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ARTICLE

Effects of a 16-week physical training on clinical outcomes in patients with hypertension and chronic kidney disease: NEPHROS post-trial follow-up

Os efeitos de um treinamento físico de 16 semanas sobre desfechos clínicos em pacientes com hipertensão e doença renal crônica: o estudo NEPHROS de seguimento pós-ensaio

Efectos de un entrenamiento físico durante 16 semanas en los resultados clínicos de pacientes afectados de hipertensión y enfermedad crónica de riñón: NEPHROS seguimiento post ensayo

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Abstract

The NEPHROS is a randomized controlled trial which applied a 16-week aerobic and resistance training to patients with chronic kidney disease (CKD) and high blood pressure. This report describes a long-term post-trial follow-up, comparing survival, health-related quality of life (HRQoL), and estimated glomerular filtration rate (GFR) change between the intervention and control groups according to in-trial cardiovascular risk factors. Three years after the original trial, NEPHROS participants were re-evaluated. Cox proportional hazards model was used to compare survival time and linear regression for changes in GFR and physical and mental HRQoL summary scores between intervention and control groups according to age, sex, and in-trial GFR, C-reactive protein, glucose, lipids, ankle-brachial index (ABI), functional capacity, and blood pressure. Of the 150 participants of NEPHROS, 128 were included in the long-term analysis. The previous exercise training had no effects on survival, GFR, or HRQoL. Baseline in-trial GFR (HR = 0.95, 95%CI: 0.92; 0.98) and ABI (HR = 0.03, 95%CI: 0.002; 0.43) were positive independent predictors for survival. Lower ABI (coefficient = 9.00, 95%CI: 0.43; 17.5) and higher systolic blood pressure (coefficient = -0.13, 95%CI: -0.24; -0.03) were independent predictors for GFR decline. A 16-week exercise program had no long-term effect on survival, quality of life, or glomerular filtration in patients with CKD stages 2 to 4. Lower GFR and ABI and higher systolic blood pressure were associated with poorer prognosis among CKD patients.

Chronic Kidney Disease; Hypertension; Exercise; Survival; Ankle Brachial Index

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Introduction

The burden of non-communicable chronic diseases (NCD), including hypertension, diabetes, and chronic kidney disease (CKD), is increasing worldwide [1,2]. The scenario is especially worrisome in emerging countries such as Brazil, characterized by rapid urbanization and the population's increasingly sedentary lifestyle, a greater access to high-calorie diets, with persisting inequalities in access to health care [3].

NCDs frequently affect each other, and the prognosis worsens progressively according to the number of comorbidities [4]. Around 80% of CKD patients also have hypertension. Moreover, higher blood pressure is usually associated with faster decline in glomerular filtration rate (GFR) and increased mortality [5]. GFR lowering, in turn, has a linear association with higher cardiovascular mortality [6].

Cohort studies indicate that daily physical activity decreases installation and progression of both high blood pressure and CKD [7]. The positive effects of physical activity are attributed to improved inflammatory and metabolic profiles, among others [8]. Some randomized controlled trials have also shown positive short-term effects of structured exercise interventions on cardiovascular disease risk factors [9,10], including NEPHROS trial [11,12]. However, the long-term effects have been poorly investigated. Practicing physical exercise regularly is difficult, even with motivational and material support [13]. Data on exercise maintenance after structured short-term training and its effects on clinical endpoints, particularly in CKD patients, is still incipient.

This study reports a long-term post-trial follow-up of participants of the NEPHROS randomized controlled trial, in which CKD patients from stages 2 to 4 underwent a 16-week aerobic and resistance training. The exercise was associated with decreased high sensitivity C-reactive protein and fasting plasma glucose, and increased functional capacity, with no effects on estimated GFR (eGFR) decline, different than usual care [12]. The main objective of this follow-up was to analyse the effects of the exercise intervention and baseline cardiovascular disease risk factors on survival, quality of life, and CKD progression.

Methods

This report describes the findings of a post-trial observational follow-up study (of 3 years) of patients who underwent a 16-week exercise training or usual care (control group). The randomized controlled trial was designed to verify how a physical training program affects GFR , blood pressure, glucose and lipids, health-related quality of life (HRQoL), ankle-brachial index (ABI), and the functional capacity (Time Up-and-Go, 2-Minute Step and 30-Second Chair-Stand tests) of hypertensive adults with CKD stages 2 to 4 [11].

Summary description of the NEPHROS trial

The inclusion criteria were non-diabetic patients over 18 years old diagnosed with high blood pressure and with eGFR between 15 and 59mL/minute/1.73m^2 or proteinuria above 300mg in 24 hours. Exclusion criteria were patients with severe disability or amputated lower limbs without prosthesis, a history of acute myocardial infarction in the last 6 months, and previous kidney transplantation.

The medical records of about 8,000 hypertensive adults registered in 17 primary health care units in the municipality of Pelotas, Rio Grande do Sul State, Brazil, were reviewed and 935 eligible patients were identified. A total of 114 individuals were excluded and 671 refused to participate, whereas 150 were included in baseline measurements and randomly allocated to the exercise group (n = 76) or the control group (n = 74). The study protocol was approved by the Ethics Research Committee of the Federal University of Pelotas (UFPEL; approval n. 01/11), affiliated with the Brtazilian National Research Council; and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. All included patients signed an informed consent form, and Clinical Trial Registration (NEPHROS – NCT01935297, https://clinicaltrials.gov/).

