

Exercício aeróbico baseado no primeiro limiar ventilatório em pacientes com excesso de peso e doença renal crônica: impacto sobre a capacidade cardiorrespiratória e funcional

Impact of training at ventilatory threshold on cardiopulmonary and functional capacity in overweight patients with chronic kidney disease

Autores

Danilo Takashi Aoiike¹
Flavia Baria¹
Mariana Leister Rocha¹
Maria Ayako Kamimura¹
Marco Túlio de Mello¹
Sergio Tufik¹
Adriano Ammirati²
Lilian Cuppari^{1,2}

¹Universidade Federal de São Paulo – UNIFESP.

²Fundação Oswaldo Ramos – UNIFESP.

Data de submissão: 19/10/2011
Data de aprovação: 25/02/2012

Correspondência para:

Lilian Cuppari
Rua Pedro de Toledo, 282
Vila Clementino
São Paulo – SP – Brasil
CEP 04039-000
E-mail: lcuppari@uol.com.br

Suporte financeiro:
FAPESP

O referido estudo foi realizado na UNIFESP/EPM e no CEPE/AFIP.

Os autores declaram a inexistência de conflitos de interesse.

RESUMO

Introdução: O excesso de peso e a doença renal crônica (DRC) estão associados à baixa capacidade cardiorrespiratória (CR) e funcional (CF). Já foi observado que o treinamento aeróbico (TA) melhora a CR e CF. Métodos indiretos e subjetivos são comumente empregados para a prescrição da intensidade do TA. O limiar ventilatório (LV) é um método direto e objetivo que permite prescrever a intensidade do TA de acordo com a capacidade física do paciente. **Objetivos:** Avaliar o impacto do TA com base na intensidade do LV sobre a CR e CF de pacientes com excesso de peso e portadores de DRC na fase não dialítica. **Métodos:** Dez pacientes (oito homens; $49 \pm 10,1$ anos, IMC $30,4 \pm 3,5$ kg/m², depuração de creatinina $39,4 \pm 9,8$ mL/min/1,73m²) foram submetidos à TA 3 vezes por semana durante 12 semanas. CR (ergoespirometria), CF e parâmetros clínicos foram avaliados. **Resultados:** O TA promoveu aumento de 20% no consumo pico de O₂ (VO_{2PICO}), 16% na velocidade alcançada no VO_{2PICO} e melhora em 9,2% na caminhada de seis minutos, 20,3% na marcha estacionária, 35,7% no sentar e levantar, 16,3% na resistência muscular de membro superior e 15,3% no tempo de ir e voltar. A pressão arterial diminuiu sem modificação nos anti-hipertensivos, no peso ou no consumo de sódio. **Conclusão:** Os resultados indicam que o TA baseado na intensidade do LV melhora a CR, CF e pressão arterial de pacientes portadores de DRC com excesso de peso. Isso sugere que o TA baseado na intensidade LV é eficaz e pode ser empregado com segurança nesses pacientes.

ABSTRACT

Introduction: Chronic kidney disease (CKD) and obesity are both associated with reduced physical capacity. The potential benefit of aerobic training on physical capacity has been recognized. The exercise intensity can be established using different methods mostly subjective or indirect. Ventilatory threshold (VT) is a direct and objective method that allows prescribing exercise intensity according to individual capacity. **Objectives:** To evaluate the impact of aerobic training at VT intensity on cardiopulmonary and functional capacities in CKD patients with excess of body weight. **Methods:** Ten CKD patients (eight men, 49.7 ± 10.1 years; BMI 30.4 ± 3.5 kg/m², creatinine clearance 39.4 ± 9.8 mL/min/1.73 m²) underwent training on a treadmill three times per week during 12 weeks. Cardiopulmonary capacity (ergoespirometry), functional capacity and clinical parameters were evaluated. **Results:** At the end of 12 weeks, VO_{2PEAK} increased by 20%, and the speed at VO_{2PEAK} increased by 16%. The training resulted in improvement in functional capacity tests, such as six-minute walk test (9.2%), two-minute step test (20.3%), arm curl test (16.3%), sit and stand test (35.7%), and time up and go test (15.3%). In addition, a decrease in systolic and diastolic blood pressures was observed despite no change in body weight, sodium intake and antihypertensive medication. **Conclusion:** Aerobic exercise performed at VT intensity improved cardiopulmonary and functional capacities of overweight CKD patients. Additional benefit on blood pressure was observed. These results suggest that VT can be

Palavras-chave: Doença Renal Crônica. Obesidade. Exercício. Terapia por Exercício.

effectively applied for prescribing exercise intensity in this particular group of patients.

