

# Aerobic Exercise Improves Physical Capacity in Patients under Chronic Hemodialysis

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## **Abstract**

Background: In the general population, regular practice of physical exercises is associated with improved physical capacity and reduction of cardiovascular events. Concerning patients with chronic kidney disease, a population with significant impairment of physical capacity and high rates of cardiovascular mortality, few studies have evaluated the effects of physical activity.

Objective: To evaluate the effect of aerobic exercise during hemodialysis on the physical capacity and blood pressure of patients with chronic renal failure.

Methods: We evaluated 14 patients with chronic kidney disease under hemodialysis, before and after 12 weeks of aerobic exercise performed during hemodialysis sessions. Patients underwent ambulatory blood pressure monitoring for 24 hours, 6-minute walk test and cardiopulmonary exercise test before and after the exercise period.

Results: After the exercise, there was a significant increase in the distance walked during the 6-minute walk test from  $509 \pm 91.9$  m to  $555 \pm 105.8$  m, and a significant reduction in systolic blood pressure of  $151 \pm 18.4$  mmHg to  $143 \pm 14.7$  mmHg, diastolic blood pressure of  $94 \pm 10.5$  mmHg to  $91 \pm 9.6$  mmHg and average arterial pressure from  $114 \pm 13.0$  mmHg to  $109 \pm 11.4$  mmHg.

Conclusion: Aerobic exercise conducted during hemodialysis sessions contributed to the improvement of physical capacity and control of hypertension in patients with chronic kidney disease. (Arq Bras Cardiol. 2010; [online]. ahead print, PP.0-0)

Key words: Exercise; vital capacity; renal dialysis; walking; blood pressure.

# Introduction

In the general population, the practice of physical activity (PA) is associated with improved physical capacity (PC), contributing to the control of hypertension (SAH) and reduced relative risk of death (RR)<sup>1</sup>. In patients with chronic kidney disease (CKD), in which over 50% of deaths are secondary to cardiovascular disease<sup>2</sup>, the practice of PA is uncommon and the literature does not provide specific recommendations regarding its performance<sup>3</sup>.

Nevertheless, it has been confirmed that the practice of PA reduces morbidity and mortality in patients with chronic renal failure<sup>4</sup>. O'Hare et al<sup>5</sup> compared a group of sedentary chronic renal patients with a physically active group and observed RR of death 62% higher in the sedentary group<sup>5</sup>. Stack et al<sup>6</sup> also reported that physical exercises performed four to five times a week reduced by about 30% the risk of death of physically active patients under hemodialysis, when compared to sedentary patients<sup>6</sup>. Based on these observations,

some nephrology services have encouraged chronic renal failure patients to exercise, both in the interdialytic period and during hemodialysis sessions (HD)<sup>7,8</sup>.

Establishing a PA routine during HD brings advantages such as greater patient's willingness to practice exercise, convenient schedules, reducing the boredom of HD sessions and ease of medical care. In addition, PA in chronic renal failure patients under HD is associated with improved physical capacity (PC) and reduced blood pressure (BP). It also contributes to improving patients' quality of life<sup>8-10</sup>. Early works performed by our group confirm these benefits<sup>8</sup>.

In this study, we assessed the impact of an individualized aerobic exercise program (AE) supervised and carried out during HD sessions, on PC and BP of chronic renal failure patients.

# **Methods**

This is an experimental study in which 14 adult volunteering patients were evaluated (10 women and four men) with an average age of 48 years under hemodialysis in the Department of Nephrology of the University Hospital of *Universidade Federal de Juiz de Fora* for at least three months. For inclusion in the study, patients had to be sedentary for six months or more. All patients signed an informed consent pursuant to Resolution nº 196/96 issued by the

National Health Council. The project was approved by the Ethics Committee on Research of the University Hospital of *Universidade Federal de Juiz de Fora* under number 290/2005 dated December 15, 2005.

Exclusion criteria were acute heart and lung disease; acute infectious diseases; hemoglobin < 10 g/dl and hematocrit < 30%; glucose > 300 mg/dl; physical or mental disability preventing the proper performance of the protocol; cancer and pregnancy.

