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Five Months of Physical Exercise in Hemodialysis Patients: Effects on Aerobic Capacity, Physical Function and Self-Rated Health

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Key Words
Physical exercise · Physical fitness · Hemodialysis · Chronic renal failure · Quality of life

Abstract
Background: The number of chronic renal failure patients treated by hemodialysis (HD) is continuously increasing. Most patients have reduced physical capacity and have a high risk of cardiac and vascular diseases. The aim of this study was to determine the effects of 5 months physical exercise of HD patients' physical capacity, self-rated health and risk factors for cardiovascular disease. ***Methods:*** 33 HD patients were included in the study. *Inclusion criteria:* HD for more than 3 months, age >18 years. *Exclusion criteria:* Diabetes mellitus, symptomatic cardiovascular disease, musculoskeletal limitations, severe peripheral polyneuropathy, inability to speak Danish or English, dementia or other mental disorders. The patients were randomly assigned to an exercise group (EG, n = 22) or a control group (CG, n = 11). Prior to randomization, baseline testing was performed. The effects were measured by aerobic capacity, '2-min stair climbing', 'squat test', self-rated health (SF36), blood pressure and lipids. All tests were carried out by blinded testers. The intervention consisted of 1 h of physical exercise twice a week for 5 months. ***Results:*** 20 patients completed the intervention. Attendance was 74% of all sessions. There were no dropouts caused by complications related to the intervention. The EG had a significant increase in aerobic capacity, 'squat test' and Physical Function and Physical Component Scale (SF36). No significant changes were observed in any of the parameters in the CG. ***Conclusion:*** Physical exercise twice a week for 5 months increases physical function and aerobic capacity in HD patients. An exercise program with only two exercise sessions per week seems easy to implement in clinical practice with high attendance among participants. Further investigation is needed to determine the effects on blood pressure and lipids. There were no medical complications related to the exercise program.

Introduction

The prevalence of chronic renal failure patients treated by hemodialysis (HD) has continuously increased over the last decades. In Denmark the increase was 968 (144.5%) from 1991 to 2000 [1]. This was primarily due to an increase in the number of patients with diabetic nephropathy and acceptance of treating older patients.

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Previous studies have found that physical and aerobic capacity are extremely limited in HD patients compared to healthy subjects [2, 3]. Inactivity and disease-specific changes in muscle morphology are important reasons for this [3]. These factors affect the ability to perform daily activities and stay independent.

Furthermore, this group of patients suffers from comorbidities like hypertension and dyslipidemia, which are well-known cardiovascular risk factors. Mortality is high in HD patients and in Denmark 47.2% of HD patients die from cardiac and vascular diseases [1] compared to 33.2% in the general population in Denmark [4].

Several studies have investigated the effects of physical exercise in HD patients [3, 5, 6]. Most studies use interventions consisting of three or more exercise sessions per week [3, 5, 6], which may be unrealistic to implement in clinical practice. In addition to this, physical capacity has frequently been evaluated by testing aerobic capacity on stationary ergometer whereas physical function is rarely measured [3, 5, 6]. Furthermore, most exercise studies have not randomized participants and testers have not been blinded [3, 5, 6]. A recent non-controlled study with resistance training twice weekly demonstrated effects on physical function assessed by 6-min walk test, gait speed and sit-to-stand-to-sit test [7].

This study was designed to determine the effects of physical exercise on aerobic capacity, physical function, self-rated health and cardiac and vascular risk factors in a group of HD patients.

Subjects and Methods

Participants

The study took place at the Department of Medical Orthopaedic and Rehabilitation and the Department of Nephrology P, University Hospital of Copenhagen, Rigshospitalet, Denmark. From the Dialysis Centre, 100 HD patients from a total of 260 were invited to participate in the study. To be included the participants had to be over 18 years of age and treated by HD for more than 3 months. Patients with diabetes mellitus, symptomatic heart disease, orthopedic limitations, severe peripheral polyneuropathy, dementia and participation in other trials with the risk of affecting the results were excluded. Inability to speak either Danish or English excluded patients from the entire study, whereas those patients able to speak English were only excluded from the questionnaire.

Thirty-three patients volunteered for the study and completed baseline tests prior to randomization. The participants were randomly assigned to either the intervention or the control (ratio 2:1). Randomization was performed by 2 blinded persons by the envelope method. The participants were retested after the intervention. All tests were carried out by blinded testers.

The exercise tests were performed with exactly the same relation to the dialysis procedure for each individual before and after the intervention period. Informed consent was obtained from all patients. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the local ethical committee.

