



## ACUTE CARDIOVASCULAR ALTERATIONS IN HYPERTENSIVE RENAL PATIENTS DURING EXERCISE WITH CONSTANT LOAD IN THE INTERDIALYTIC PERIOD

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### ABSTRACT

**Purpose.** The study investigated acute cardiovascular alterations during aerobic exercise in interdialytic phase. **Basic procedures.** Seven hypertensive men with chronic renal disease (CRD) and seven healthy men (C) were matched according to the age (CRD:  $48.5 \pm 8.5$ ; C:  $45.28 \pm 9.3$ ) and body mass index (CRD:  $24.2 \pm 2.8 \text{ kgm}^{-2}$ ; C:  $26.7 \pm 2.7 \text{ kgm}^{-2}$ ). The exercise was executed on a cycloergometer during 6 minutes at 75% of  $\text{HR}_{\text{max}}$  and 3 minutes of recovery without load at 55–60 rpm. The patients came twice and were controlled only on an occasion at the hospital at 9.00 am. The exercise was performed before and 24 hours after haemodialysis (HD). The blood samples were drawn immediately before and 24 hours after HD for hematocrit and hemoglobin analysis. The statistical difference was verified by the ANOVA and two-tailed unpaired Student's t-test only for  $p < 0.05$ . **Main findings.** After HD, the systolic blood pressure (SBP) shows reduction in the first stage (~14%;  $p < 0.05$ ) and in the recovery period of exercise (~18%;  $p < 0.05$ ). A hypotension effect of HD was better observed in the diastolic blood pressure (DBP) from the 5<sup>th</sup> to 9<sup>th</sup> min of exercise (~20%;  $p < 0.05$ ). The HD did not modify biochemical (hematocrit and hemoglobin), physiological (Rest  $\text{SpO}_2$ ; rest SBP; rest DBP and  $\text{VO}_{2\text{max}}$ ) and body weight parameters. **Conclusions.** The study showed a significant reduction in blood pressure levels during the exercise, principally in DBP 24 hours after HD, suggesting that exercise executed during this period can induce better tolerance to exercise in dialyzed patients.

Key words: haemodialysis, hypertension, blood pressure, physical test

### Introduction

The regular physical activity is related to beneficial effects to renal patients, such as a reduced risk of cardiovascular mortality, improvement in blood pressure (BP), control among hypertensive individuals and improvement in health-related quality of life as a result of enhanced psychological well-being and improved physical functioning [1, 2]. Given that cardiovascular mortality is the number-one cause of death among patients with end-stage renal disease (ESRD) in the United States and approximately 80% of incident ESRD patients have a history of hypertension [3], there is great potential to reduce the death rate as a result of exercise participation in this population. Despite the myriad potential benefits of exercise, dialysis patients are extremely inactive [4], and nephrologists rarely assess patients' physical activity levels or counsel patients to increase activity [5]. The lack of exercise assessment and counseling is almost certainly multifactorial, re-

lated to such factors as competing medical issues that lead to limited time available for exercise counseling, lack of training in exercise prescription, and fear of adverse events related to exercise in this population. For example, it is possible that, although exercise participation could lead to greater benefits among patients with renal disease than in the general population, dialysis patients may also incur greater risk because of underlying heart or musculoskeletal disease.

The rationale for prescribing exercise in this patient population is extremely strong. However, barriers to regular exercise participation are many, which may explain the persistent sedentary behavior of this cohort. Motivation to exercise has been problematic, particularly when training is performed on non-dialysis days [6].

In addition, pre-dialysis and interdialytic (44 h) ambulatory systolic and diastolic BP decreased after the 4<sup>th</sup> month of training, a finding that persisted after the 6<sup>th</sup> month of training. Previous studies with dialyzed patients showed a chronic beneficial effect in BP control during haemodialysis after training [7, 8]. Intradialytic exercise also can induce positive psychological adaptations in this cohort by reducing symptoms of anxiety, depression, and fatigue and enhancing various compo-

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nents of QOL, including general health, vitality, and perceptions of physical functioning.