Keywords: Chronic Kidney Disease. Obesity. Exercise. Exercise Therapy.

INTRODUCTION

Patients with chronic kidney disease (CKD) have low cardiopulmonary and functional capacities that are expressed by reduced oxygen uptake (VO_2), decreased daily activity and low exercise tolerance.^{1,2} Low cardiopulmonary fitness and functional capacity of these patients become evident when one notes that the peak of VO_2 (VO_{2PEAK}) is on average 50% lower than that of healthy sedentary individuals of the same age.^{2,3} In addition, they have a reduction of about 40 to 50% in muscle strength^{2,3} as a consequence of muscle atrophy, reduced capillarization, increased peripheral vascular resistance⁴ and decreased arterial compliance.⁵

Physical inactivity, a condition commonly seen in over weight and obese individuals, is in general associated with low cardiopulmonary and functional capacities as well. Recent data demonstrated that the prevalence of excess of body weight has remarkably increased among patients with CKD.⁶ The association of both diseases may aggravate the physical capacity and consequently the quality of life of these patients. Indeed, low cardiopulmonary fitness and functional capacity are associated with greater risk of mortality, hospitalization and morbidity in patients with CKD.^{7,8} On the other hand, exercise improves cardiopulmonary and various aspects of functional capacity in CKD patients.^{2,9}

Exercise intensity can be prescribed based upon ratings of perceived physical exertion, metabolic equivalent, estimated or measured maximal heart rate and measured VO_{2PEAK} . The methods based on the relationship between different percentages of maximal heart rate or VO_{2PEAK} have been the most commonly used strategies for exercise prescription in general population.¹⁰ The ideal physical exercise protocol has not been established for patients with CKD.¹¹ The effective exercise prescription should not only ensure a sufficient training stimulus to yield the relevant health benefits, but should also do it without over-exertion and unnecessary discomfort, thereby promoting safety and exercise adherence.¹⁰⁻¹²

In line with these assumptions, the use of the ventilatory threshold (VT) as a target for determining the exercise intensity seems to be a more appropriate

method to be used for patients with CKD. The VT is defined as the maximum exercise intensity fully supported by aerobic metabolism, representing in general a mild to moderate exercise intensity.^{13,14} Additionally, since the VT is a direct and objective measure of cardiopulmonary capacity, the intensity of the exercise is determined individually according to physical capacity and it is independent of the patient's motivation.¹⁵

Studies using the VT for prescribing the exercise intensity for patients with severe chronic diseases are scarce, but in most of them the benefits achieved were similar to those of higher intensity.^{15,16} To our knowledge, only two studies have used the VT for prescribing the training intensity in patients with CKD and both were performed with patients on dialysis.^{17,18} The purpose of the present study was to investigate in overweight patients with CKD the impact of an aerobic training prescribed according to VT on cardiopulmonary and functional capacities.

METHODS

PATIENTS

Ten patients with CKD in the non-dialysis stage (stages 3 and 4) were recruited from the outpatient clinic from the Oswaldo Ramos Foundation according to the following criteria, body mass index (BMI) > 25 kg/m², age between 18 and 65 years, systolic blood pressure (BP) < 180 mmHg and diastolic BP < 100 mmHg, serum hemoglobin > 11 g/dL, glycated hemoglobin (HbA1c) < 8%, and absence of chronic obstructive pulmonary disease, congestive heart failure or active coronary disease. Patients using beta blockers or erythropoietin and with positive ergometric test were not included.

Patients were informed of the purpose of the study protocol and signed an informed consent form. The study was approved by the Ethics Committee of the Federal University of São Paulo.

