physical exercise, optimization of the medical treatment and discussion of implications on daily life.

The group sessions with a doctor, a nurse, a dietician or a psychologist was scheduled once a week for 1 h for the first 8 weeks. The education included information on pathophysiology, risk factors, treatment, diet and coping mechanisms for living with AF.

The exercise programme was conducted as 1-h sessions twice a week for 12 weeks and supervised by a cardiac rehabilitation physiotherapist. Each training session consisted of at least 30 min of aerobics  $\geq 70\%$  of maximum exercise capacity estimated from a maximum cycle ergometer test with ECG monitoring and graded on the Borg scale (score 14–16) and interval training with elements of strengthening exercises (13).

Patients were encouraged to be moderately physically active  $\geq 30$  min each day and, if they missed a group training session, to perform 30 min of high-intensity activities.

### Medication

The medical treatment was optimized according to the current guidelines.

### Quality of life

At inclusion and after 3, 6 and 12 months, all participants completed the following disease-specific QoL questionnaires: Health-related Quality of Life in patients with Atrial Fibrillation (AF-QoL-18) and Atrial Fibrillation Effect on Quality of Life (AFEQT) and the generic QoL questionnaires: Generalised Anxiety Disorder Assessment (GAD-7), Patient Health Questionnaire (PHQ-9) and EuroQol 5D (EQ-5D).

AF-QoL-18 includes 18 questions on 3 domains: psychological, physical and sexual activity. The answer score range from zero (worst) to 100 (best). AFEQT includes 20 questions on treatment, symptoms and daily activity during the last 4 weeks. The score range from 20 (best) to 140 (worst).

GAD-9 assesses anxiety and results range from zero (worst) to 21 (best). PHQ-9 focuses on depression symptoms during the latest 2 weeks ranging from zero (best) to 27 (worst). EQ-5D consists of 5 questions on mobility, self-care, usual activities, pain/discomfort, anxiety/depression and a visual analogue scale (EQVAS) assessing self-estimated health status.

### Physical exercise tests

At inclusion and after 3 and 6 months, all participants were tested by an ergometer cycle test, a 6-min walk (6MW) test and a 5-repetition-sit-to-stand (5RSS) test.

The ergometer cycle test was performed in accordance with the standard for exercise testing of the American Heart Association (14). The maximal physical capacity test was used as an indirect measure of the maximum exercise capacity. Participants started at 50 Watt (W), with a 25-W load increase for each 2 min until the participants could no longer maintain a speed of 60 rotations/min due to fatigue/dyspnoea.

The 6MW test is a simple, safe and inexpensive test to estimate submaximum exercise capacity. The test results correlate well with functional capacity and can be used prognostically (15).

The 5RSS test is also a simple, safe and inexpensive test evaluating the strength of the lower extremities by the patient standing up from a sitting position as quickly as possible 5 times in a row (16).

All tests were performed by one of 2 trained physiotherapists, who were blinded to whether the participant participated in rehabilitation.

### Statistical analysis

**Quality of life.** From the study by Arribas et al. in 2010 (17), mean and standard deviation (SD) of AF-QoL-18 in a population of Spanish patients with AF were stated to be: mean 38.9 and

(SD 21.5). With a level of significance of 0.05, a power of 0.8 and a difference between groups of 17 (corresponding to, for example, means 39 and 22), the necessary number of patients in each randomization arm is  $n=26$ . No power calculation was made in relation to the other questionnaires.

**Maximum exercise capacity.** Hegbom et al., in 2006 (7), compared changes in maximum exercise capacity between 2 groups of patients with AF, of which only one group received active exercise therapy. From this paper, mean and SD of changes in measure of maximum exercise capacity (CW max) are stated as 0.3 and 0.26 ( $W \times \min$ ), respectively. With a level of significance of 0.05, a power of 0.8 and a difference between groups of 0.3 (corresponding to, for example, means before/after of 1.3/1.6 for the active group and 1.3/1.3 for the passive group), the necessary number of patients in each randomization arm is  $n=16$ .

The differences in time course in mean outcome values between the 2 randomization groups at baseline and at 3, 6 and 12 months were analysed by repeated measures ANOVA, taking into account the within-patient correlation. All hypotheses were specified *a priori*, thus, no corrections for multiple testing were made (18). Assumptions of normality and variance homogeneity were assessed by residual plots. Sensitivity analyses were performed using robust variance estimation to manage potential variance heterogeneity, using log-transformed data to accommodate right skewness and using bootstrap when assumptions in general were not met. Stata statistical software (version 13; StataCorp LP, College Station, TX, USA) was used for randomization and analyses. Two-tailed  $p$ -values  $<0.05$  were considered statistically significant.

#### Ethical issues

All patients received oral and written information, emphasizing that participating in the study was voluntary and withdrawing their informed consent at any time would not affect the present or future treatment. The project was approved by the local ethics committee (approval number N-20120002) and conducted in conformity with the Declaration of Helsinki.