The study was divided into pre and post AE phase. In the pre-AE phase, each volunteer underwent medical evaluations and physical therapy followed by laboratory tests and an electrocardiogram at rest (ECG), Doppler echocardiography (ECO) and ambulatory blood pressure monitoring (ABPM). For evaluation of PC, a 6-minute walk test (6MWT) and cardiopulmonary exercise test (CPET) were performed. After these assessments, the volunteers underwent supervised AE during HD sessions for 12 weeks. In the post-exercise phase, laboratory tests, ABPM, 6MWT and CPET were repeated.

The medical evaluation consisted of anamnesis and clinical general examinations and active search for signs and symptoms related to physical stress. Meanwhile, the physical therapy evaluation aimed at designing a stretching and warm-up program that would be consistent with the musculoskeletal condition of patients.

Conventional ECG was performed in Ecafix electrocardiograph model ECG6 and analyzed according to the classic electrocardiographic diagnostic criteria<sup>11</sup>. The ECG was performed by an echocardiographer accredited by the Brazilian Society of Cardiology in a GE-branded ultrasound equipment model Logic500.

For ABPM, an oscillometric blood pressure monitor (SpaceLabs, 90207) validated by the British Society of Hypertension was used<sup>12</sup>. The examination was performed and evaluated according to the Guideline for Ambulatory Blood Pressure Monitoring<sup>13</sup>. During this examination, patients were instructed to maintain their usual activities and medications.

The 6MWT was used for initial assessment of PC, before and after the AE phase. In this test, patients are instructed to walk as fast as possible for 6 minutes on a flat track of 30 m, recording the final distance in meters. Patients can slow down, stop and rest, without stopping the clock. Running or jogging is not allowed. Two tests were performed on the same day with an interval of 30 minutes. For the purposes of valid result, the longest distance achieved was considered <sup>14</sup>.

The CPET was performed on a treadmill ergometer, Inbraesporte brand, with Micromed's Elite software. We used the ramp protocol according to the Guideline on Techniques and Equipment to Perform Ergometry and Ergospirometry Tests¹⁵. For the analysis of exhaled gases (airflow and volume and exhaled fractions of  $\rm O_2$  and  $\rm CO_2$ ), the gas analyzer  $\rm VO_{2000}$  was used. During the test, ECG and heart rate (HR) were recorded continuously through CM5. The variables evaluated through CPET were peak oxygen consumption ( $\rm VO_{2PEAK}$ ), which expresses the physical capacity¹⁵ and the decrease of HR in the first minute of recovery, which evaluates the vagal tone¹⁶. The values considered normal for  $\rm VO_{2PEAK}$  vary according to sex and age and are calculated

using mathematical equations<sup>17</sup>. Regarding the decrease of HR, a reduction greater than 12 beats in the first minutes of recovery is considered appropriate<sup>16</sup>.

All tests were performed at the greatest interdialytic period. Those patients who were submitted to dialysis on Mondays, Wednesdays and Fridays performed ABPM, 6MWT and CPET on Tuesday and those receiving dialysis on Tuesdays, Thursdays and Saturdays performed it on Wednesday. All drugs used regularly by the patient were maintained throughout the study.

The intervention consisted of performance of AE during HD sessions three times a week and for 12-week period. Such exercise consisted of a warm-up phase, performance of aerobic exercise on stationary bicycle and, finally, the "cooling" stage. We used a Moviment-branded horizontal electromagnetic cycle ergometer, model BM 4000.

In the warming up, patients underwent passive stretching of lower limbs and aerobic activity on the bicycle with the lowest load applicable to the ergometer used, which was 0.5 KPM, and rotation close to 35 rpm for 5 minutes.

After the warm-up phase, we performed a conditioning phase, with 30 minutes of exercise during the first two hours of HD in order to avoid physical stress in the second half of the session, when patients' hemodynamic conditions are unfavorable. HR was monitored continuously using a Polarbranded heart rate monitors model F1, and BP was measured at rest every 5 minutes of exercise and after cooling.

On cooling, after 2 minutes on the bicycle with minimal load and rotation of 35 RPM, passive stretching of lower limbs were applied again. Then, the AT session was discontinued.