STUDY PROTOCOL

This was a prospective, non-controlled interventional study. All patients were seen by a nephrologist at baseline, 6 weeks and 12 weeks. Clinical, physical, laboratorial and quality of life assessments were

performed at baseline and after 12 weeks. The training sessions using a treadmill were performed in the Psychobiology and Exercise Study Center. All sessions were performed under supervision in regards to intensity and duration of the exercise.

TRAINING PROTOCOL

The training program was conducted in accordance with the recommendations of the American College of Sports Medicine.¹² All training sessions were preceded by stretching of large muscle groups and heating (five minutes) and, at the end, by cool down and stretching (five minutes). The program lasted 12 weeks with three sessions per week on alternate days. The aerobic training was continuous, with an increment of ten minutes in duration every four weeks. The intensity was prescribed according to VT, characterized by the highest intensity of physical exertion fully maintained by aerobic energy pathways. The VT is considered a marker of exercise consistent with mild to moderate intensity and is usually found between 40 to 60% maximum VO_2 ($\text{VO}_{2\text{MAX}}$).¹⁹⁻²¹ The intensity control was done by means of the heart rate value obtained at VT.

ERGOMETRIC AND CARDIOPULMONARY EXERCISE TEST

The tests were performed on a treadmill. Ergometric test was performed by a physician for cardiac evaluation and as an adaptation to minimize the learning effect in cardiopulmonary exercise testing. The Bruce's modified protocol was applied for the ergometric test.²² The cardiopulmonary exercise test was used to determine the $\text{VO}_{2\text{PEAK}}$ since patients with severe chronic diseases usually do not meet the criteria for determining the $\text{VO}_{2\text{MAX}}$.⁹ The test began with a fixed inclination of 1%. The initial velocity was 3 km/h during the first three minutes with increments of 0.5 km/h every minute until the patient reaches physical exhaustion.

The ventilatory variables were measured using a gas analyzer (Quark PFT Cosmed 4, Rome, Italy) and were collected by the method of breath by breath. Before each test, the analyzer was calibrated with reference gases. The highest VO_2 obtained during the last stage reached was considered the $\text{VO}_{2\text{PEAK}}$. The VT was determined as the stage preceding the first occurrence of the exponential increase in ventilation, increase in the ventilatory equivalent for oxygen (VE/VO_2) and increase in expired fraction of oxygen. The respiratory compensation point (RCP) was determined as the stage preceding the second occurrence of

the exponential increase in ventilation, increase in the ventilatory equivalent for carbon dioxide (VE/VCO_2) and decrease in end-tidal carbon dioxide. Data were analyzed by the average of 20 seconds.

FUNCTIONAL CAPACITY TESTS

Functional capacity was assessed using a variety of objective measures. These included six-minute walk test (maximal distance walked along an internal corridor during six minutes), two-minute step test (maximal number of steps achieved in stationary walking during two minutes, used to quantifying the aerobic power), sit-to-stand test (maximal sit to stand cycles achieved in 30 seconds, used to quantifying the muscular endurance of the legs), arm curl test (maximal number of arm curl cycles in 30 seconds, used to quantifying the muscular endurance of the arms), sit and reach test (maximal distance achieved in the Wells bench, used to quantifying the general flexibility), back scratch test (maximum amplitude of the arms used to quantifying the arms flexibility) and time up and go test (shorter time to rise from a chair, walk three meters and sit back, used to quantifying the functional mobility). In order to minimize the effect of learning, the patients were previously submitted to a pre-test. All tests were applied in accordance with the methods described by Rikli.²³

QUALITY OF LIFE ASSESSMENT

The Short-Form Health Survey (SF-36) questionnaire was applied to assess the quality of life.²⁴ The scores for each domain range from 0 to 100%. The higher scores define a better quality of life. The questionnaire was applied individually in a clear and quiet room with the patient rested.

