ORIGINAL ARTICLE

Aerobic exercise effects in renal function and quality of life of patients with advanced chronic kidney disease

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SUMMARY

BACKGROUND: *To date, the therapeutic effects of exercise have not yet been evaluated regarding renal function parameters and quality of life specifically in patients with advanced chronic kidney disease. Thus, the study aim was to evaluate the effects of aerobic exercise in renal function and quality of life in patients with advanced chronic kidney disease.*

METHODS: *A quasi-experimental prospective study [NCT03301987] was carried out. Nine patients with advanced chronic kidney disease were recruited from a hospital nephrology unit. Kidney function parameters such as creatinine, creatinine clearance, urea clearance, glomerular filtration rate, and creatinine/weight proportion, as well as the Kidney Disease Quality of Life SF-36 (KDQoL-SF36) were measured at baseline and after 1 month of aerobic exercise.*

RESULTS: *Significant increases ($P < .05$) were observed for creatinine/weight proportion as well as symptoms, effects, charge, and physical domains of the KDQoL-SF36 after 1 month of therapeutic exercise. The other parameters did not show any statistically significant difference ($P > .05$).*

CONCLUSIONS: *Aerobic exercise may cause improvements in renal function and quality of life of patients with advanced chronic kidney disease. Further studies about therapeutic exercise protocols specifically in patients with advanced stages of chronic kidney disease should be carried out in order to study their effectiveness and safety.*

KEYWORDS: *Exercise. Kidney Diseases. Physical Therapy Modalities. Quality of Life.*

INTRODUCTION

Kidney disease is characterized by the impairment of renal function and causes accumulation of blood metabolites, which alter the electrolyte balance[1], as well as severe comorbidities such as cardiovascular conditions [2] or chronic obstructive pulmonary disease. [3] Indeed, chronic kidney disease (CKD) is considered renal function impairment when it lasts for at least 3 months [4].

Worldwide, CKD is considered a major public health problem [4]. In Spain, this condition may reach up to 9.16% of the total population with a prevalence of 4,300,000 patients with CKD. Indeed, CKD incidence will increase over the next decade as a consequence of other comorbidities such as diabetes and hypertension in conjunction with population aging. The economic burden of CKD is very high and may reach up to $50 billion in the United States and 3% of the total national health burden in Spain[5,6].

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Considering the CKD clinical practice guidelines[1,7], CKD stages are measured according to glomerular filtration [8]. Indeed, albuminuria, measured based on the albumin/creatinine ratio, may be considered as an independent marker of endothelial damage and a risk factor independent from cardiovascular conditions [2]. The averages of urea and creatine clearance (measured at the last 24 hours) are recommended parameters for measurement in patients with advanced CKD, according to the kidney disease guidelines[1,7].

Patients with CKD are more likely to present physical activity limitations and impaired quality of life than the general population [9]. In addition, physical activity may be considered a key predictor of quality of life in these patients[10].

Exercise practice is considered a key therapeutic intervention in patients with CKD and may reduce cardiovascular risk, increase cardiorespiratory, metabolic, neuromuscular, and cognitive functions, as well as improve physical function secondary to muscular tissue increase and minimize the risk of functional impairment through improved quality of life[11].

Consequently, the practice of physical exercise is a key factor for the clinical management of patients with CKD[11], as well as in patients under maintained hemodialysis treatment and patients under peritoneal dialysis intervention[12]. Domiciliary exercise practice has shown to improve renal function in patients with CKD before starting the dialysis treatment[13]. Nevertheless, the effects of therapeutic exercise have not yet been evaluated regarding renal function parameters and quality of life in patients with advanced CKD. Therefore, the aim of this study was to evaluate the effects of aerobic exercise in renal function parameters and quality of life in patients with advanced CKD.

METHODS

Study design

A quasi-experimental prospective study was carried out in order to determine the effects of therapeutic exercise in renal function parameters and quality of life in patients with advanced CKD. A sample of 9 patients with advanced CKD was recruited at the Galdakao Hospital (Spain) from October to December 2017. In addition, this research was conducted according to the Template for Intervention Description and Replication (TIDieR) checklist and guidelines[14]. The Clinical Intervention Ethics Committee from the University of León (Spain; code ÉTICA-ULE-018-2017) approved this study, and subjects signed an informed consent form subjects before the study started. Furthermore, this study was prospectively registered at ClinicalTrials.gov [NCT03301987].