Aerobic Capacity

The aerobic capacity was measured at baseline and again with the same workloads up to 10 days after completing the intervention program. The standard test chosen is previously described and has been used in studies of other chronically weakened patients (rheumatoid arthritis) [8]. The test was performed on an electrically braked Krogh bicycle ergometer with the person placed in a chair 5 cm above the crank. The test consisted of two submaximal workloads (45 t and 65% of the estimated maximal capacity (pre-training) of the person) with a pedalling rate of 60 rpm each maintained for steady state (5 min). The test was terminated after a 1- to 2-min spin at the expected maximal workload and with the highest possible pedalling rate ('supramaximal workload'). The oxygen uptake as well as heart rate (ECG) was measured continuously during the test (breath by breath (Medical Graphics CPX express)) and the peak value regarded as max VO_2. Blood pressure was measured before and after the test.

Physical Function

Physical function was measured by (1) 2-min stair-climbing test [9] – the number of steps covered ascending and descending two flights of stairs as many times as possible for 2 min were registered; (2) squat test [10] – the time to perform ten consecutive standardized unsupported squats was registered (a modified version of the original). These tests have been validated in other old and chronically ill patients [9, 10].

Self-Rated Health

To investigate self-rated health, the Danish version of the questionnaire Short Form 36 (SF36) was used [11]. The questionnaire comprises eight dimensions covering physical, mental and social aspects of health. On each dimension a score from 0 to 100 was calculated according to standard procedure. Scores were also transformed into a physical component scale and a mental component scale. Higher score indicates better health.

Blood Pressure

Blood pressure was measured before three consecutive HD sessions and was calculated as an average. The use of antihypertensives through the study period was registered as well.

Lipids

Plasma total cholesterol and triglyceride were measured enzymatically (Autoanalyser; Hitachi). Plasma high-density lipoprotein (HDL) cholesterol was measured after the precipitation of very-low-density lipoprotein (VLDL) and low-density lipoprotein (LDL) with phosphotungstic acid (Boehringer Mannheim, Germany). Plasma LDL cholesterol was calculated by Friedewald's formula: LDL cholesterol = total cholesterol – (HDL cholesterol + VLDL cholesterol), where VLDL cholesterol = 0.47 · triglyceride.

Intervention

The exercise group (EG) participated in 1 h of physical exercise twice a week for a period of 5 months. The program consisted of

10 min of warm-up, 20–30 min of strength and aerobic exercises like step and circuit training, high and low impact aerobics and 15–20 min spin on a Monark stationary ergometer at variable intensity. The exercise program was supervised by a physiotherapist.

In general, the intensity was adjusted to 14–17 using Borg's rating of perceived exertion [12]. The spin on ergometers included at least 9 times of spin in 20 s on an intensity rated as 17 on the Borg Scale. The session was concluded by 5–10 min stretching and cooling down. During the intervention period the intensity was individually adjusted. In the first 2 months the intensity was adjusted every week and thereafter every second week. The exercise program was tested in a pilot study before the present study [unpubl. data]. Participants in the control group (CG) were requested to continue their normal way of living.

Statistical Analysis

Statistical analysis was carried out using the SPSS 10.0 statistical package. Data are presented as median and range. Wilcoxon-Mann-Whitney test was used to compare the exercise and the CG at baseline and to investigate differences in the changes after the observation period between the exercise and the CG. Wilcoxon signed ranks test on paired observations was used within groups to investigate the changes from baseline to after the exercise period. All tests were two-tailed at a significance level of $p \leq 0.05$.

Table 1. Age, sex and clinical data. Data are expressed as median (range)

	Exercise (n = 22)	Control (n = 11)
Age, years	59 (25–58)	48 (23–58)
Sex, f/m	8/14	3/8
Duration of disease, months	114 (4–720)	60 (3–192)
Duration of HD, months	23.5 (4–180)	17 (3–60)
Hemoglobin, mmol/l	7.3 (6.4–7.9)	7.6 (6.0–8.0)
Diagnosis		
Polycystic kidneys	5	1
Glomerulonephritis	11	3
Renis contractus bilat.	1	0
Chronic pyelonephritis	1	0
Obstructive uropathy	1	0
Vascular	0	1
Unknown	3	6

Results

Participants

The basic characteristics of the participants are presented in table 1. There were no significant differences between the EG and the CG.

From a total of 33 patients, 11 from the EG and 9 from the CG completed the study. The reasons for dropping out of the EG were: regret participating in the study or lack of time (n = 8) and medical complications not related to the intervention (n = 3). The reasons for dropping out of the CG were: moving to another dialysis center (n = 1) and disinterest (n = 1). Demographic data and duration of chronic renal failure as well as duration of dialysis in the dropouts did not differ from those who completed the study. Attendance in the EG was 74% of all exercise sessions.

No statistical significant difference was found between the two groups in any of the tests at baseline (tables 2–4). The exercise tests were performed on a non-dialysis day in 17 patients and immediately before dialysis in 3 patients both at baseline and after the intervention period.