ANTHROPOMETRIC, LABORATORY AND CLINICAL MEASUREMENTS

Body weight and height were measured to determine body mass index (BMI). Blood was collected with the patient fasted for eight hours. Serum creatinine, urea, glucose, sodium, potassium, calcium, phosphorus, glycated hemoglobin, albumin (bromocresol green), hemoglobin, pH, bicarbonate (automated potentiometer) were determined. Twenty four-hour urine was collected for determination of creatinine clearance, urinary sodium and urea. Protein equivalent of nitrogen appearance (PNA) was determined using 24-hour urinary urea nitrogen, according to Sargent & Gotch's equation.²⁵ Blood pressure and resting heart rate were measured before the cardiopulmonary exercise test.

STATISTICAL ANALYSIS

Data are presented as mean and standard deviation or median and interquartile. Skewed variables were log or squared root transformed. Paired Student's *t*-test or Wilcoxon test were used to compare variables between baseline and 12 weeks. *P*-values < 0.05 were considered statistically significant. The SPSS® software version 15.0 for Windows (SPSS Inc., Chicago, IL, USA) was used for analysis.

RESULTS

The study included ten CKD patients (eight men; eight stage 3 and two stage 4; 49.7 ± 10.1 years, BMI 30.4 ± 3.5 kg/m²). The etiologies of kidney disease were hypertensive nephropathy (*n* = 4), tubule interstitial nephropathy (*n* = 2), chronic glomerulo nephritis (*n* = 2) and polycystic kidneys (*n* = 2). Only one patient had diabetes mellitus. At baseline, all patients were in use of antihypertensive medication, and sodium bicarbonate had been prescribed for nine patients. During the follow-up, one patient required a reduction in the angiotensin converting enzyme inhibitor dosage, and for another patient the dose of sodium bicarbonate was reduced by half. No other changes in medication were needed. All enrolled patients completed the study period. Eight patients attended more than 80% of the maximum of 36 sessions during the 12 weeks. The remaining two patients attended at least 75% of the sessions.

The cardiopulmonary parameters during the follow-up are depicted in Table 1. As can be seen, both absolute and relative VO_{2PEAK} increased after 12 weeks of training. The increase of these parameters was on average 20.7% (95%CI 12 – 29%) and 20% (95%CI 11 – 29%), respectively. Consistent with the increase in VO_{2PEAK} , the maximal ventilation and the speed in VO_{2PEAK} were significantly increased. Variables at VT, such as VO_2 , % VO_{2PEAK} and heart rate remained unchanged. However, the speed at VT increased significantly. Moreover, at RCP, an increase of VO_2 and speed with no change in % VO_{2PEAK} and heart rate were observed. Figure 1 shows the speed achieved at VT, RCP and at VO_{2PEAK} at baseline and after 12 weeks. It is noteworthy that the speed achieved at VT after 12 weeks (5.9 ± 0.7 km/h) was similar to the speed achieved at RCP at baseline (6.0 ± 0.7 km/h, *p* = 0.86).

The results of functional capacity tests are demonstrated in Table 2. Except for sit and reach test, stand and reach test, and back scratch test, that remained unchanged, all other tests were improved. The six-minute walk test and two-minute step test increased by an average of 9.2% (95%CI 5.1 – 13.2%) and 20.3%

(95%CI 11.8 – 28.8%) respectively. The arm curl test and sit and stand test increased by an average of 16.3% (95%CI 8.9 – 23.7%) and of 35.7% (95%CI 17 – 54.4%) respectively. The time up and go test reduced by 15.3% (95%CI 7.8 – 22.9%) after 12 weeks.

As seen in Table 3, improvement in the functional domain and a tendency to increase the general health perception were found in the SF-36. Table 4 summarizes the clinical and laboratory characteristics of patients at baseline and after 12 weeks of training. Body weight, as well as most laboratory parameters, remained unchanged. Serum urea and PNA decreased significantly, and there was a trend of increasing serum bicarbonate. Both systolic and diastolic blood pressure decreased significantly. The resting heart rate tended to decrease. No cardiovascular, metabolic, osteoarticular or skeletal-muscle adverse events were observed during the follow-up.

DISCUSSION

In the present study, we found that the use of VT as a target for establishing the exercise intensity was well-tolerated and resulted in improvement of cardiopulmonary and functional capacity of the non-dialyzed CKD patients with excess of body weight.