Sample size calculation

The sample size was calculated using the software from Unidad de Epidemiología Clínica y Bioestadística, Complexo Hospitalario Universitario de A Coruña, Universidade da Coruña (available at http://www.fisterra.com/mbe/investiga/9muestras/9muestras2.asp). Considering the prevalence of 4,300,000 patients with CKD in Spain in 2010 [6], the sample size calculation for an α level of 0.05 (confidence interval, α-1 = 95%), a proportion of 5% and a precision of ± 15 %, provided at least n = 8 cases. Also, assuming information loss of 10%, at least n = 9 patients with CKD needed to be included in the study.

Participants

A sample of 9 patients with advanced CKD (for the etiology, comorbidities, and status of CKD in the recruited patients, see Appendix 1) was recruited using a consecutive sampling method. The setting was performed at the Nephrology Unit from the Galdakao Hospital (Spain). The inclusion criteria comprised patients with older than 18 years, who signed the informed consent form, with a diagnosis of stage 4–5 CKD and stable kidney function for at least 1 year[13]. The exclusion criteria comprised not signing the informed consent form, patients with a physical impairment that did not allow for physical exercises, such as uncontrolled hypertension and cardiac failure, motor disorders[13], and dementia, or any degree of cognitive impairment[15].

Intervention

The aerobic exercises were performed according to the recommended Spanish exercise guidelines[1,7]. The patients carried out exercise activities, such as brisk walking (30 min/day) or completing from 8,000 to 10,000 steps/day. The measurement of the physical exercise performed was assessed with an accelerometer pedometer (Kenz Lifecorder, EX 1-axial) with a sensor of acceleration (Suzuken Co-Ltd., Nagoya, Japan). The accelerometer pedometer was continuously used for 1 month and was only removed for bathing or sleeping. The main physical exercise parameter was the number of steps per day[13].

Outcome measurements

Descriptive data such as sex, age, height, weight, body mass index (BMI), and kidney disease chronicity (years) were extracted from the electronic and paper medical records by the same authorized researcher. The stage of the CKD was determined according to the recommended clinical practice guidelines[1,7]. According to the glomerular filtration [8], the stages of the CKD were established as follows: stage I for values higher than 90 ml/min/m^2; stage II for values from 90 to 60 ml/min/m^2; stage III for values from 60 to 30 ml/min/m^2 (specifically, stage IIIA from 60 to 45ml/min/m^2 and stage IIIB from 45 to 30ml/min/m^2); stage IV for values from 30 to 15ml/min/m^2; and stage V for values lower than 15ml/min/m^2. In addition, CKD was classified in a non-numeric way, considering slight CKD for stages with glomerular filtration higher than 60ml/min/m^2; slight-moderate CDK for stages with glomerular filtration from 60 to 45ml/min/m^2; moderate-severe CDK for stages with glomerular filtration from 45 to 30ml/min/m^2; severe CKD for stages with glomerular filtration from 30 to 15ml/min/m^2; and terminal CKD for stages with glomerular filtration lower than 15ml/min/m^2 [1,7,8].

Kidney function parameters such as creatinine, creatinine clearance, urea clearance, glomerular filtration rate, and creatinine/weight proportion were measured at baseline and after 1 month of therapeutic exercise. The glomerular filtration rate (ml/min/1.73 m^2)[16], which was calculated from the serum creatinine and urinary protein levels, was used as the kidney function index.

The Kidney Disease Quality of Life SF-36 Short Form (KDQoL-SF36™; Spanish Version 1.2; RAND, University of Arizona, Unites States) was measured at baseline and after 1 month of therapeutic exercise. The symptoms, effects, charge, physical and mental domains were registered. The KDQoL™ is a commonly used 134-item instrument designed to assess generic and kidney-disease targeted aspects of quality of life for patients on dialysis[17]. An abbreviated version of the KDQoL™, the KDQoL-SF36™, has been translated to Spanish and used in the United States (rand.org/health/surveys_tools/kdqol.html); it was validated into Spanish by Ricardo et al.[18] for the Spanish population with CKD.