The outcome variables were measured eight weeks after enrollment and by the end of the intervention (16th week). The intervention included 60-minute aerobic and resistance training three times a week. The control group received usual care. After the intervention, patients of both groups were advised to maintain regular exercise according to their capacity and available resources, such as walking, jogging, cycling, or swimming for at least 30 minutes, 5 days a week. Additional details about the trial have been published previously [11,12].

Post-trial observational follow-up study

- **Subjects**

All 150 patients included in the randomized controlled trial in control or intervention groups were searched for three years after the baseline assessment. The initial approach was by telephone, followed by outpatient clinic evaluation. Patients who were still alive were invited for serum creatinine measurement and HRQoL evaluation and questioned about regular physical activities and exercise with the following question: "Do you currently practice any type of exercise or sport regularly (i.e., 2 or 3 times a week?)".

- **Predictors**

The previous exercise intervention (intervention vs. control group) was the main exposure in the outcome analysis. The following in-trial cardiovascular disease risk factors were analyzed as secondary predictors: age (in years), sex (male/female), smoking status (no, current, or former smoker) and the mean of the measurements (baseline, 8th week, and 16th week) of fasting plasma glucose (g/dL), total cholesterol and in fractions (mg/dL), triglycerides (mg/dL), high sensitivity C-reactive protein (mg/dL), blood pressure (mmHg), ABI (excluded if above 1.4), HRQoL scores, functional capacity tests, and body mass index – BMI (kg/m^2).

Outcomes

- **Survival**

The time and cause of death were obtained from relatives by telephone calls. NEPHROS participants who were declared dead by relatives and those whose relatives could not be located were searched for in the public death registry system.

- **Changes in eGFR**

Plasma creatinine was measured using the Jaffe method and Roche chemicals in the same laboratory by an examiner blind to the subjects' allocation. The GFR was estimated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. The difference between the GFR estimated 35 months after the intervention and the mean of the 3 in-trial GFRs was considered a long-term change in GFR.

- **Changes in HRQoL**

The health-related quality of life was measured using the Medical Outcomes Study 36-Item Short Form (SF-36) health survey, which assesses quality of life in eight domains and has been validated for the Brazilian population [14]. The difference between the HRQoL measured 35 months after the trial and the mean of the three in-trial HRQoL assessments was considered a long-term change in HRQoL.

Statistical analysis

The mean of the variables during the trial (in-trial) was compared between survivors, non-survivors, and patients lost to the three-year follow-up by ANOVA, Kruskal-Wallis test, or chi-square test (χ^2). The association of intervention status (exercise or control group) and cardiovascular disease (CVD) risk factors with outcomes was initially tested by Kaplan-Meier curves with log-rank test (categorical predictors), univariate Cox proportional hazards (continuous predictors), or univariate linear regression analysis. After collinearity was discarded, differences in distribution of baseline characteristics according to the intervention status (intervention or control group) with $p \leq 0.25$ were considered potential confounders and included in the multivariable model to test the exposure to exercise. Cox proportional hazards regression was used for adjusted survival analysis. Linear regression was used for adjusted analysis of change in GFR and HRQoL. All predictors with $p \leq 0.25$ were initially included in the models. The assumptions for Cox (proportionality) and linear regression (normality and homoscedasticity of residuals, collinearity, and linearity) were tested. Variables were tested for normality using the Shapiro-Wilk test. In case of skewed distribution, commands (ladder and gladder) were used to suggest transformation options that provided parametric distribution. After the regression, residual distribution was tested using graphical methods. A p-value < 5% was considered as significant. All statistical analyses were performed using Stata software v. 15.1 (https://www.stata.com).

Results

After 1,028.78 (standard error – SE = 23.88) days from the trial inception, 128 patients or relatives were located, of which 23 refused to reevaluate GFR and HRQoL. All located patients were included in the survival analysis and 105 in the linear regression analysis for changes in GFR and HRQoL (Figure 1).

Table 1 summarizes the baseline characteristics of the sample in the randomized controlled trial according to the survival status at follow-up. Participants had a mean age of 65 years and were mostly white women, overweight or obese (mean BMI = 29.9, SE = 0.7kg/m^2), and with slightly reduced renal function (eGFR = 63.4, SE = 2.3mL/minute/1.73m^2). No significant in-trial differences were found between the patients included in the survival analysis and those with loss of follow-up (Table 1).