Data were collected according to the principles of good clinical practice and the project was reported to the Danish Data Protection Agency (2008-58-0028).

## RESULTS

A total of 823 patients were screened. The majority of patients did not meet the inclusion criteria (Fig. 1). The low inclusion rate (7%) was explained mainly by exclusion of patients who were eligible for other rehabilitation programmes or experienced comorbidities. Consequently, 90 patients eligible for inclusion were invited to participate in the study, of whom 58 (64%) accepted the invitation. Barriers to participation were mostly time-consumption or not being able to participate due to the patients' work.

Two patients from the rehabilitation group and 4 from the control group did not return the questionnaires and were lost to follow-up. Over 80% of the intervention group participated in  $\geq 75\%$  of the rehabilitation programme.

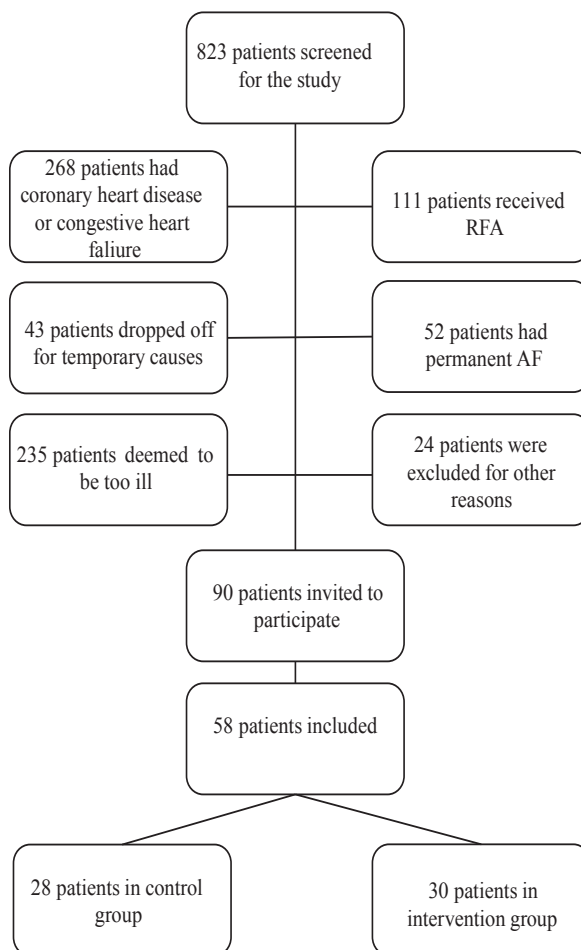
Baseline characteristics of participants are listed in Table I.

#### Questionnaires

For all QoL questionnaires, the trend was an increase in QoL from the baseline to 6 months questionnaire, which was higher in the intervention group than in the control group, although not all differences were statistically significant.

Using the AF-QoL-18 questionnaire, we found that the intervention group had a significantly higher increase in score during the first 6 months, but only a minor not statistically significant difference at 12 months (Table II and Fig. 2a). When separating the AF-QoL-18 into the 3 domains (physical, psychological and sexual activity), we found the same trend in all 3 sub-analyses, with the most pronounced effect in the physical domain (data not shown).

Results from the AFEQT questionnaire were similar (Table II and Fig. 2b).



**Fig. 1.** Flowchart of participants. RFA: radio frequency ablation, AF: atrial fibrillation.

**Table I.** Baseline characteristics of participants. All values are given as numbers unless otherwise stated in the table

	Control group (n = 24)	Intervention group (n = 28)	p-value for difference
Age, years, mean (SD) [range]	60.2 (8.9) [42.7–73.4]	62.2 (10.0) [32.6–77.6]	0.447
Female, n (%)	7 (29)	11 (39)	0.562
AF type, n (%)			0.177
Paroxysmal	9 (38)	16 (57)	
Persistent	15 (63)	12 (43)	
CHADS2VA2Sc score, n (%)			0.673
0	9 (38)	6 (21)	
1	8 (33)	11 (39)	
2	5 (21)	7 (25)	
3	2 (8)	4 (14)	
Symptoms, n (%)			
Fatigue	11 (46)	12 (43)	1.000
Dyspnoea	9 (38)	11 (39)	1.000
Palpitations	10 (42)	14 (50)	0.588
Dizziness	6 (25)	11 (39)	0.376
Syncope	1 (4)	3 (10)	0.615
Chest pain	10 (42)	7 (25)	2.450
Asymptomatic	3 (13)	5 (18)	0.711
Smoker, n (%)	1 (4)	1 (4)	1.000
BMI, kg/m <sup>2</sup> , mean (SD) [range]	27.8 (3.9) [22.1–40.4]	27.9 (5.1) [21.1–43.4]	0.963
Oxygen uptake, l/min/kg, mean (SD) [range]	31.7 (8.3) [15.4–50.1]	29.0 (7.3) [16.5–42.0]	0.230
Medical treatment, n (%)			
Warfarin	11 (46)	11 (39)	0.779
Dabigatran	3 (13)	2 (7)	0.652
ASA	2 (8)	2 (7)	1.000
Beta blocker	16 (67)	18 (64)	1.000
Amiodarone	2 (8)	3 (11)	1.000
Flecainide	4 (17)	3 (11)	0.690

BMI: body mass index; AF: atrial fibrillation; SD: standard deviation; ASA: acetylsalicylic acid.