Statistical analysis

The statistical SPSS 22.0 software (IBM SPSS Inc., Chicago, IL, USA) was used for the data analysis. A 95% confidence interval (CI) and a statistically significant difference of *P*-value < .05 were considered. Firstly, the Shapiro-Wilk test was used to assess normality. Secondly, the data were described by means of the mean ± standard deviation (SD) and 95% CI limits (upper and lower limits) for the parametric data (age, height, renal function parameters, and KDQoL-SF36 domains), median ± interquartile range (IR) for the non-parametric data (weight and BMI), as well as frequencies and percentages (%) for the categorical data (sex and kidney disease degree). In paired samples, the Student *t*-test was applied to assess differences before and after the intervention for all the renal function parameters and KDQoL-SF36 domains measurements (due to all of them were parametric data). Box-plots were used to illustrate the KDQoL-SF36 domains differences before and after 1 month of therapeutic exercise.

RESULTS

Descriptive data

A total sample of 9 patients, 3 females (30%) and 6 males (60%), age mean± SD of 66.22 ± 7.08 years, height mean ± SD of 1.66 ± 0.10 m, weight median ± IR of 74.00 ± 11.50 kg, BMI median ± IR of 27.02 ± 6.91 kg/cm^2, with advanced CKD completed the research course. The frequencies (%) of the CKD stages were 5 cases of grade IV (55.5%) and 4 of grade V (44.4%).

Renal function parameters

Regarding Table 1, a statistically significant increase (*P* = .018) was observed for the creatinine/weight proportion after 1 month of therapeutic exercise. The other renal function parameters did not show any statistically significant difference (*P* > .05).

Kidney disease and quality of life domains

Regarding Table 2 and Figure 1, statistically significant increases (*P* < .05) were observed for the symptoms, effects, charge and physical domains of the KDQoL-SF36 after 1 month of therapeutic exercise. Nevertheless, the mental domain of the KDQoL-SF36 did not show any statistically significant difference (*P* = .972).

TABLE 1 – RENAL FUNCTION PARAMETERS OF PATIENTS (N = 9) WITH ADVANCED CKD BEFORE AND AFTER 1 MONTH OF THERAPEUTIC EXERCISE.

Renal function parameters	Therapeutic exercise	Mean	SD	Lower limit	Upper limit	Mean difference	SD difference	t-test P-value (t)
Creatinine	Baseline	3.41	1.35	2.37	4.45	0.12	0.34	.328 (1.042)
	1 month	3.53	1.58	2.31	4.75			
Creatinine clearance	Baseline	26.92	10.95	18.40	35.24	1.13	5.38	.546 (0.630)
	1 month	27.95	11.10	-3.00	5.27			
Urea clearance	Baseline	10.85	2.72	8.76	12.94	-0.26	1.49	.616 (-0.522)
	1 month	10.59	3.78	8.86	12.32			
Glomerular filtration rate	Baseline	18.66	6.67	13.52	23.79	-0.38	3.39	.743 (-0.3340)
	1 month	19.04	6.61	13.95	24.13			
Creatinine/weight	Baseline	16.23	1.95	14.72	17.74	0.95	0.97	.018 (2.951)
	1 month	17.18	1.60	15.95	18.41			

Abbreviations: CKD, chronic kidney disease. In all the analyses, p < .05 (with a 95% confidence interval) was considered statistically significant.

TABLE 2 – KDQOL-SF36 DOMAINS OF PATIENTS (N = 9) WITH CKD BEFORE AND AFTER 1 MONTH OF THERAPEUTIC EXERCISE.