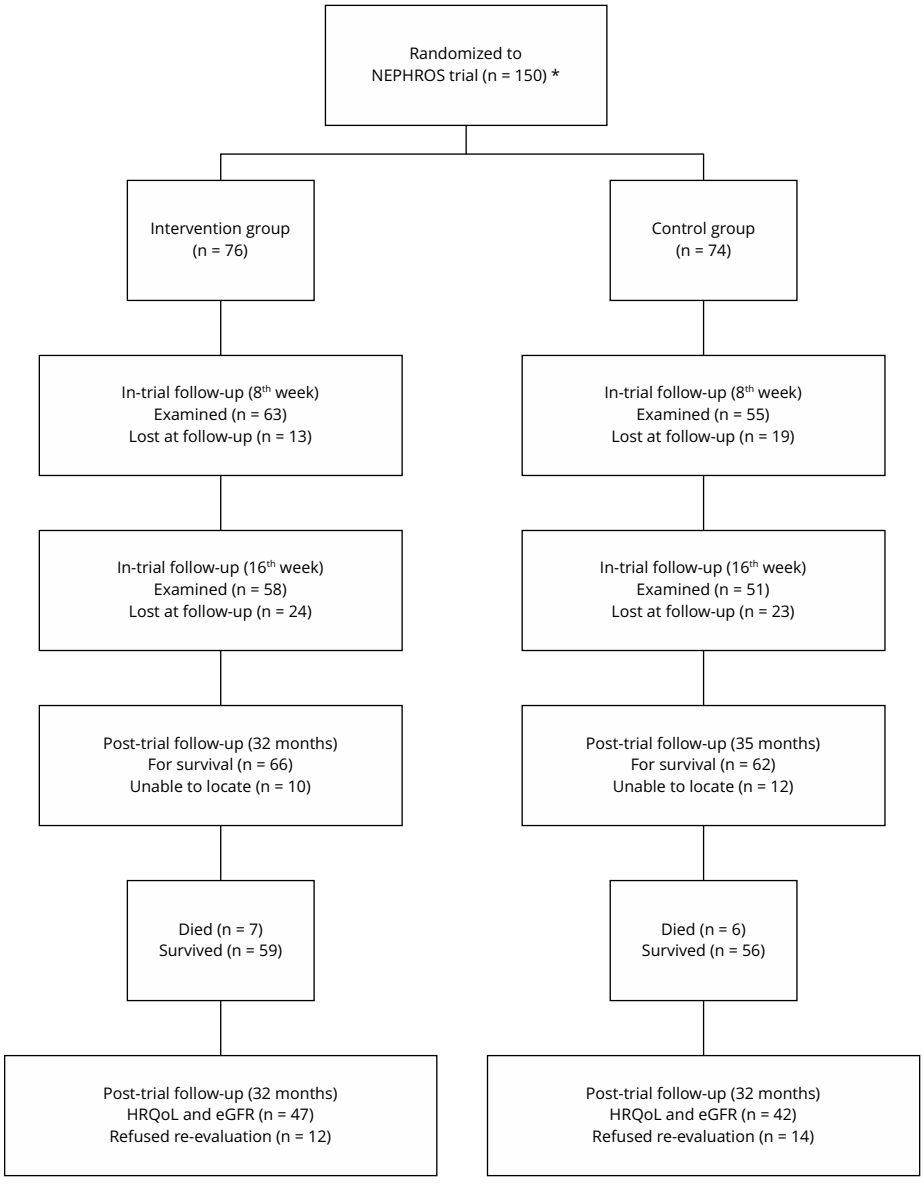
Of the 128 patients initially located, 13 died (10.2%) after 3 years (7 in the intervention group and 6 in the control group), of which 2 were related to cancer, 4 to cardiovascular disease, and the others to unidentified causes. The patients died after a mean of 764.58 (SE = 11.1) days after randomization. Figure 2 shows the three-year survival probability after the trial. No differences were found in survival between the NEPHROS control (no-exercise) and intervention (exercise) groups (log-rank test, p = 0.94) in univariate intention-to-treat analysis (Table 2 and Figure 2). The per-protocol analysis, which included only patients who attended more than 70% of the exercise sessions during the trial, had similar results (data not shown). During the 32-month post-trial follow-up, no participant declared to maintain regular exercise.

The in-trial eGFR (HR = 0.95, 95%CI: 0.92; 0.98, p = 0.002) and in-trial ankle-brachial systolic index (HR = 0.03, 95%CI: 0.002; 0.43, p = 0.01) were significantly associated with survival in univariate analysis. The independent variables age, in-trial plasma triglycerides, and in-trial BMI were associated ($p < 0.25$) with the outcome in univariate analysis and therefore included in the initial multivariable adjustment model. After adjusted analysis, in-trial GFR (HR = 0.95, 95%CI: 0.92; 0.98, p = 0.002) and in-trial ABI (HR = 0.03, 95%CI: 0.001; 0.54, p = 0.02) remained as independent predictors of survival (Figure 3). The proportional hazards assumption was fulfilled when time-dependent covariates were included in the model. The final model presented probability > χ^2 = 0.0003, LR $\chi^2(2)$ = 16.04.

Univariate analysis for change in GFR showed no influence of the exercise group in the NEPHROS trial (β = -0.01, coefficient = -0.41, 95%CI: -6.66; 5.85, p = 0.89) (Table 2), but the GFR was significantly associated with in-trial ABI (β = 0.25, coefficient = 10.44, 95%CI: 1.68; 19.20, p = 0.02) and in-trial systolic blood pressure (β = -0.26, coefficient = -0.14, 95%CI: -0.25; 0.02, p = 0.02). The in-trial SF-36 physical function domain, in-trial serum triglycerides, and in-trial high-density lipo-

Figure 1

Flowchart for NEPHROS in-trial and post-trial follow-up and re-evaluation. NEPHROS * trial randomization is described elsewhere [10].



eGFR: estimated glomerular filtration rate; HRQoL: health-related quality of life.