Few exercise studies have been performed with patients in the non-dialysis stage of CKD and, to the best of our knowledge, none of them employed VT for establishing the training intensity. All studies with this group of CKD patients used indirect methods, such as arbitrary percentage of VO_{2PEAK} ,²⁶ the percentage of maximum effort in conjunction with the Borg scale²⁷ or the percentage of heart rate reserve.²⁸ Although valid, the mentioned methods do not guarantee that the intensity of exercise coincides with that based on VT, which ensures a fully aerobic intensity and guarantee that the exercise is performed according to the capacity of each patient. Indeed, depending on the percentage of VO_{2PEAK} chosen, the intensity of the exercise can be inappropriately high. In the present study, the % VO_{2PEAK} found at VT was on average 64.5%, varying from 42.9 to 88.8%. Since the % VO_{2PEAK} at VT has a large inter-subject variability, the precision of indirect methods in relation to VT can be compromised, implicating for very low intensity for some or inappropriate high for others.

It is well known that repeated sessions at high intensity may increase the risk of over-reaching or over-training. Since overweight/obese CKD patients are potentially at high risk of cardiovascular disease²⁹ and osteoarticular and skeletal muscle

TABLE 1 CARDIOPULMONARY PARAMETERS BEFORE AND AFTER 12 WEEKS OF TRAINING (n = 10)

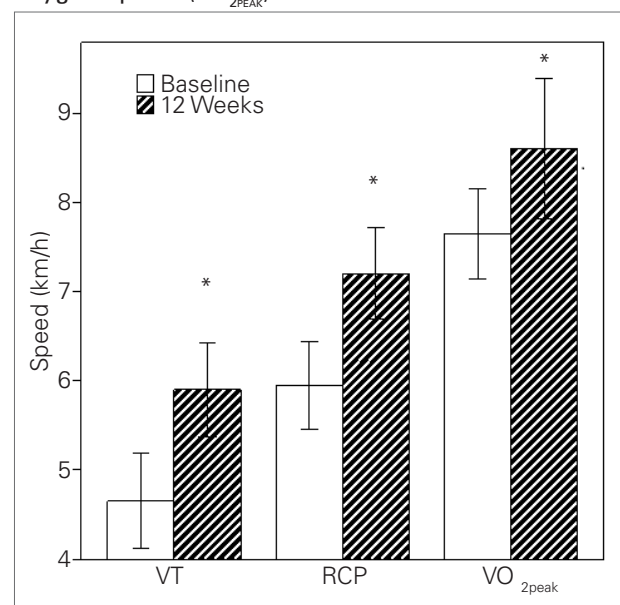
Variables	Baseline	12 weeks	p-value
VO _{2PEAK} absolute (mL/min)	1878.8 ± 426.5	2254.4 ± 539.8	0.002
VO _{2PEAK} relative (mL/kg/min)	23.1 ± 5.3	27.6 ± 6.7	0.003
Maximal heart rate (bpm)	159.3 ± 13.3	160.0 ± 13.9	0.87
Maximal ventilation (L/min)	85.3 ± 23.7	98.2 ± 16.8	0.02
Speed in VO _{2PEAK} (km/h)	7.5 (7.0–8.0)	8.7 (7.5–9.5)	0.007
VO ₂ in VT (mL/kg/min)	14.4 ± 3.2	16.2 ± 3.9	0.12
%VO _{2PEAK} in VT	64.5 ± 16.0	59.3 ± 6.8	0.47
Heart rate in VT (bpm)	115.1 ± 12.0	111.6 ± 9.6	0.43
Speed in VT (km/h)	4.7 ± 0.7	5.9 ± 0.7	0.001
VO ₂ in RCP (mL/kg/min)	17.4 ± 3.6	21.5 ± 4.9	0.009
%VO _{2PEAK} in RCP	77.1 ± 13.2	78.6 ± 8.5	0.76
Heart rate in RCP (bpm)	130.4 ± 16.4	137.6 ± 12.2	0.27
Speed in RCP (km/h)	6.0 ± 0.7	7.2 ± 0.7	0.001

Data are presented as mean ± standard deviation or median and interquartile. VO₂: oxigenuptake; VT: ventilatory threshold; RCP: respiratory compensation point.