The PHQ9 and GAD questionnaires showed that patients in both groups achieved a higher QoL after 6 months, but the increase was statistically significantly higher in the intervention group. From 6 to 12 months a lower QoL was found in both groups without statistical significance at the end of the study (Table II and Figs 2c and 2d).

A similar trend was found using the EQVAS, with an initial not statistically significant increase in QoL for the intervention group that decreased at the end of the study (Table II and Fig. 2e).

### Physical training

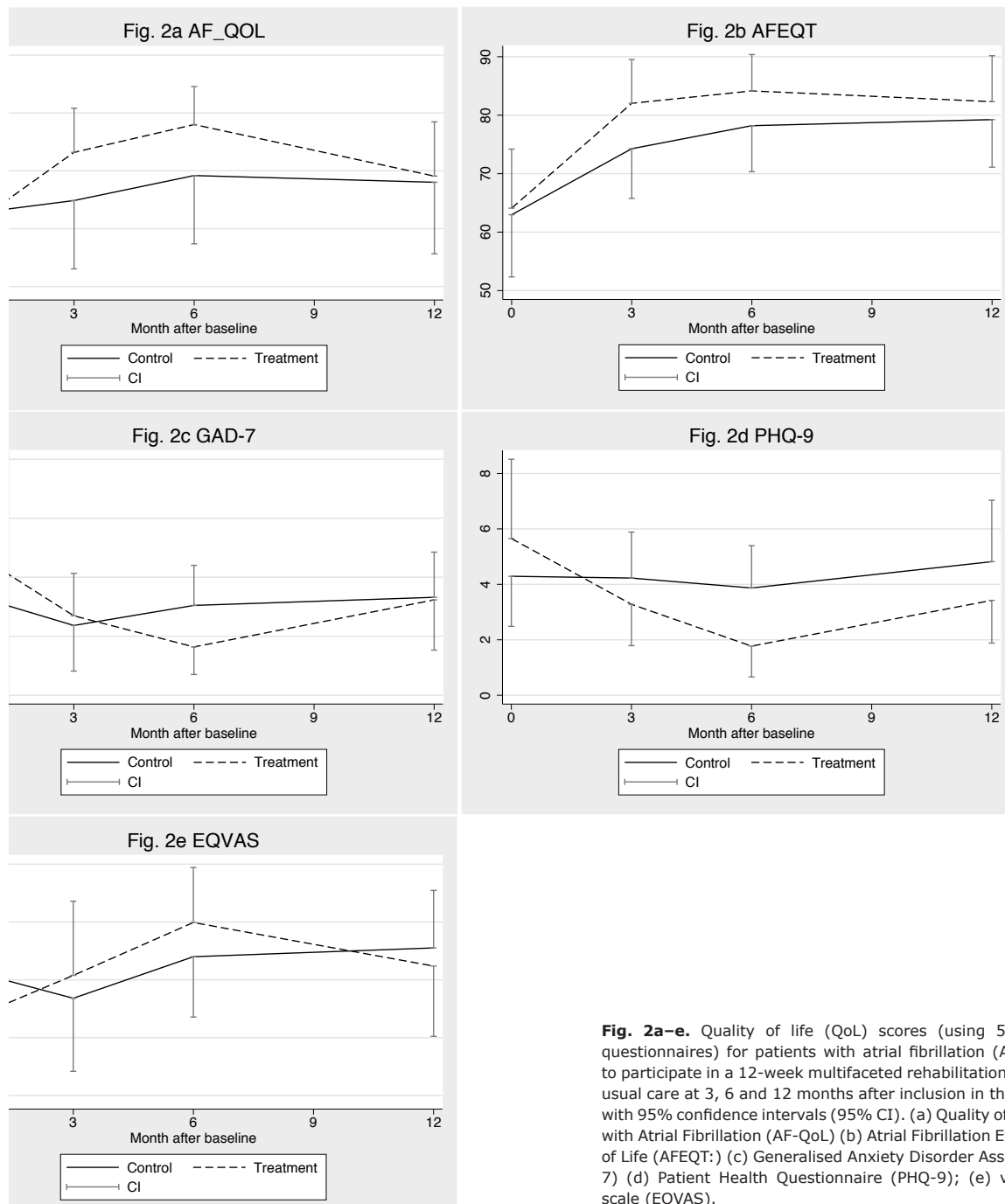
As shown in Fig. 3 and Table III, the participants in the intervention group had a lower maximum exercise capacity and oxygen (O<sub>2</sub>) uptake and an inferior performance in the 5RSS test at baseline than the control group despite the electronic randomization. The control group did not improve their exercise capacity and O<sub>2</sub> uptake during the study, whereas in the intervention group, the maximum exercise capacity increased significantly from baseline to 3 months and remained steady