* Randomized to NEPHROS trial (n = 150).

protein (HDL) cholesterol were also included in the adjustment model after showing some association ($p < 0.25$) with the outcome. In the adjusted analysis, in-trial systolic blood pressure ($\beta = -0.26$, coefficient = -0.13, 95%CI: -0.24; -0.03, $p = 0.01$) and in-trial ABI ($\beta = 0.22$, coefficient = 9.00, 95%CI: 0.43; 17.57, $p = 0.04$) remained as independent predictors for CKD progression (Figure 4). The final model was significant (probability > F = 0.003, R-squared = 13%) and fulfilled the assumptions of normality of residuals (Shapiro-Wilk $p = 0.31$), homoscedasticity of residuals (white test $p = 0.84$), no collinearity

Table 1

Sample characteristics at baseline (in-trial), according to the main outcome (survival status) 35 months after the NEPHROS trial.

	Survivors	Non-survivors	Lost at follow-up	p-value *
NEPHROS (E/C) [n]	59/56	7/6	10/12	0.86
Age (years) [mean, SD]	64.8 (11.1)	70.0 (9.8)	63.5 (10.1)	0.11
Sex (F/M) [%]	72.6/83.6	9.5/7.3	17.9/9.1	0.27
White [%]	62.6	53.8	54.5	0.31
Schooling (years) [median, IQR]	5.0 (3.0; 7.0)	2.0 (1.0; 4.0)	4.0 (2.0; 5.0)	0.08
Smoker (c/f) [%]	5.2/34.8	7.7/30.8	18.2/27.3	0.19
SF-36 MCS [median, IQR]	72.0 (56.0; 84.0)	76.0 (56.0; 88.0)	68.0 (40.0; 76.0)	0.17
SF-36 PCS [median, IQR]	66.7 (48.3; 80.0)	46.7 (33.3; 68.3)	76.7 (40.0; 86.7)	0.16
2-Minute Step Test [n] [mean, SD]	126.8 (44.1)	101.4 (22.8)	112.6 (47.2)	0.26
30-Second Chair-Stand Test [mean, SD]	10.8 (2.9)	9.8 (3.5)	9.9 (3.6)	0.46
Timed Up-and-Go Test (s) [median, IQR]	6.0 (4.9; 7.1)	5.9 (5.5; 9.3)	6.5 (5.3; 7.8)	0.61
SBP (mmHg)	156.5 (25.9)	161.8 (18.7)	155.8 (30.5)	0.77
BMI (kg/m^2) [median, IQR]	28.6 (26.1; 33.0)	31.0 (27.2; 34.0)	27.6 (26.0; 31.0)	0.33
ABI [median, IQR]	1.0 (0.9; 1.2)	1.01 (0.9-1.1)	1.05 (0.9-1.1)	0.11
eGFR (mL/minute/1.73m^2) [mean, SD]	63.1 (17.4)	45.3 (29.9)	62.1 (16.5)	0.003
TG (mg/dL) [median, IQR]	128.5 (95; 188)	157 (128; 334)	150 (95.7; 178)	0.04
TC (mg/dL) [mean, SD]	200.8 (39.3)	204.6 (42.6)	189.4 (42.5)	0.68
HDL (mg/dL) [mean, SD]	57.8 (12.0)	50.1 (10.1)	55.6 (13.1)	0.39
LDL (mg/dL) [median, IQR]	120.1 (95.8; 137.1)	106.4 (93.5; 112.4)	99.8 (95.0; 122.2)	0.35
hs-RCP (mg/L) [median, IQR]	2.1 (1.0; 5.9)	3.4 (1.5; 7.7)	2.9 (1.1; 10.2)	0.46
Glucose (mg/dL) [median, IQR]	94.8 (88.3; 103.8)	93.0 (90.3; 94.3)	97.7 (86.0; 136.0)	0.67

ABI: ankle-brachial index; BMI: body mass index; c: current; E/C: Exercise/Control; eGFR: estimated glomerular filtration rate; F: female; f: former; HDL: high-density lipoprotein; hs-RCP: high-sensitivity reactive C-protein; IQR: interquartile range; LDL: low-density lipoprotein; M: male; MCS: mental component summary; PCS: physical component summary; s: seconds; SBP: systolic blood pressure; SD: standard deviation; TC: total cholesterol; TG: triglycerides.

* p-value calculated by ANOVA (parametric variables), Kruskal-Wallis test (non-parametric variables) or χ^2 test (categorical variables).

(variance inflation factor – VIF = 1.02), and linearity (scatter plot). Exercise intervention (Table 2) and other potential in-trial predictors showed no association with changes in the SF-36 mental or physical components summary.