KDQoL-SF36 domains	Therapeutic exercise	Mean	SD	Lower limit	Upper limit	Mean difference	SD difference	t-test P-value (t)
Symptoms	Baseline	71.96	8.72	65.25	78.67	17.67	9.35	<.001 (5.667)
	1 month	89.64	6.53	84.62	94.67			
Effects	Baseline	75.25	9.31	68.09	82.41	9.23	10.81	.033 (2.563)
	1 month	84.49	9.29	77.00	91.63			
Charge	Baseline	53.47	30.79	29.80	77.14	18.05	20.59	.030 (2.630)
	1 month	75.52	24.22	52.90	90.15			
Physical	Baseline	37.41	10.83	29.08	45.74	4.43	4.79	.024 (2.776)
	1 month	41.85	11.85	32.73	50.96			
Mental	Baseline	48.68	7.50	42.91	54.45	-0.10	8.98	.972 (-0.036)
	1 month	48.57	7.21	43.02	54.12			

Abbreviations: CKD, chronic kidney disease; KDQoL-SF36, kidney disease quality of life SF36. In all the analyses, p < .05 (with a 95% confidence interval) was considered statistically significant.

DISCUSSION

This is the first study to support novel evidence about the effects of aerobic exercise in renal function parameters and quality of life in patients with advanced CKD. Although we prioritized renal function parameters and quality of life, a prior systematic review [19] suggested that exercise improved stress and inflammation biomarkers in patients with CKD.

Likewise Kosmadakis et al.[20], our study obtained improvements after 1 month of aerobic exercise; the same was observed regarding the quality of life and uremic symptom scores. On the other hand, Chang et al. [21]did not observe any improvements in the physical component score of the KDQoL-SF36 after 3 months of intervention. Therefore, this suggests that aerobic exercise may be a key therapeutic factor in the clinical management of patients with CKD, but this is not yet completely clear.