**Table II.** Scores from quality of life (QoL) questionnaires at baseline and after 3, 6 and 12 months. The first column with p-values stems from the unpaired comparison between treatment groups at baseline. Subsequent p-values stem from unpaired comparisons of changes from baseline

Questionnaire		Baseline		3 months		6 months		12 months	
		Mean (SD)	p-value	Mean (SD)	p-value	Mean (SD)	p-value	Mean (SD)	p-value
AF-QoL-18	Control	52.2 (22.1)		57.3 (24.7)		59.2 (27.28)		58.0 (28.0)	
	Intervention	48.4 (22.8)	0.555	63.2 (18.9)	0.014*	68.0 (15.21)	0.031*	59.1 (23.2)	0.359
AFEQT	Control	66.3 (26.5)		78.2 (20.9)		82.3 (18.7)		83.4 (19.3)	
	Intervention	67.5 (26.3)	0.841	86.4 (19.5)	0.194	88.6 (15.1)	0.822	86.7 (20.5)	0.812
GAD-7	Control	3.6 (3.9)		2.4 (3.5)		3.0 (3.1)		3.3 (3.5)	
	Intervention	5.3 (4.9)	0.092	2.7 (3.6)	0.071	1.6 (2.1)	0.003*	3.2 (4.2)	0.074
PHQ-9	Control	4.3 (4.3)		4.2 (3.7)		3.9 (3.5)		4.8 (5.0)	
	Intervention	5.8 (7.3)	0.251	3.3 (3.6)	0.082	1.8 (2.5)	0.023*	3.4 (3.8)	0.028*
EQVAS	Control	76.2 (13.2)		73.4 (14.4)		77.0 (12.1)		77.8 (11.0)	
	Intervention	71.0 (15.9)	0.184	75.4 (15.9)	0.062	80.0 (11.0)	0.099	76.2 (15.0)	0.362

\*p-values from analysis of variance (ANOVA) test of difference between groups from baseline to time-point

QoL: quality of life; SD: standard deviation; AFEQT: Atrial Fibrillation Effect on Quality of Life; GAD-7: Generalised Anxiety Disorder Assessment; PHQ-9: Patient Health Questionnaire; EQ-5D: EuroQol 5D.



**Fig. 2a–e.** Quality of life (QoL) scores (using 5 different QoL questionnaires) for patients with atrial fibrillation (AF) randomized to participate in a 12-week multifaceted rehabilitation programme vs usual care at 3, 6 and 12 months after inclusion in the study. Shown with 95% confidence intervals (95% CI). (a) Quality of Life in patients with Atrial Fibrillation (AF-QoL) (b) Atrial Fibrillation Effect on Quality of Life (AFEQT:) (c) Generalised Anxiety Disorder Assessment (GAD-7) (d) Patient Health Questionnaire (PHQ-9); (e) visual analogue scale (EQVAS).