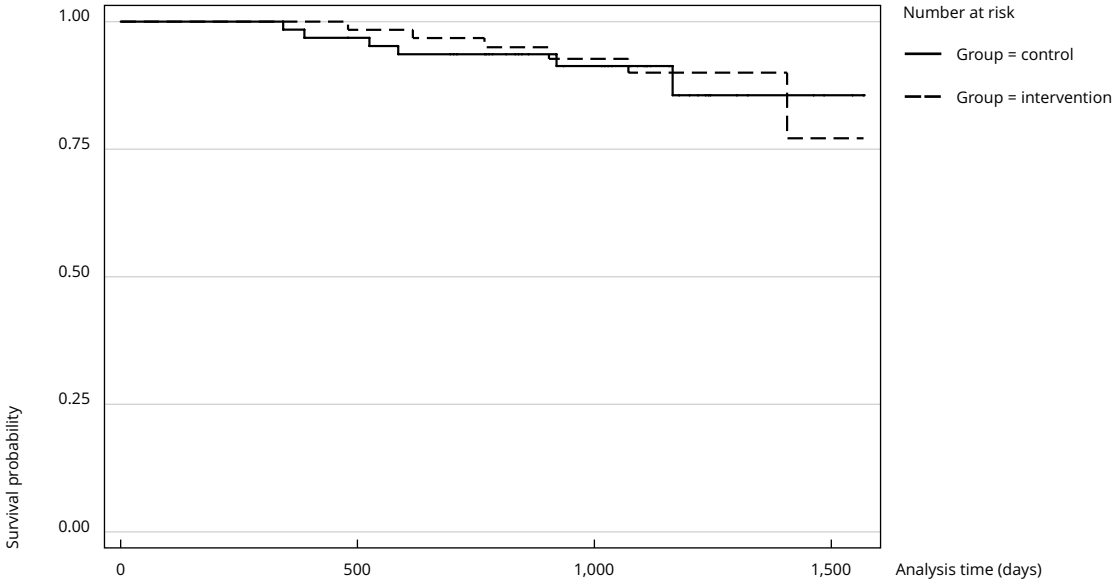
Discussion

This NEPHROS post-trial follow-up investigated the effects of a structured exercise intervention and in-trial cardiovascular disease risk factors on all-cause mortality, GFR, and health-related quality of life in a hypertensive CKD population. Patients who underwent physical training and control patients had no differences in survival or in GFR and HRQoL after a mean of 35 months, despite the short-term positive effects of exercise on functional capacity, metabolism, and inflammatory factors.

The long-term effects of short-time supervised physical interventions in healthy or diseased populations are poorly known. The few reports describe different results [12,15,16,17,18,19,20,21,22], usually showing benefit preservation only among patients who remain exercising [18]. Mustata et al. [16] found that arterial stiffness in CKD patients undergoing hemodialysis improved with 3-month aerobic training, but reverted to pre-exercise levels after one month of detraining. Boyce et al. [17] randomized hypertensive pre-dialysis CKD patients to a 4-month exercise intervention or usual care and found a significantly reduced blood pressure and improved functional capacity, which returned to baseline levels after two months of detraining. Korpelainem et al. [18] found that Finnish older women

Figure 2

Kaplan-Meier survival estimates according to intervention or control randomization group in the NEPHROS trial.



Note: Log-rank test p = 0.94.

Table 2

Results of the follow-up evaluation (35 months) and changes in the in-trial measures over time.