The prescription of exercise intensity was based on Borg's Perceived Exertion Scale<sup>18</sup>. According to this scale, patients assign a score to the intensity of fatigue that varies from 6 to 20 points. During the AE, at every 5 minutes, patients were asked about the score they would assign to their fatigue at that moment, and the bicycle load was maintained to achieve an intensity of stress enough to determine a score of fatigue between 11 and 13 points, which corresponds to an exercise of "mild" intensity to "quite hard" in this scale. The rotation speed on the bicycle pedal should remain close to 50 rpm within the 30 minutes of exercise in order to achieve a stable exercising intensity.

At the beginning of HD, the AE session would be discontinued if the patient presented systolic BP > 180 mmHg and/or diastolic BP > 110 mmHg, interdialytic weight gain > 5 kg, difficult vascular access or any symptom that could impair the exercise. Once the AE started, the criteria for discontinuing the exercise were reports of intense physical fatigue (Borg scale > 15), chest pain, hypoglycemia, dizziness, paleness, fainting, pre-syncope, dyspnea disproportionate to the intensity of exercise, arrhythmia, hypotension or hypertensive response.

The evaluation of dialysis quality was determined by Kt/V, a dimensionless index that measures the clearance of urea, based on the distribution of urea in total body water<sup>19</sup>. An index of Kt/V  $\geq$  1.4 is considered optimal. We obtained the medical records of patients before and after the AE period, as well as serum urea, creatinine, hemoglobin, hematocrit, triglycerides, total cholesterol and fractions.

Statistical analysis was performed using SPSS version 13.0 (SPSS, Chicago, IL, USA) and the pre and post AE values were compared by Student t test. Differences were considered statistically significant when the p value was  $\leq 0.05$ .

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## Results

#### **Demographic and clinical variables**

Table 1 shows the main demographic and clinical characteristics. The average age was  $48 \pm 12.8$  years, including four male patients (28.6%) and 10 (71.4%) women. The average hemodialysis time was  $94 \pm 43.9$  months and the most frequent cause of CKD was chronic glomerulonephritis, followed by hypertension. Out of the 14 patients studied, 12

Table 1 - Table of demographic and clinical characteristics of patients evaluated

Characteristics	Patients
Age	47.6 ± 12.79
Sex (male/female)	4/10
Race (whites/blacks)	5/9
HD time (months)	93.7 ± 43.90
CKD biology	
Chronic glomerulonephritis	7 (50.0%)
Hypertension	4 (28.7%)
Diabetes mellitus	1 (7.1%)
Obstructive uropathy	1 (7.1%)
Renal amyloidosis	1 (7.1%)

HD - hemodialysis; CKD - chronic kidney disease.

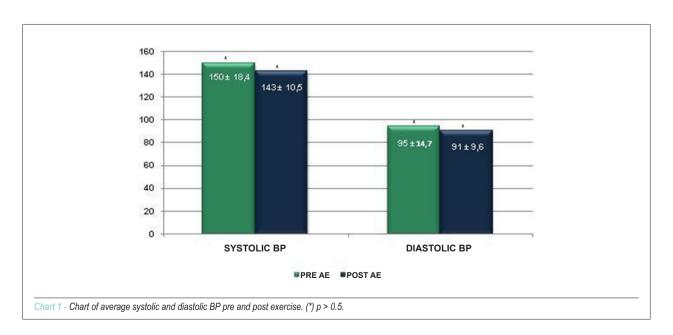
(85%) were hypertensive and were under medical treatment. During the study, there were no significant changes in the class or dose of antihypertensive drug. Patients' dry weight was similar before and after the AE period and ranged from  $56.8 \pm 12.99$  kg before exercise to  $56.4 \pm 12.72$  kg at the end of the study.

The average number of patients willing to take exercise sessions was 82% and the goal of 30 minutes of tolerance to exercise was achieved by patients around the fourth week. In the first week of exercise, the average time in exercise sessions was equal to  $21.29 \pm 9.19$  minutes. At the end of 12 weeks, this time increased to  $33 \pm 4.22$  minutes, with a statistically significant difference compared to the first week of exercise. It is worth noting the absence of relevant clinical complications during the exercise, with only one episode of pre-syncope, which led to the discontinuation of that exercise session and exercise was resumed at the next session of hemodialysis.