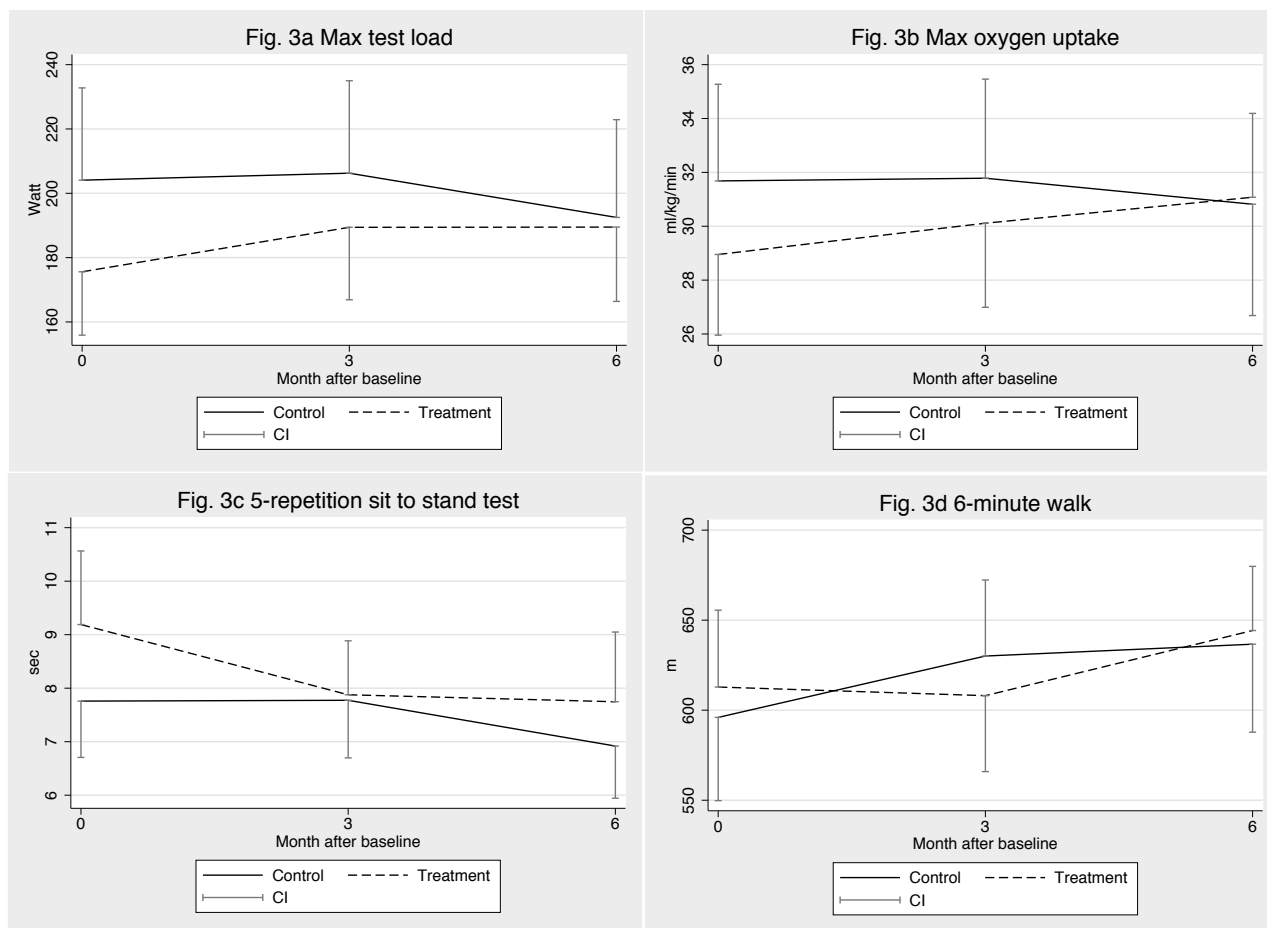
until 6 months. The maximum O<sub>2</sub> uptake increased from 29.0 ml O<sub>2</sub>/kg (SD 7.3) at baseline to 31.1 (SD 7.4) after 6 months.

In the 5RSS test, the rehabilitation group improved during the first 3 months and remained approximately the same for the next 3 months. The control group remained at the same level during the first 3 months but improved from 3 to 6 months. Thus, the difference

between the 2 groups was the same at 6 months as at baseline (Fig. 3 and Table III).

In the 6MW test, the baseline mean distance was similar between groups. A small improvement was observed in both groups from baseline to 6 months, but no statistically significant difference between groups.

Nine patients had AF during one or more of the physical tests. Stratification for AF or sinus rhythm did



**Fig. 3a–d.** Results from physical tests for patients with atrial fibrillation (AF) randomized to participate in a 12-week rehabilitation programme including physical exercise and education vs usual care at baseline and 3 and 6 months after inclusion in the study. Shown with 95% confidence intervals (95% CI). (a) Maximum exercise capacity; (b) maximum O<sub>2</sub> uptake; (c) Five-repetition-sit-to-stand test; (d) 6-min walk test.

not change the results of the physical tests significantly, but wider confidence intervals were observed.

Plots of residuals showed no violations of model assumptions. Sensitivity analyses confirmed our findings. Hence, the conclusions did not depend on a normal distribution of data or variance/covariance structure of data. Stratification by physical capacity at baseline, age, sex and type of AF did not differ from the main results.

No patients experienced adverse events during training.

During the study period, 38 patients had at least one readmission for cardiac reasons, mostly AF (rehabilitation group: 20 and control group: 18), 25 had at least one direct current cardioversion (rehabilitation group: 13 and control group: 12) and 11 had a radiofrequency ablation (rehabilitation group: 7 and control group:

**Table III.** Results of physical score tests at baseline and after 3 and 6 months. The first column with p-values stems from the unpaired comparison between treatment groups at baseline. The subsequent p-values stem from unpaired comparisons of changes from baseline