Mechanisms underlying this enhancement of dialysis adequacy likely include increased blood perfusion between the working muscle and bloodstream, thereby enabling more thorough removal of the damaging solutes through haemodialysis (HD) treatment [9]. These benefits also may translate into the long term enhancement of dialysis adequacy (Kt/V) [10], although this hypothesis has not been rigorously investigated in a randomized controlled trial involving exercise training.

Miller et al. [11] demonstrated that hypertensive patients could significantly reduce pre-dialysis and post-dialysis systolic blood pressure after 3 months of intradialytic cycling. The reduction in BP was accompanied by a reduction in antihypertensive medications (−36%,  $p < 0.018$ ) resulting in cost savings of USD \$ 885 per patient annually. Additional trials have observed reduced resting BP [12, 13], and BP during maximal exercise [13] with 1–3 months of aerobic, or combined training. However, little importance has been given to acute cardiovascular alterations during exercise executed in interdialytic phase. This study focuses on the available data regarding tolerance exercise among renal patients before and one day after HD.

## Material and methods

### Subjects

The present study involved seven hypertensive men with chronic renal disease (CRD) that underwent periodic haemodialysis and seven healthy men (controls [C]) who were matched for age, body mass index (BMI) (Tab. 1). The patients were recruited randomly from a Renal Therapy Unit of University Hospital. Informed consent was obtained for the study in accordance with Resolution 196/96 of the National Council of Health in Brazil, which was approved by local Ethics Committee. All had been treated by three-week maintenance haemodialysis for at least one year. Dialysis access was by arterio-venous fistula. None had recirculation demonstrable on ultrasound dilution (Transonics). None had current angina or any other clinically apparent condition likely to impair their capacity to perform stationary cycling. All patients took regular antihypertensive medications, with diagnostic of hypertension in the Renal Therapy Unit of University Hospital in accordance with the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7).

Table 1. Clinical characteristics of the study population (means  $\pm$  SEM)

	Renal (n = 7)	Control (n = 7)
Age (years)	48.5 $\pm$ 8.5	45.28 $\pm$ 9.3
Height (m)	1.7 $\pm$ 0.06	1.73 $\pm$ 0.07
Weight (kg)	70.61 $\pm$ 11.7	79.8 $\pm$ 4.2
BMI (kgm <sup>-2</sup> )	24.2 $\pm$ 2.8	26.7 $\pm$ 2.7
Rest systolic blood pressure (mm Hg)	169.5 $\pm$ 6.4*	129.5 $\pm$ 7.8
Rest diastolic blood pressure (mm Hg)	105.7 $\pm$ 6.8*	82.8 $\pm$ 7.1
VO <sub>2max</sub> (mL/kg/min)	15.1 $\pm$ 1.6*	23.1 $\pm$ 1.7

Values are means  $\pm$  SE

\* Significant difference compared to control group at  $p < 0.05$  (two-tailed unpaired Student's t-test)

### Dialysis technique

Dialysis was carried out using a Fresenius Medical Care 4008H machine. All patients were treated exclusively using high-flux synthetic membranes, predominantly polysulfone. Dialysers were reused with peracetic acid (Renalin, Minntec Inc., USA) as the main processing agent. Bicarbonate was used as buffer. Ultra-pure water was used for all dialysis-related processes. Stringent bacteriological standards were maintained. Dialysis was prescribed and monitored using a two-pool kinetic model to ensure a Kt/V of 1.2. This was a composite of Kt/V (renal) and Kt/V (dialysis). Mean dialysis time was 180 min (range 140–225 min). The midweek dialysis session was chosen for the studies. Blood flow rates and dialysate flow rates were kept constant over the study period. Dialysis fluid temperature was maintained at 36°C throughout the procedures. No ultrafiltration was performed during the study period.

### Protocol of exercise

The indirect VO<sub>2max</sub> was determined using equation [14]. The protocol of exercise was performed using a cycloergometer (Bicycle Technology-BM 2800 PRO) with lower-limb use, pedaling in a sitting position according to the indirect protocol of Astrand and Rodahl [14]. The patients were asked to exercise for 9 minutes (6 minutes at 75% of HR<sub>max</sub> and 3 minutes of recovery without load) 75% of their theoretical maximum heart rate (HR<sub>max</sub>) for age (using tables from the American Heart Association). The load was adjusted for individuals to find intensity (75% of HR<sub>max</sub>) and with pedal cadency at 55–60 rpm.