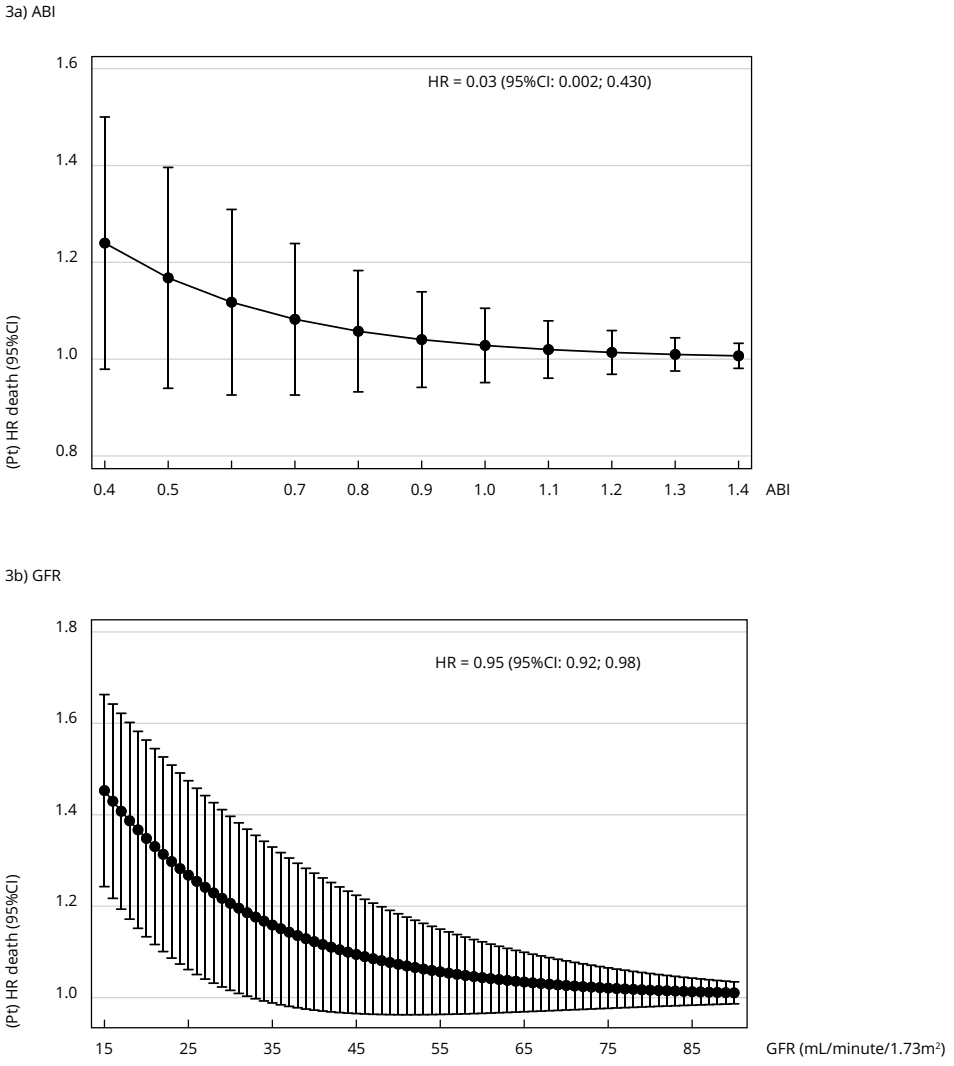
	35 months of follow-up			Changes in the in-trial		
	Exercise	**Control**	**p-value**	**Exercise**	**Control**	**p-value**
Deaths (n)	7/66	6/62	0.86			
e-GFR (mL/minute/1.73m^2)	69.8 (22.2)	67.1 (23.8)	0.58	4.7 (15.0)	5.1 (13.8)	0.89
SF-36 Health Survey						
Physical functioning	70 (45; 85)	70 (35; 85)	0.77	5 (-15; 15)	0 (-10; 10)	0.51
Physical role limitations	75 (0; 100)	50 (0; 100)	0.51	3.3 (-45; 18)	7.5 (-27; 29)	0.22
Bodily pain	51 (41; 72)	52 (31; 72)	0.93	32.2 (23; 44)	42.7 (23; 61)	0.24
General health perception	72 (55; 82)	62 (45; 87)	0.44	-3 (-12; 11)	6 (-6; 17)	0.32
Vitality	65 (50; 80)	57 (40; 80)	0.27	-2 (-15; 10)	1 (-7; 15)	0.53
Social role functioning	88 (50; 100)	75 (50; 100)	0.43	31 (-5; 62)	31 (-13; 62)	0.72
Emotional role limitations	100 (35;100)	83.5 (0; 100)	0.58	0 (-33; 11)	0 (-11; 11)	0.39
Mental health	76 (56; 96)	68 (56; 88)	0.23	5.3 (-9.3; 12)	3.3 (-4.7; 11)	0.93
PCS	63 (42; 81)	57 (41; 80)	0.54	8 (-2; 21)	10 (-9; 20)	0.61
MCS	73 (54; 86)	65 (48; 84)	0.38	5 (-12; 21)	9 (-9; 19)	0.90

MCS: mental component summary; PCS: physical component summary.

Note: results in mean (SD – standard deviation) or median (IQR – interquartile range), p-value for t-test (parametric variables) or Mann-Whitney test (non-parametric variables).

Figure 3

Predicted hazard ratio (HR) for death until 35 months after the intervention according to ankle-brahila index (ABI) and glomerular filtration rate (GFR) means during the in-trial follow-ups (from Cox regression analysis).

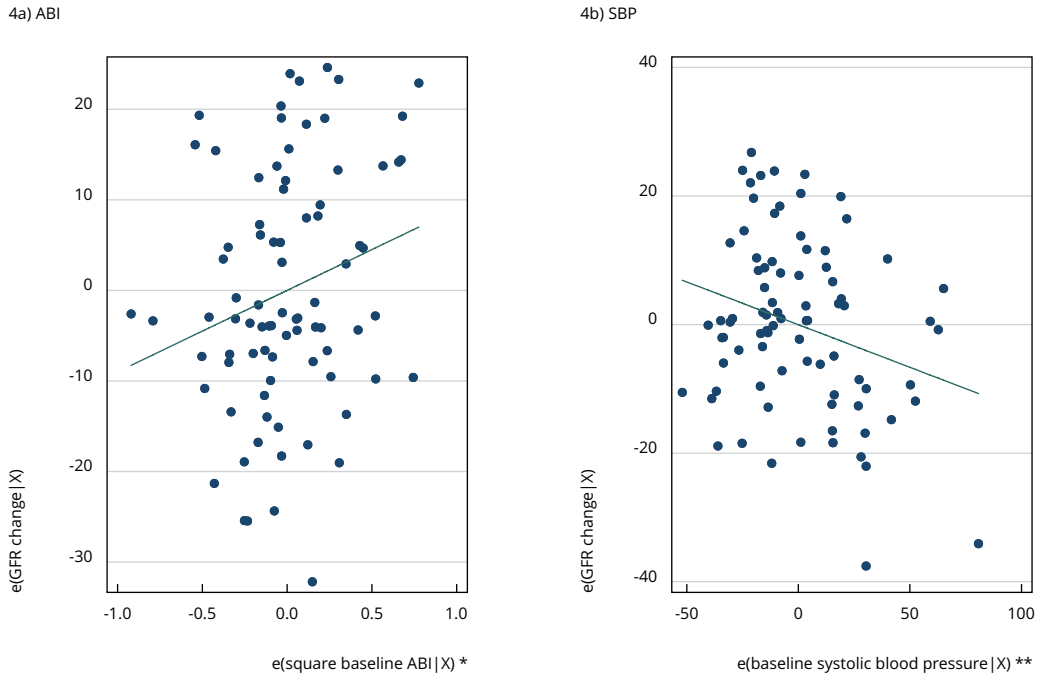


95%CI: 95% confidence interval.