Physical score test		Baseline		3 months		6 months	
		Mean (SD)	p-value	Mean (SD)	p-value	Mean (SD)	p-value
Maximum exercise capacity, Watt	Control	204 (68)		206 (68)		193 (65)	
	Intervention	176 (48)	0.073	189 (56)	0.012*	190 (55)	0.026*
O <sub>2</sub> uptake, ml/kg/min	Control	31.7 (8.3)		31.8 (8.7)		30.8 (8.8)	
	Intervention	29.0 (7.3)	0.200	30.1 (7.7)	0.125	31.1 (7.4)	0.079
5-repetition-sit-to-stand test, s	Control	7.8 (2.4)		7.8 (2.6)		6.9 (2.1)	
	Intervention	9.2 (3.2)	0.058	7.8 (2.5)	0.011*	7.8 (3.1)	0.490
6-min walk test, m	Control	596 (104.3)		630 (100)		637 (104)	
	Intervention	613 (96)	0.951	608 (104)	0.138	644 (84)	0.734

\*p-values from analysis of variance (ANOVA) test of difference between groups from baseline to time-point. SD: standard deviation.

4). There was no statistically significant difference between groups.

## DISCUSSION

This study found that a full rehabilitation programme including group education and physical training for patients with paroxysmal or persistent AF was beneficial, with statistically significant improvement of QoL measured with both disease-specific (AF-QoL-18, AFEQT) and non-disease-specific (GAD-7, PHQ-9, EQ-5D) questionnaires during the first 6 months, after which the effect attenuated.

Five different questionnaires were used to assess different aspects of QoL. In all questionnaires, there was an increase in QoL for all participants from the start to the end of the study, which was consistent with results from other studies (19, 20). The intervention group experienced a higher increase in QoL during the first 6 months (although not statistically significant in all questionnaires) and a subsequent attenuation of the intervention effect compared with the control group. An earlier study regarding the AFEQT questionnaire suggested that a mean change of approximately 12 points was correlated with a small improvement and <5.3 points was an unimportant improvement (21). Our study showed a difference of 7.6 points after 3 months, potentially suggesting a small clinical importance.

In addition, a positive effect was found on maximum O<sub>2</sub> uptake, whereas no convincing improvement was found in the other physical tests.

At baseline, there was a statistically significant difference between the intervention and the control group in the performance of the physical tests despite randomization. However, this did not have any statistically significant effect on the results, as stratification by O<sub>2</sub> uptake at baseline did not show a different effect of training in patients with a low O<sub>2</sub> uptake compared with those with a high uptake.

Physical exercise has been shown to reduce the risk and magnitude of, for example, hypertension, diabetes mellitus and obesity, and has been shown to be beneficial for patients with CHD and congestive heart failure (22, 23). Thus, physical exercise may potentially lead to a reduction in the risk of developing AF. However, long duration of vigorous training may increase the risk of developing AF (8), although it seems that moderate physical exercise have a protective effect on patients with permanent AF (8, 24). Regarding physical exercise and non-permanent AF, Malmo et al. (25) found that aerobic interval training reduced the time in AF and improved QoL estimated from the Short Form-

36 (SF-36) questionnaire. Furthermore, training also significantly improved AF symptoms, VO<sub>2</sub> peak, left atrial and ventricular function.

Risom et al. (26) conducted a 12-week randomized trial on rehabilitation for patients with paroxysmal or persistent AF after catheter ablation. The authors found an improved physical capacity assessed by VO<sub>2</sub> peak, which is in line with our results. The authors did not find a statistically significant improvement in the 6MW test in the training group compared with the control group, which was comparable with our results. They did not find an improvement of the mental health based on a non-disease specific questionnaire. As radiofrequency ablation was an exclusion criterion in our study the results cannot be directly compared.

Skjelboe et al. included 76 patients with paroxysmal or persistent AF who were randomized to high- or low-intensity exercise for 12 weeks. Both groups improved their peak VO<sub>2</sub> significantly (11). QoL was not measured. Recent studies have compared AF patients and non-AF patients who joined a cardiac rehabilitation programme for other cardiovascular diseases or cardiovascular risk factors. Younis et al. found that patients with AF initially had lower physical capacity than non-AF participants, but improvement in physical capacity diminished the risk of total mortality and cardiovascular hospitalization for both groups (27). In a case control study Reed et al. found that rehabilitation improved QoL in both groups, but to a greater extent in patients without AF (28).

Although patients with paroxysmal AF may be in sinus rhythm most of the time, they may be less likely to be physically active because of anxiety about initiating AF (29). Even when patients were in sinus rhythm, this study showed that QoL and physical capacity could be improved. We also found an improvement of the 6MW test in the control group, perhaps because participating in the study encouraged patients to be more physically active even though they were in the control group. The bicycle tests favoured the intervention group, probably because bicycle training was a central part of the physical exercise programme.

Establishing whether physical exercise in patients with AF would be beneficial to reduce the risk of comorbidities and the burden of AF will require larger studies with longer follow-up.