The measurements taken were blood pressure (BP; mercury column), heart rate (HR; Polar – T-61), and peripheral oxygen saturation (SpO<sub>2</sub>; pulse oximeter – Nonimim) immediately before, at different moments and after exercise session. The subjective perceived exertion was rated by Borg scale used during exercise session [15].

The patients came twice, in random order, to hospital at 9.00 am after an overnight without medicament use (antihypertensive). For the first time, the patients performed exercise before HD session. For the second time, the exercise was performed 24 hours after HD procedure. The controls visited the hospital at 9.00 am for exercise procedure only once.

#### Laboratory measurements

The blood samples (5 mL) were drawn in random order, to hospital at 9.00 am, immediately before and 24 hours after HD procedure for hematocrit (Hct) and hemoglobin (Hgb) analysis. Hematocrit measurement was carried out according to Goldenfarb et al. [16] and the values found were expressed as a percentage of the total blood volume. Hemoglobin rate was determined by the cyanometahemoglobin method according to Collier [17], and its values were expressed in g/dL of blood.

#### Statistical analysis

All data are expressed as means  $\pm$  SEM. The statistical analyses of clinical characteristics of the study population data were carried out by two-tailed unpaired Student's t-test. The one-way analysis of variance (ANOVA) was performed to verify the difference between pre, post-haemodialysis and the control groups. A  $p < 0.05$  was considered significant. Post-hoc analysis was carried out, when appropriate, by the Student-Newman-Keuls test.

#### Results

The HD did not modify biochemical (hematocrit and hemoglobin), Physiological (Rest SpO<sub>2</sub>; rest SBP; rest DBP; VO<sub>2max</sub> and rest heart rate) and body weight parameters quantified immediately before exercise realization. Regardless of HD realization (Pre-haemodialysis or post-haemodialysis), the CRD patients had a lower value for hematocrit ( $-20\%$ ;  $p < 0.05$ ), hemoglobin ( $-19\%$ ;  $p < 0.05$ ), VO<sub>2max</sub> ( $-35\%$ ;  $p < 0.05$ ) and higher values for rest SBP ( $+24\%$ ;  $p < 0.05$ ) only in relation to the control group (Tab. 2). However, the rest systolic

blood pressure (SBP) has a little reduction ( $-11.5\%$ ;  $p < 0.05$ ) after HD procedure (no significant) between CRD patients, but have higher values ( $+16\%$ ;  $p < 0.05$ ) and significant difference when compared to the control group.

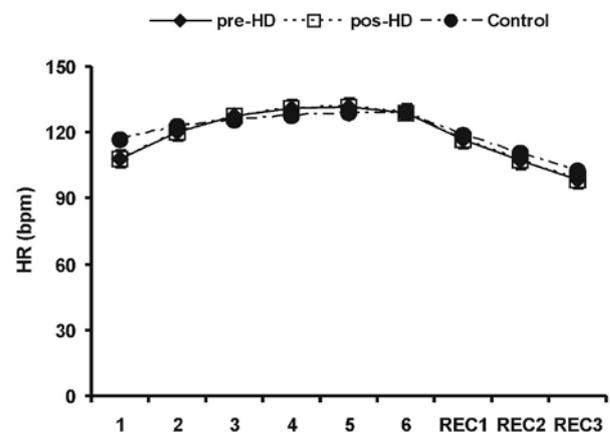
Table 2. Physiological and biochemical parameters in hypertensive renal patients before and 24 hours after dialysis procedure compared with healthy control non-dialyzed