#### Cardiovascular variables and physical capacity

Upon ECG at rest, all patients had sinus rhythm, seven patients (50%) presented abnormal ventricular repolarization, and three (21%) with diagnostic criteria for left ventricular hypertrophy. ECG detected left ventricular hypertrophy in eight patients, which accounted for 57% of the sample. In addition, it also detected ascending aorta ectasia in one patient (7%), increased end-diastolic diameter of LV in two patients (14%) and ejection fraction smaller than 60% in four patients (28 %).

At baseline, 24-hour average systolic BP, diastolic BP and mean BP were respectively equal to  $150 \pm 18.4$  mmHg,  $95 \pm 10.5$  mmHg and  $114 \pm 13.0$  mmHg (Chart 1). At the end of the AE, there was a statistically significant reduction in systolic BP to  $143 \pm 14.7$  mmHg, diastolic BP to  $91 \pm 9.6$  mmHg and average BP to  $109 \pm 11.4$  mmHg, despite maintaining the same doses of antihypertensive drugs and the dry weight of patients. Before the AE, most patients (13/14) presented



reduced nocturnal sleep pressure with reduction values of systolic and diastolic BP respectively equal to  $0 \pm 1.1\%$  and  $2 \pm 9.1\%$ . After the AE, these values increased significantly to  $3 \pm 9.3\%$  and  $5 \pm 10.7\%$ , respectively. However, both decreases did not reach minimum regular values (10%).

Upon PC assessment, there was a significant increase in 6MWT distance of  $509 \pm 91.9$  m in the pre-exercise to  $555 \pm 105.8$  m at the end of the AE period corresponding to an increase of about 10%. Despite the increase in the distance run, the perceived exertion according to the Borg scale was stable and was equal to  $12 \pm 1.5$  before the AE and  $12 \pm 1.1$  after the AE, a finding that suggests improved tolerance to exercise.

After the AE period, the VO $_{\rm 2PEAK}$  values determined by CPET ranged from 20.7  $\pm$  6.91 ml/kg.min $^{-1}$  in the pre-AT phase to 21.3  $\pm$  10.13 ml/kg.min $^{-1}$  after the AE with no statistically significant difference. Another variable assessed in the CPET, the decrease of heart rate in the first minute of recovery, also presented non-significant increase of 16  $\pm$  4.2 beats to 18  $\pm$  5.7 beats after the exercise period.

#### Laboratory variables

After the AE phase, there was a statistically significant increase in hemoglobin and triglyceride levels, and significant reduction in creatinine levels. The increase in hemoglobin was combined with a slight reduction of weekly dosage of erythropoietin required to achieve the target of 11 g/l of hemoglobinemia.

## **Discussion**

In this study, we observed that aerobic exercise sessions held during HD was associated with increased PC, better control of hypertension and improved anemia.

Patients under HD have significant reduction of physical capacity compared to healthy sedentary individuals of the same sex and same age<sup>20</sup>. While CPET is the gold standard in PC measurement<sup>17</sup>, this test involves relatively high costs, use of special equipment and performance by specially trained professional, which impairs its frequent use in clinical practice. The 6MWT has also been used in this study because it is one of the tests most commonly used in literature to estimate PC, since it is easy to use, inexpensive and it represents daily activities<sup>14</sup>. This test has been widely used in patients with cardiac and lung diseases, but its application in patients with CKD is often limited to clinical research.

The average distance achieved in the 6MWT in the preexercise phase was similar to that achieved in other studies, which evaluated patients with CKD under HD<sup>21-23</sup>. Then, after 12 weeks of AE, the distance run in the 6MWT increased by 10%, indicating considerable improvement in PC. These findings are consistent with the study by Parsons et al<sup>23</sup>, who observed a 14% increase of PC in 6MWT after exercise of 13 patients under HD for 20 weeks.

Along with the increased distance run in the 6MWT, most patients assessed have an improved feeling of fatigue as measured by the Borg scale. Furthermore, the patients showed a 35% increase in the time of tolerance to aerobic exercises at the end of 12 weeks of AE. These findings suggest the benefit of a supervised exercise program on the improvement of PC.