The rehabilitation programme seemed to have the highest impact on reducing anxiety and depression and increasing physical and psychological well-being (estimated by questionnaires with focus on these domains: AF-QoL-18, GAD-7 and PHQ-9) and alleviating patients' symptoms (as assessed by AFEQT).



### Strengths

The strengths of this study include a complete rehabilitation programme, the use of disease-specific individualized training programmes and exercise tests performed by physiotherapists who were blinded to the 2 groups.

The study included patients with paroxysmal or persistent AF, whereas other studies have primarily included patients with permanent AF. Thus, in general, participants in our study seemed to have higher baseline scores compared with an unselected population of AF (17). Dudrik et al. have previously shown that progression from paroxysmal to persistent AF is associated with a decrease in health-related quality of life (30). We therefore performed stratified analyses on type of AF, but we did not find any differences in the effect of rehabilitation between the 2 groups.

This study examined the effect of a complete rehabilitation programme for patients with AF. Previous studies have shown beneficial effects of education about anticoagulation treatment on treatment compliance and found that physical training was beneficial regarding physical capacity and QoL (7, 9, 24, 28). In addition, non-randomized studies indicated a beneficial effect of physical exercise, weight loss, and aggressive risk factor management (5–7).

### Limitations

The primary limitation was the number of participants, although it was comparable with other studies in patients with AF (7–11). The physical training of the control group was not monitored. Due to logistics we could not include all relevant patients. Patients could not be included if they were admitted for a short period when no nurse or physicians leading the study were on duty. However, this is non-systematic selection and could therefore not influence the study results. Also, a precise registration of the AF burden would have been optimal, e.g. implanting a loop-recorder. However, the economy of the study was restricted. No information was collected regarding the degree of the patients' physical activity during the follow-up period, which could affect the QoL scores.

Thus, this study has limitations. No long-term positive effect of patient education and physical training on QoL of the studied patients was found. Therefore, the cost-effectiveness of this rehabilitation programme for this patient group is questionable.

### Conclusion

This study indicated that a multifaceted rehabilitation programme including education and physical training in patients with paroxysmal or persistent AF may have

a beneficial short-term (but no long-term) effect on QoL and physical exercise capacity estimated with disease-specific and generic QoL questionnaires.

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### REFERENCES

- Anderson L, Taylor RS. Cardiac rehabilitation for people with heart disease: an overview of Cochrane systematic reviews. *Cochrane Database Syst Rev* 2014; 12.
- McCabe PJ, Schad S, Hampton A, Holland DE. Knowledge and self-management behaviors of patients with recently detected atrial fibrillation. *Heart Lung J Acute Crit Care* 2008; 37: 79–90.
- Qureshi WT, Alirhayim Z, Blaha MJ, Juraschek SP, Keteyian SJ, Brawner CA et al. Cardiorespiratory fitness and risk of incident atrial fibrillation results from the Henry Ford exercise testing (FIT) project. *Circulation* 2015; 131: 1827–1834.
- Pathak RK, Elliott A, Middeldorp ME, Meredith M, Mehta AB, Mahajan R, et al. Impact of CARDIOrespiratory FITNESS on arrhythmia recurrence in obese individuals with atrial fibrillation the CARDIO-FIT Study. *J Am Coll Cardiol* 2015; 66: 985–996.
- Pathak RK, Middeldorp ME, Meredith M, Mehta AB, Mahajan R, Wong CX, et al. Long-term effect of goal-directed weight management in an atrial fibrillation cohort: a long-term follow-up study (LEGACY). *J Am Coll Cardiol* 2015; 65: 2159–2169.
- Pathak RK, Middeldorp ME, Lau DH, Mehta AB, Mahajan R, Twomey D, et al. Aggressive risk factor reduction study for atrial fibrillation and implications for the outcome of ablation: the ARREST-AF cohort study. *J Am Coll Cardiol* 2014; 64: 2222–2231.
- Hegbom F, Sire S, Haldal M, Orning OM, Stavem K, Gjesdal K. Short-term exercise training in patients with chronic atrial fibrillation: effects on exercise capacity, AV conduction, and quality of life. *J Cardiopulm Rehabil* 2006; 26: 24–29.
- Giacomantonio NB, Bredin SSD, Foulds HJA, Warburton DER. A systematic review of the health benefits of exercise rehabilitation in persons living with atrial fibrillation. *Can J Cardiol* 2013; 29: 483–491.
- Osbak PS, Mourier M, Kjaer A, Henriksen JH, Kofoed KF, Jensen GB. A randomized study of the effects of exercise training on patients with atrial fibrillation. *Am Heart J* 2011; 162: 1080–1087.
- Osbak PS, Mourier M, Henriksen JH, Kofoed KF, Jensen GB. Effect of physical exercise training on muscle strength and body composition, and their association with functional capacity and quality of life in patients with atrial fibrillation: a randomized controlled trial. *J Rehabil Med* 2012; 44: 975–979.
- Skjelboe AK, Bandholm TQ, Hakmann S, Mourier M, Kalleose T, Dixen U. Cardiovascular exercise and burden of arrhythmia in patients with atrial fibrillation – a randomized controlled trial. *PLoS One* 2017; 12: 1–16.