Aerobic Capacity

The EG improved significantly in VO_2 max ($p = 0.012$). No change was observed in the CG and the difference in between groups was significant. Data are presented in table 2.

Physical Function

In the squat test, the EG increased significantly ($p = 0.004$), while there was no change in the CG. The difference in between groups was not significant. In the 2-min stair-climbing test, no change was observed in any of the groups (table 2).

Self-Rated Health

SF36 scores and changes are presented in table 3. Physical function score increased significantly ($p = 0.001$) in the EG, while there was no change in the CG. Difference in between groups in physical function was statistically significant after the intervention ($p = 0.004$). Physical component scale score increased significantly in the EG with no significant change in the CG. The difference in between groups was not significant. Bodily pain changed significantly in the TG. Two patients from the CG did not complete the questionnaire because of inability to speak Danish.

Blood Pressure

Blood pressures are shown in table 4. No significant changes were observed in blood pressure and in use of antihypertensive drugs in either of the two groups.

Lipids

The results of total cholesterol, HDL, LDL and triglyceride are shown in table 4. No significant changes were observed in either of the two groups.

Table 2. Physical function and aerobic capacity before and after intervention; median (range)

Outcome	Group (n)	Baseline	Retest	p
Squat, s	EG (10)	17.03 (12.61–26.58)	14.43 (9.84–23.51)	0.004
	CG (7)	16.25 (13.83–24.43)	18.18 (12.47–26.00)	NS
Stair climbing	EG (10)	219.5 (146–406)	234 (152–495)	NS
Number of steps	CG (7)	282 (121–330)	247 (132–363)	NS
VO_{2max}, ml/min/kg	EG (9)	18.8 (0.89–2.13)	20.9 (0.95–2.48)	0.012*
	CG (9)	23.1 (0.76–2.27)	24.0 (0.93–2.07)	NS

* Significant difference between groups.

Table 3. SF36 score before and after intervention; median (range)

Outcome	Group (n)	Baseline	Retest	p
Physical function	EG (11)	80 (45–90)	85 (65–95)	0.01*
	CG (7)	75 (60–90)	80 (30–90)	NS
Role physical	EG (10)	50 (0–100)	75 (0–100)	NS
	CG (7)	100 (0–100)	75 (0–100)	NS
Bodily pain	EG (11)	84 (31–100)	100 (62–100)	0.03
	CG (7)	62 (32–100)	84 (62–100)	NS
General health	EG (11)	60 (15–100)	57 (20–100)	NS
	CG (7)	52 (32–72)	72 (5–87)	NS
Vitality	EG (11)	70 (35–100)	70 (45–100)	NS
	CG (7)	55 (50–90)	75 (5–85)	NS
Social functioning	EG (11)	100 (50–100)	100 (62.5–100)	NS
	CG (7)	88 (25–100)	100 (62.5–100)	NS
Role emotional	EG (10)	100 (0–100)	100 (33.33–100)	NS
	CG (7)	100 (33–100)	100 (0–100)	NS
Mental health	EG (11)	88 (52–100)	84 (68–100)	NS
	CG (7)	84 (56–100)	76 (52–100)	NS
Physical component scale	EG (10)	46.6 (25–53)	47.0 (33–56)	0.004
	CG (7)	41.1 (32–52)	48.9 (26–56)	NS
Mental component scale	EG (10)	59.7 (35–65)	55.2 (43–63)	NS
	CG (7)	51.7 (40–65)	55.1 (34–62)	NS

* Significant difference between groups.

Table 4. Blood pressures and lipids before and after intervention; median (range)

Outcome	Group (n)	Baseline	Retest	p
Systolic blood pressure	EG (11)	139 (108–183)	141 (93–155)	NS
mm Hg	CG (8)	145 (118–162)	144.5 (118–189)	NS
Diastolic blood pressure	EG (11)	78 (53–98)	77 (53–110)	NS
mm Hg	CG (8)	88.5 (60–106)	85.5 (60–114)	NS
Cholesterol, mmol/l	EG (11)	4.8 (3.2–6.7)	4.9 (3.4–6.1)	NS
	CG (9)	4.6 (3.5–5.4)	4.2 (2.7–5.9)	NS
High-density lipoprotein	EG (11)	1.0 (0.8–2.4)	1.2 (0.8–2.2)	NS
mmol/l	CG (9)	1.3 (0.8–2.4)	1.3 (0.73–1.99)	NS
Low-density lipoprotein	EG (11)	2.9 (1.4–4.8)	2.2 (0.6–4.3)	NS
mmol/l	CG (9)	2.5 (1.3–3.4)	2.5 (1.1–3.2)	NS
Triglyceride, mmol/l	EG (11)	1.33 (0.58–3.54)	1.32 (0.19–3.34)	NS
	CG (9)	1.04 (0.47–4.25)	0.99 (0.64–1.92)	NS

Discussion

This randomized clinical trial differs from many exercise trials in HD patients by focusing on self-rated and objective measured physical function and by introducing an intervention with two exercise sessions per week.