	Pre-haemodialysis (n = 7)	Post-haemodialysis (n = 7)	Control (n = 7)
Hematocrit (%)	34.9 $\pm$ 4.1*	36.5 $\pm$ 3.0*	43.2 $\pm$ 2.2
Hemoglobin (g/dL)	11,8 $\pm$ 1.1*	12.2 $\pm$ 1.4*	14,6 $\pm$ 0.8
Rest heart rate (bpm)	81.2 $\pm$ 6.1	76.3 $\pm$ 5.4	78.7 $\pm$ 6.1
Rest SpO <sub>2</sub> (%)	99.0 $\pm$ 0.3	99.5 $\pm$ 0.4	98.8 $\pm$ 0.5
Rest systolic blood pressure (mmHg)	169.5 $\pm$ 6.4*	150.0 $\pm$ 9.0*	129.5 $\pm$ 7.8
Rest diastolic blood pressure (mmHg)	105.7 $\pm$ 6.8	95.4 $\pm$ 7.1	75.7 $\pm$ 3.7
Body weight (kg)	70,6 $\pm$ 11.7	71.2 $\pm$ 9.0	79.8 $\pm$ 4.2
VO <sub>2max</sub> (mL/kg/min)	15.1 $\pm$ 1.6*	14.9 $\pm$ 1.5*	23.1 $\pm$ 1.7

Values are means  $\pm$  SE

\* Significant difference compared to control group at  $p < 0.05$  (one-way analysis of variance)

A protocol of physical test was realized before and after 24 hours of HD with objective to verify the effects of dialysis in the cardiovascular parameters during exercise at 75% of HR<sub>max</sub>. The HR and SpO<sub>2</sub> were not different in the different phases of physical test between pre, pos-HD and the control group (Fig. 1).

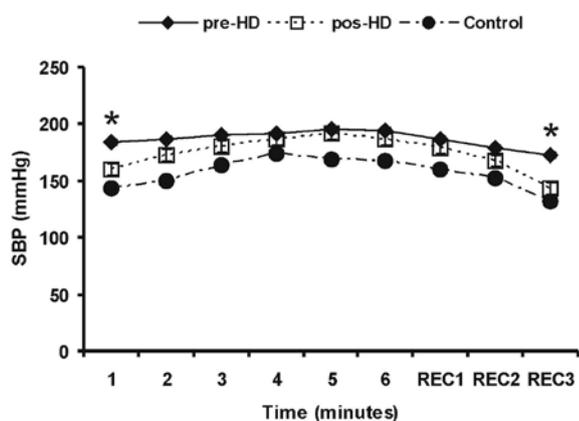


Values are means  $\pm$  SE; \*Significant difference compared to dialyzed and control group at  $p < 0.05$  (one-way analysis of variance)

Figure 1. Heart (beat) rate during protocol of exercise and recovery period (REC) before (pre-HD) and after 24 hours of haemodialysis (pos-HD) in hypertensive CRD patients ( $n = 7$ ) compared to healthy control non-dialyzed ( $n = 7$ )

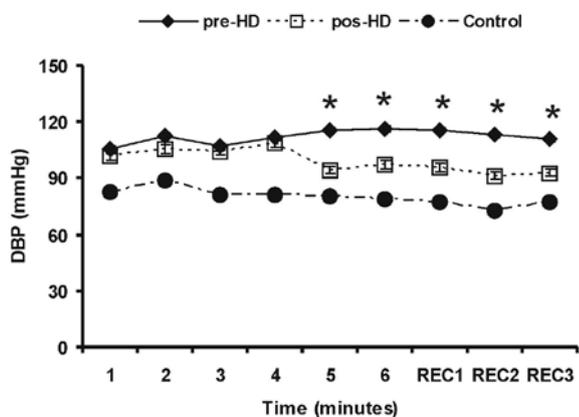
After dialysis, the SBP procedure has a reduction only at the first stage (Pre-HD vs Post-HD:  $-14\%$ ;  $p < 0.05$ ) and at the end of recovery period of physical test (Pre-HD vs Post-HD:  $-18\%$ ;  $p < 0.05$ ; Fig. 2).

A hypotension effect of HD in the patients was more evident in the diastolic blood pressure, where there was a reduction from the 5<sup>th</sup> to 9<sup>th</sup> min of physical test (Pre-HD vs Post-HD:  $-20\%$ ;  $p < 0.05$ ; Fig. 3). The peripheral oxygen saturation was not different between CRD patients (pre and post-HD) and control ones in the different phases of physical test, having a variation of approximately 97–99% (data is not shown here).