Unlike prior studies [13], our study showed signif-

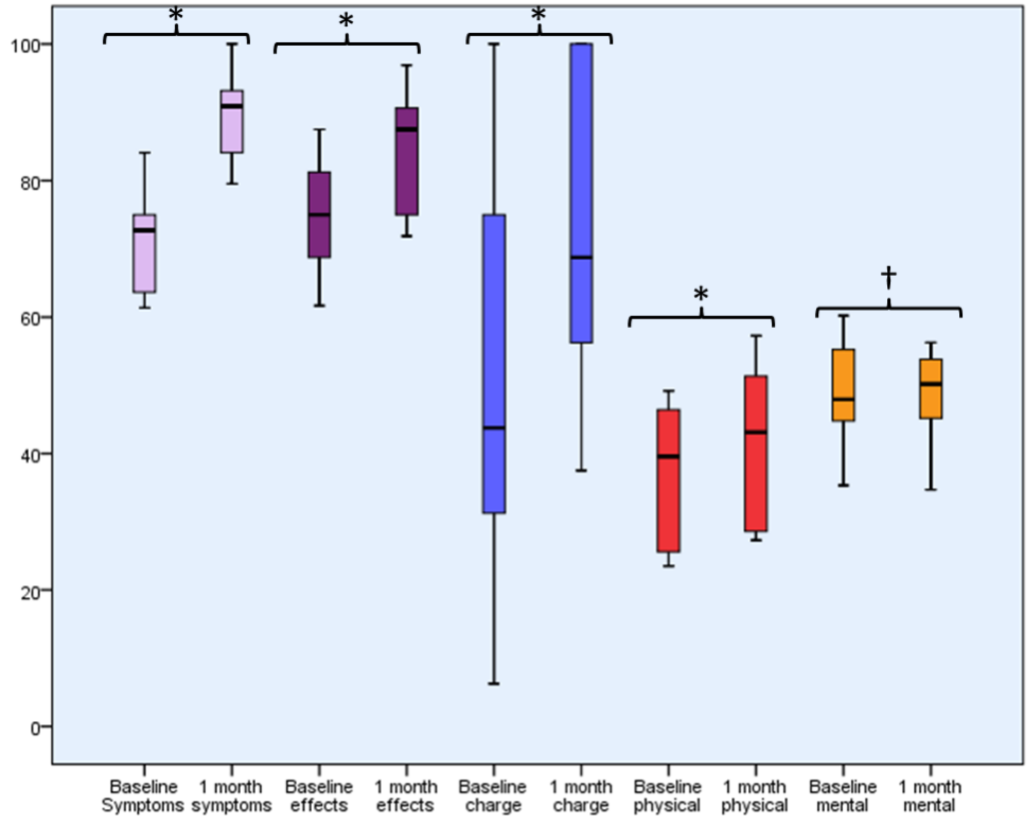

FIGURE 1. Box-plots to illustrate the differences in KDQoL-SF36 domains in patients with CKD before and after 1 month of therapeutic exercise. Abbreviations: CKD, chronic kidney disease; KDQoL-SF36, kidney disease quality of life SF36. *Statistically significant differences with P < .05 (with a 95% confidence interval). †No statistically significant differences with P > .05 (with a 95% confidence interval).

icant improvements in renal function, while others reported improvements in muscle strength, although renal function was not modified. Nevertheless, there is a lack of consensus on the effect of exercise on kidney function. Further research studies are needed to clarify the effect of exercise in the physiopathology of the renal function.

Relevance for physical therapy

Exercise recommendation, prescription, and supervision supported by specialized physical therapists may be effective in helping patients with advanced CKD remove the difficulties to adhere to these kinds of programs. Currently, there is not a unified protocol for prescribing exercise, and there is a disagreement with respect to the prescription moment as well as exercise type, intensity, and duration for these specific patients. In addition, these patients present a high risk of cardiovascular diseases. Consequently, the prescription of exercise should be individualized, and the physical therapist must define the duration and systematic procedure of the aerobic exercise in order to participate actively in the decision making during the prescription of physical exercise.

Regarding the coordination of aerobic exercise care, physical therapists, nephrologists, and physicians play a key role in the adherence of advanced CKD patients to aerobic exercise protocols, which should be supported by multidisciplinary teams.

Limitations

Several limitations should be considered for future studies about therapeutic exercise in patients with advanced CKD. First of all, despite the sample size calculation provided, future studies with a higher precision and sample size should be carried out. Second, despite the prospective trial registry, this study had a case series design. Thus, randomized clinical trials should be carried out with control groups. Finally, the effects of therapeutic exercise must be studied depending on the stages IV and V of advanced CKD.

CONCLUSIONS

In conclusion, aerobic exercise may cause improvements in renal function and quality of life of patients with chronic kidney disease. However, further studies about protocols for therapeutic exercise in patients with advanced stages of chronic kidney disease should be carried out in order to study their effectiveness and safety.

Conflict of interest

The authors declare there are no conflicts of interest.

RESUMO

OBJETIVO: *Até o momento, os efeitos do exercício terapêutico ainda não tinham sido avaliados quanto aos parâmetros de função renal e qualidade de vida em pacientes com doença renal crônica avançada, especificamente. Assim, o objetivo do estudo foi avaliar os efeitos do exercício aeróbico na função renal e na qualidade de vida em pacientes com doença renal crônica avançada.*

MÉTODOS: *Um estudo prospectivo quase experimental [NCT03301987] foi realizado. Nove pacientes com doença renal crônica avançada foram recrutados de uma unidade de nefrologia hospitalar. Parâmetros de função renal como creatinina, depuração de creatinina, liberação de ureia, taxa de filtração glomerular e creatinina/peso, bem como a qualidade de vida da doença renal SF-36 (KDQoL-SF36) foram medidos no início e após um mês de atividade aeróbica.*

RESULTADOS: *Aumentos significativos (P<0,05) foram mostrados para a proporção de creatinina/peso, bem como sintomas, efeitos, carga e domínios físicos do KDQoL-SF36 após um mês de exercício terapêutico. Os demais parâmetros não apresentaram diferença estatisticamente significante (P>0,05).*

CONCLUSÕES: *O exercício aeróbico pode produzir melhorias na função renal e na qualidade de vida de pacientes com doença renal crônica avançada. Especificamente, novos estudos sobre protocolos de exercícios terapêuticos em pacientes com estágios avançados de doença renal crônica devem ser realizados a fim de estudar sua eficácia e segurança.*

PALAVRAS-CHAVE: *Exercício. Nefropatias. Modalidades de fisioterapia. Qualidade de vida.*

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