had reduced hip fracture and mortality rates in a seven-year follow-up after 30 months of physical training. However, the intervention was mainly home-based and a trainer would visit them regularly during the long follow-up to promote exercise practice. Participants of the NEPHROS trial had no additional incentive to keep exercising, except for verbal advice at the end of the study. A post-trial exercise offer was planned, but not implemented due to the lack of funding. No sample (control and exercise groups) in this post-trial follow-up declared the practice of any exercise modality during re-evaluation. Furthermore, no additional subjective or objective measurement of exercise practice or physical activity was obtained.

Figure 4

Adjusted regression for glomerular filtration rate (GFR) changes according to ankle-brachial index (ABI) and systolic blood pressure (SBP) (linear regression).



* Coefficient = 9.0013947, SE = 4.3075079, t = 2.09;

** Coefficient = -0.132804, SE = 0.05351108, t = 2.48.

Limited long-term follow-up data concerns randomized controlled trials on exercise training and most interventional studies. However, the economic burden of maintaining long-term clinical trials often contributes to this obstacle. A post-trial observational follow-up study is an easier alternative that has been widely used [23,24,25], providing highly valuable new information, sometimes very different from the in-trial results. This combination of designs, however, has limitations. A cohort study is based on data that occur in real life without interference from the investigator, which increases the tendency to bias. This is why results of post-trial observational follow-ups should always be confirmed (or discarded) by further studies or innovative designs, such as the recently described cohort multiple randomized controlled clinical trial [26].

These considerations particularly concern exploratory data analysis, used in this study on the association between baseline cardiovascular disease risk factors and clinical outcomes. In-trial lower GFR and ABI were associated with shorter survival, even after adjustment for sex, age, and other CVD risk factors. The large Chronic Kidney Disease Prognosis Consortium had already provided robust evidence on the inverse association between GFR and all-cause and cardiovascular mortality [6]. The ankle-brachial index is a surrogate marker for cardiovascular disease. Index below 0.9 shows a high specificity for peripheral artery disease, which is usually associated with atherosclerosis in other sites. Recent guidelines from the American Heart Association and American College of Cardiology consider ABI as an auxiliary tool for quantitative CVD risk assessment in treatment decision-making [27]. An abnormal ABI has been associated with higher mortality in diabetic patients [28] and in the general population [29]. Studies mainly with patients in hemodialysis indicate that lower ABI predicts higher all-cause and cardiovascular mortality in patients with advanced CKD [30,31,32,33,34,35,36,37]. Our analysis

suggests that this occurs in earlier stages of CKD in non-diabetic patients. However, this result should be carefully considered given the events that occurred during follow-up.

The GFR remained mostly stable after the almost three years of follow-up possibly because of the sample, which included older hypertensive and non-diabetic patients, most without proteinuria. Higher systolic blood pressure and lower ABI were associated with a greater decline in GFR. Uncontrolled blood pressure is greatly associated with a faster progression of chronic kidney disease [5], but the role of ABI has been less investigated. An analysis of the Framingham Heart Study [38] and the Atherosclerosis Risk in Communities (ARIC) study cohorts has already described this association for the general population [39]. The ankle-brachial index is a surrogate of atherosclerotic burden, which acts as predictor of both death and GFR decline and emphasizes the interrelated nature of cardiovascular and kidney diseases, especially in older adults, even after adjustment for classical risk factors. The lack of a baseline quantitative measure of albuminuria, a known risk factor for CKD progression, greatly limits our findings. The use of antihypertensive drugs has also not been recorded. Furthermore, around one sixth of the sample could not be located and another one sixth had not its GFR estimated in the final assessment. Finally, this follow-up study can be significantly underpowered. However, since we followed best-practice and current recommendations and used secondary analyses, the interpretation of our findings was based on the direction and magnitude of the associations. The predictive power of ABI for survival and the GFR decline in earlier stages of CKD should be especially investigated in future properly designed and powered studies. If confirmed the role of ABI, chronic kidney disease in older hypertensive patients could be nearer from the cardiovascular disease constellation than is currently estimated.

The strengths of this study include the focus on patient-oriented outcomes, such as survival and quality of life, based on a comprehensive set of baseline in-trial data measured thrice each, with participants subjected to clinical and laboratory analysis at follow-up, contrary to analysis of secondary data from multipurpose databases. To the best our knowledge, no previous post-trial follow-up of exercise in CKD patients assessed clinical endpoints. Although research is still incipient, short-term benefits of exercise on surrogate endpoints for CKD patients do not imply long-term advantages in patient-oriented outcomes if infrastructure and life-course educational and motivational support are not provided for a healthy lifestyle.