Values are means  $\pm$  SE; \*Significant difference compared to dialyzed and control group at  $p < 0.05$  (one-way analysis of variance)

Figure 2. Systolic blood pressure (SBP) during a protocol of exercise and recovery period (REC) before (pre-HD) and 24 hours after haemodialysis (post-HD) in hypertensive CRD patients ( $n = 7$ ) compared to healthy control non-dialyzed ( $n = 7$ )



Values are means  $\pm$  SE; \*Significant difference compared to dialyzed and control group at  $p < 0.05$  (one-way analysis of variance)

Figure 3. Diastolic blood pressure during a protocol of exercise and recovery period (REC) before (pre-HD) and 24 hours after haemodialysis (post-HD) in hypertensive CRD patients ( $n = 7$ ) compared to healthy control non-dialyzed ( $n = 7$ )

## Discussion

The investigators showed that training on non-dialysis days yielded significantly greater cardiorespiratory adaptations [8, 18]. In addition, patients engaged in the intradialytic training program significantly improved cardiorespiratory outcomes compared with non-exercising controls [18]. Mechanisms underlying this enhancement of dialysis adequacy likely include increased blood perfusion between the working muscle and bloodstream, thereby enabling more thorough removal of the damaging solutes through HD treatment [10].

The investigators concluded that it is difficult to persuade patients to maintain exercise programs on non-dialysis days [8, 18]. Therefore, exercising during HD is often recommended as a more feasible, convenient, and time-effective solution to promote exercise adherence [3, 8, 18].

Hypertension commonly occurs in the chronic renal patients. At the beginning of the haemodialysis treatment, approximately 80 to 90% of the patients are hypertensive and, after this initial period, around 60% still remain with elevated values of SBP and DBP [19]. In the hypertensive patients, the aerobic exercise has been utilized as complementary to the treatment of hypertensive status, aimed at (treatment for a disease, which is not the case, we presume) reduction in tensional levels. However, so far the chronic [6, 13] or acute effect of exercise 24 hours after dialysis on blood pressure levels have been studied a little.

Anderson et al. [6] investigated the effect of an exercise program on blood pressure in renal patients during the third and sixth month of HD. The results showed a significant reduction in SBP ( $138.4 \pm 19.6$  mm Hg to  $125.7 \pm 20$  mm Hg;  $p < 0.05$ ) and DBP ( $83.2 \pm 10.2$  mm Hg to  $74.7 \pm 9$  mm Hg;  $p < 0.05$ ).

In previous studies, it was recommended to do exercise only in the first two hours after the HD procedure, in order to avoid cardiovascular instability with fall in blood pressure after this phase [20]. On the other hand, in present study, we investigated the acute cardiovascular alterations in hypertensive renal patients during exercise with constant load (75% of  $HR_{max}$ ) for 24 h after HD. In this period of 24 h after HD there was observed a reduction in systolic ( $-14\%$ ;  $p < 0.05$ ) and principally in diastolic blood pressure ( $-20\%$  stages;  $p < 0.05$ ) only during exercise execution, but not at rest. Other studies have shown a blood pressure reduction only in rest situation after an exercise program [6, 13]. The DBP reduction during predominant aerobic exercise (constant load) executed after HD occurs probably as a function of enhancement in blood perfusion

or lower in sympathetic tonus in this interdialytic period. The hypotension effect observed 24 hours after HD in our study did not induce significant alterations in health markers (HR; SpO<sub>2</sub> and VO<sub>2max</sub>) and perceived exertion ratings (Borg scale) during exercise.

### Conclusions

In summary, the present study showed a significant hypotension effect during the exercise realization observed principally in DBP 24 hours after HD treatment in chronic renal patients. These patients have been recommended to do the exercise during HD and only for the first two hours after HD in order to avoid cardiovascular complications and enhanced clinical indicators. In the present study, we showed a little reduction in DBP 24 hours after HD only during exercise, which did not represent deleterious effect on health in the period of 24 hours after HD and can enhance performance indicators and better tolerance to exercise in the hypertensive and renal patients.

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