Paradoxically, in the sample, the application of CPET after the AE period showed no significant difference in VO<sub>2PFAK</sub> when compared to test results before exercise. These findings contrast with some publications reporting an average increase of 20% in the  $VO_{\tiny 2PFAK}$  in chronic renal patients undergoing AE<sup>24-26</sup>, which is also opposite to the findings obtained in the 6MWT. These discrepancies may be related to technical difficulties for examination, such as age, comorbidities, difficult to understand. Accordingly, there have been reports of dissociation between the value of  $VO_{\mbox{\tiny 2PEAK}}$  and the prognosis of patients with severe heart disease<sup>27-29</sup>. In this study, this hypothesis was reinforced by the intolerance of many patients to the procedures required to perform CPET. These complications have often led to discontinuation of the test. Another aspect to be considered was the fact that the AT was carried out on a stationary bicycle, because patients are required to remain seated during HD sessions, while the CPET was performed on a treadmill. This fact may have influenced patients' performance, once immediate functional muscle adaptations responsible for early physical capacity improvements are linked to the type of exercise<sup>30-32</sup>.

In addition to VO $_{\rm 2PEAK'}$  CPET was also used to assess vagal tone, by analyzing the decrease of HR in the first minute of recovery. In this test, reductions smaller than 12 beats relate to improper vagal tone and are associated with higher relative risk of death $^{16}$ . In the sample studied, the decrease of HR in the first minute of recovery was equal to 16  $\pm$  4.2 bpm before the AE, with a non-significant rise to 18  $\pm$  5.7 bpm after the AE. These findings are consistent with an appropriate vagal response.

The pressure evaluation was performed by ABPM, which is the reference standard for indirect measurement of BP, which has been frequently used in literature to assess the pressure behavior of chronic renal patients<sup>33-35</sup>. The findings showed that 12 patients (85%) were hypertensive, most of which used three or more antihypertensive agents. After the AT, there was significant reduction in blood pressure, despite the maintenance of anti-hypertensive therapy and absence of changes in estimated dry weight. In addition, we also observed decreased nocturnal sleep blood pressure in most patients, although the average reduction in BP during sleep has not yet reached normal values<sup>13</sup>. These findings, also observed in a previous study8, are compatible with the antihypertensive effect of aerobic exercise and have been confirmed by other authors with individual measures of BP33,34. In one of the few studies that used ABPM to assess BP, Anderson et al<sup>35</sup> studied 19 patients who had significant improvement in blood pressure control after three and six months of AE. These data are consistent with the results of this study and suggest the ABPM as an effective method for pressure evaluation of patients with chronic renal failure.

As for laboratory data, it is worth mentioning the smaller need for erythropoietin to maintain target levels of hemoglobinemia after the AE period, suggesting the beneficial effect of AE on the control of anemia in CKD. A similar benefit was reported by Goldberg et al<sup>36</sup> after a period of exercise in a group of patients under chronic hemodialysis. Although we know the effect of exercise in improving lipid

profiles in different populations, including CKD, the results of this study showed increased levels of triglycerides and LDL cholesterol. Thus, we can speculate about dietary factors associated with these findings, such as reduction of appetite loss among CKD patients, however, these aspects were not evaluated in this study.

At the end of the AE period, there was a slight increase of Kt/V accompanied by a significant reduction in creatinine indicating a trend of improvement in the quality of dialysis. Although this study was not focused on evaluating this aspect, it is possible that peripheral vasodilation and increased blood flow induced by the exercise have helped removing toxins during HD<sup>23,37</sup>.

In summary, AE during HD sessions is a safe strategy associated with PC improvement. It also contributes to better blood pressure control and improvement of anemia in CKD patients. However, before being extrapolated to the population of CKD patients, these data require confirmation in samples with larger number of patients.

# Conclusion

The application of a supervised program of aerobic exercise in chronic renal patients during hemodialysis was associated with improvement in physical capacity, control of hypertension and anemia.

#### **Potential Conflict of Interest**

No potential conflict of interest relevant to this article was reported.

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#### **Study Association**

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