The results demonstrate that exercise improves physical capacity in HD patients. There was a significant increase in both objective and subjective outcomes: ability to perform squats, aerobic capacity and the self-rated physical function and bodily pain. The stair-climbing test indicated a slight increase, but did not reach significant levels. There were no changes in blood pressure and lipid levels. No medical complications related to the intervention were observed.

We believe that there are two main reasons for offering physical exercise to HD patients: HD patients have seriously decreased physical capacity and a high risk of cardiac and vascular diseases. Therefore, physical exercise should be considered as both prophylaxis and rehabilitation.

Recent studies have documented impaired physical function up to 34.1% in HD patients compared to healthy controls [13]. This impairment is probably caused by reduction in muscle strength and aerobic capacity. In most exercise trials, the effect on physical capacity is only determined by testing aerobic capacity on stationary ergometer. An increase in aerobic capacity is not necessarily accompanied by an increase in physical function.

Tests with elements of everyday activities are more appropriate measures, since physical function is important for handling everyday activities and staying independent. Therefore, physical function becomes an important outcome in evaluating the effect and is used in recent trials [7, 14]. In the present study, the most pronounced improvement was found in self-rated physical function. We believe that the patients' sensation of improvement in activities related to their everyday life is an important motivating factor for adherence to exercise programs. In the mental and social dimensions of SF36, no changes were seen. The SF-36 is a generic questionnaire and may therefore not be sensitive to disease-specific changes. A Danish version of the disease specific questionnaire Kidney Disease Quality of Life-Short Form [15] was not available during the study period, but will soon be published [unpublished data by Eidemak I, Molsted S, Heaf J, but now available on www.gim.med.ucla.edu/kdqol/]. Bodily pain was diminished after the study period in the EG. This is a notable aspect, since bodily pain is significantly higher (lower score in SF36) in HD patients compared to the general population [16].

Cardiac and vascular diseases are frequently seen in HD patients. Hypertension is seen in the majority of patients and is considered one of the most important risk factors for cardiac and vascular diseases. Some trials have studied the effects of physical exercise on hypertension in HD patients, but have conflicting results [5, 17–20]. In a recent non-randomized but controlled study, exercise during dialysis reduced the use of antihypertensive medications [21]. The difference in antihypertensive medications was calculated as difference in numbers of antihypertensive drugs per patient before and after the intervention. In the present study there was no significant effect on blood pressure or in use of antihypertensive medications. This could be explained by the short intervention period, too few exercise sessions per week, or an inaccurate method for measuring blood pressure. When planning the study, the intention was to monitor blood pressure by 24-hour measurements. Unfortunately, this was not possible due to technical complications.

In healthy subjects, physical inactivity is associated with risk for mortality to a similar extent as cigarette smoking, hypertension and high cholesterol [22]. The connection between physical inactivity and mortality in HD patients has recently been studied and demonstrate association between physical inactivity and higher mortality in dialysis patients [23]. Another study found that the level of physical activity in HD patients was significantly lower than among healthy sedentary controls [2], which makes physical exercise in HD patients important.

Besides low physical function and the risk of cardiac and vascular disease, HD patients often suffer from other co-morbidities upon which exercise may have a positive effect. Reduced bone mineral density and low insulin sensitivity are well-known problems in HD patients [24, 25]. Studies in other groups of patients with the above-mentioned problems have shown positive effects of physical exercise [26, 27]. In addition to this, the costs of offering physical rehabilitation programs in dialysis centres are very low and may well prove to be cost-effective.

Fatigue in HD patients can make it difficult to motivate to physical exercise. Most previous studies have used interventions consisting of three or more exercise sessions per week. If attempting to implement such exercise programs, we would assume that attendance would be low due to fatigue and lack of time among the patients. In the present study we used an intervention with exercise sessions twice a week in relation to HD, which we believe increases attendance in clinical practice.

Patients with diabetes mellitus and severe heart disease were excluded in this study in order to minimize the risk of medical complications following high intensity exercise. However, with a lower level of intensity, these categories of patients should be able to participate and benefit from exercise programs as well.

The conclusion of this study is that a physical exercise program twice a week increases physical function and aerobic capacity in HD patients. Further investigation is needed to determine the effects on blood pressure and dyslipidemia and other complications like osteodystrophy and insulin resistance. There were no medical complications related to the exercise program.

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