12. Go AS, Hylek EM, Phillips KA, Phillips KA, Chang Y, Hecnalt LE, et al. Prevalence of diagnosed atrial fibrillation in adults. *JAMA* 2001; 285: 2370–2075.
13. Borg GA. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc* 1982; 14: 377–381.
14. Fletcher GF, Ades PA, Kligfield P, Arena R, Balady GJ, Bittner VA, et al. Exercise standards for testing and training: a scientific statement from the American Heart Association. *Circulation* 2013; 128: 873–934.
15. Du HY, Newton PJ, Salamonson Y, Carrieri-Kohlman VL, Davidson PM. A review of the six-minute walk test: its implication as a self-administered assessment tool. *Eur J Cardiovasc Nurs* 2009; 8: 2–8.
16. Bohannon RW. Test-Retest Reliability of the five repetition sit-to-stand test: a systematic review of the literature involving adults. *J Strength Cond Res* 2011; 25: 3205–3207.
17. Arribas F, Ormaetxe JM, Peinado R, Peinado R, Perulero N, Ramirez P, Badia X. Validation of the AF-QoL, a disease specific quality of life questionnaire for patients with atrial fibrillation. *Europace* 2010; 12: 364–370.
18. Perneger TV. What's wrong with Bonferroni adjustments. *Br Med J* 1998; 316: 1236–1238.
19. Hagens VE, Ranchor AV, Van Sonderen E, Bosker HA, Kamp O, Tijssen JG, et al. Effect of rate or rhythm control on quality of life in persistent atrial fibrillation: results from the rate control versus electrical cardioversion (RACE) study. *J Am Coll Cardiol* 2004; 43: 241–247.
20. Jenkins L, Brodsky M, Schron E, Chung M, Rocco TJ, Lader E. Quality of life in atrial fibrillation: the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study. *Am Heart J* 2005; 149: 112–120.
21. Dorian P, Burk C, Mullin CM, Bubien R, Godejohn D, Reynolds MR, et al. Interpreting changes in quality of life in atrial fibrillation: how much change is meaningful? *Am Heart J* 2013; 166: 381–387.e8.
22. Giannuzzi P, Mezzani A, Saner H, Bjornstad H, Fioretti P, Mendes M, et al. Physical activity for primary and secondary prevention. Position paper of the Working Group on Cardiac Rehabilitation and Exercise Physiology of the European Society of Cardiology. *Eur J Prev Cardiol* 2003; 10: 319–327.
23. O'Connor CM, Whellan DJ, Lee KL, Keteyian SJ, Cooper LS, Ellis SJ, et al. Efficacy and safety of exercise training in patients with chronic heart failure: HF-ACTION randomized controlled trial. *JAMA* 2009; 301: 1439–1450.
24. Olshansky B, Sullivan R. Increased prevalence of atrial fibrillation in the endurance athlete: Potential mechanisms and sport specificity. *Phys Sportsmed* 2014; 42: 45–51.
25. Malmo V, Nes BM, Amundsen BH, Tjonna AE, Stoylen A, Rossvoll O, et al. Aerobic interval training reduces the burden of atrial fibrillation in the short term: a randomized trial. *Circulation* 2016; 133: 466–473.
26. Risom SS, Zwisler AD, Rasmussen TB, Sibilitz KL, Madsen TL, Svendsen JH, et al. Cardiac rehabilitation versus usual care for patients treated with catheter ablation for atrial fibrillation: results of the randomized CopenHeartRFatrial. *Am Heart J* 2016; 181: 120–129.
27. Younis A, Shaviv E, Nof E, Israel A, Berkovitch A, Goldenberg I, et al. The role and outcome of cardiac rehabilitation program in patients with atrial fibrillation. *Clin Cardiol* 2018; 41: 1170–1176.
28. Reed JL, Clarke AE, Faraz AM, Birnie DH, Tulloch HE, Reid RD, et al. The impact of cardiac rehabilitation on mental and physical health in patients with atrial fibrillation: a matched case-control study. *Can J Cardiol* 2018; 34: 1512–1521.
29. Hansson A, Madsen-Hårdig B, Olsson SB. Arrhythmia-provoking factors and symptoms at the onset of paroxysmal atrial fibrillation: a study based on interviews with 100 patients seeking hospital assistance. *BMC Cardiovasc Disord* 2004; 4: 1–9.
30. Dudrik EAMP, Erkuner O, Nieuwlaet R, de Vos CB, Weijs B Capucci A, et al. The influence of progression of atrial fibrillation on quality of life: a report from the Euro Heart Survey. *Europace* 2018; 20: 929–934.