Contributors

M. Bohlke conceived and designed research, conducted experiments, and contributed to personal training, analyzed data and wrote the manuscript. F. C. Barcellos conceived and designed research and wrote the manuscript. I. S. Santos conceived and designed research, conducted experiments and analyzed data. G. I. Mielke conducted experiments, contributed to personal training, analyzed data and wrote the manuscript. M. M. Vargas conducted experiments, contributed to personal training and analyzed data. P. C. Hallal conceived and designed research, and analyzed data. All authors read and approved the manuscript.

Additional informations

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Conflict of interest

The authors declare that they have no conflict of interest.

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Resumo

O estudo NEPHROS é um ensaio controlado e randomizado que aplicou um programa de treinamento aeróbico e de força com duração de 16 semanas em pacientes com doença renal crônica e hipertensão arterial. O artigo descreve o seguimento pós-ensaio de longo prazo, comparando sobrevida, qualidade de vida relacionada à saúde (HRQoL) e mudança na taxa de filtração glomerular estimada (TFGe) entre o grupo de intervenção e o grupo controle, e de acordo com fatores de risco cardiovascular registrados durante o ensaio. Os participantes do estudo NEPHROS foram reavaliados três anos depois do ensaio original. Foi usada a razão de riscos proporcionais de Cox para comparar o tempo de sobrevida, e a regressão linear para comparar a mudança na TFGe e as pontuações gerais de HRQoL física e mental, entre os grupos de intervenção e controle, de acordo com idade, sexo e níveis durante o ensaio original de TFGe, proteína C-reativa, glicose, lipídios, índice tornozelo-braquial (ITB), capacidade funcional e pressão arterial. Entre os 150 participantes do NEPHROS, 128 foram incluídos na análise de seguimento. Não foi observado nenhum efeito do treinamento na sobrevida, TFGe ou HRQoL. As medidas durante o ensaio original de TFGe (HR = 0,95; IC95%: 0,92; 0,98) e ITB (HR = 0,03; IC95%: 0,002; 0,43) foram preditores positivos independentes de sobrevida. ITB mais baixo (coeficiente = 9,00; IC95%: 0,43; 17,5) e pressão sistólica mais alta (coeficiente = -0,13; IC95% -0,24; -0.03) foram preditores independentes de declínio da TFGe. O programa de exercício de 16 semanas não teve efeito no longo prazo sobre sobrevida, qualidade de vida ou mudança na taxa de filtração glomerular em pacientes com doença renal crônica de estágios 2 a 4. Níveis mais baixos de TFGe e ITB e pressão arterial sistólica mais elevada estiveram associados a prior prognóstico entre pacientes com doença renal crônica.

Insuficiência Renal Crônica; Hipertensão; Exercício Físico; Sobrevida; Índice Tornozelo-Braço

Resumen

NEPHROS es un ensayo controlado aleatorio que aplicó un entrenamiento de 16 semanas aeróbico y de resistencia a pacientes con enfermedad crónica de riñón y presión alta. El informe actual describe un seguimiento de largo plazo post ensayo, comparando supervivencia, calidad de vida relacionada con la salud (HRQoL) y el cambio de tasa estimada de filtración glomerular (eGFR) entre los grupos de intervención y control, y según factores de riesgo cardiovascular en el ensayo. Tras tres años del ensayo original, los participantes en NEPHROS fueron reevaluados. Se usó el modelo de Cox de riesgos proporcionales para comparar el tiempo de supervivencia y la regresión lineal para comparar el cambio en los marcadores resumen eGFR, físicos y mentales HRQoL, entre los grupos de intervención y grupos de control, y según edad, sexo, y eGFR en el ensayo, proteína C-reactiva, glucosa, lípidos, índice tobillo-brazo (ABI), capacidad funcional y presión sanguínea. De los 150 participantes de NEPHROS, 128 personas fueron incluidas en el análisis a largo plazo. No se observó un cambio en el efecto del entrenamiento físico previo en la supervivencia, eGFR o HRQoL. La base de referencia en el ensayo eGFR (HR = 0,95; 95%CI: 0,92; 0,98) y ABI (HR = 0,03; 95%CI: 0,002; 0,43) fueron predictores independientes positivos para la supervivencia. Un más bajo ABI (coeficiente = 9,00; 95%CI: 0,43; 17,5) y una presión sistólica sanguínea más alta (coeficiente = -0,13; 95%CI -0,24; -0,03) fueron predictores independientes para la disminución de la eGFR. El programa de ejercicio de dieciséis semanas no tuvo un efecto a largo plazo en la supervivencia, calidad de vida o cambio en la filtración glomerular en pacientes con etapas 2 a 4 enfermedad crónica de riñón. Una eGFR y ABI más bajos, y una presión más alta sistólica de sangre estuvieron asociadas con una prognosis más escasa entre pacientes enfermedad crónica de riñón.

Insuficiencia Renal Crónica; Hipertensión; Ejercicio Físico; Sobrevida; Índice Tobillo Braquial

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