injuries,³⁰ training at high intensity may be harmful. Therefore, the use of VT for prescribing the exercise intensity may be safer and more appropriate for these patients. Additionally, due to the low intensity, this method may offer a better compliance of the patients. In accordance, no withdraw was observed in the present study and there was a high degree of compliance to the training sessions. To date, there are only two reports with patients on dialysis that used the VT to prescribe the training. In the study by Koufaki *et al.*, 33 patients undergoing hemodialysis (HD) or peritoneal dialysis the VO_{2PEAK} increased by 15% after 12 weeks of training in a cycle ergometer 3 times per week.¹⁷ In another study, also using a cycle ergometer during 24 weeks, the increase in VO_{2PEAK} was on average 20% in a group of 24 patients on HD.¹⁸

Despite using a low intensity training, the beneficial effects, in terms of cardiopulmonary, were evident in our study. Notably, the benefits were similar or even better than that found in patients with CKD using higher intensity training. In the majority of studies with patients on dialysis whose the overload of exercise was greater, either in intensity (85% of VO_{2PEAK})³¹⁻³⁴ or in the volume of training (greater number of sessions or longer duration of session),³⁵⁻³⁸ the VO_{2PEAK} increased on average 19%, which was very similar to that found in the current study (20.7%).

Figure 1. Speed at ventilatory threshold (VT), respiratory compensation point (RCP) and peak of the oxygen uptake (VO_{2PEAK}).



Data expressed in mean and 95%CI. *p < 0.01 – baseline versus 12 weeks.

The raise in the VO_{2PEAK} was accompanied by an increase in the speed achieved at VT, as well as at RCP, indicating a higher metabolic efficiency for the same workload. Most important is the finding that the speed achieved at VT after the period of training was very similar to that achieved at RCP before training

TABLE 2 FUNCTIONAL CAPACITY PARAMETER AS BEFORE AND AFTER 12 WEEKS OF TRAINING (n = 10)

Variables	Baseline	12 weeks	p-value
Six minutes walk test (m)	578.9 ± 49.9	631.8 ± 62.7	0.001
Two minutes step test (steps)	190.5 ± 32.8	228.2 ± 38.2	< 0.001
Time up and go test (sec)	6.3 ± 0.7	5.3 ± 0.8	0.002
Sit and reach test (cm)	18.9 ± 6.5	21.0 ± 7.1	0.06
Arm curl test - right arm (repetitions)	18.7 ± 3.7	22.5 ± 4.2	0.001
Arm curl test - left arm (repetitions)	19.0 ± 3.8	22.0 ± 4.2	< 0.001
Sit and stand test (repetitions)	17.9 ± 3.9	24.1 ± 5.6	0.001
Back scratch test – right arm (cm)	4.2 ± 6.9	5.9 ± 5.8	0.29
Back scratch test – left arm (cm)	7.8 ± 8.1	3.9 ± 7.9	0.23
Stand and reach test (cm)	90.9 ± 10.4	95.1 ± 5.5	0.11

Data are presented as mean ± standard deviation.

TABLE 3 SCORE RESULTS OF SF-36 QUESTIONNAIRE BEFORE AND AFTER 12 WEEKS OF TRAINING (n = 10)

Domains	Baseline	12 weeks	p-value
Physical functioning	87.5 (78.7 – 91.2)	95.0 (90.0 – 95.0)	0.01
Role physical	92.5 ± 23.7	100.0 ± 0	0.32
Bodily pain	84.0 (67.0 – 100.0)	100.0 (67.5 – 100.0)	0.92
General health perception	62.0 ± 14.3	68.8 ± 11.6	0.06
Vitality	77.5 (63.7 – 86.2)	85.0 (65.0 – 100.0)	0.23
Social functioning	100.0 (75.0 – 100.0)	100.0 (84.38 – 100.0)	0.28
Role emotional	90.0 ± 31.6	90.0 ± 22.5	0.97
Mental health	82.8 ± 16.8	84.0 ± 12.8	0.52
Total	87.5 (75.5 – 91.5)	91.2 (79.9 – 92.4)	0.44

Data are presented as mean ± standard deviation or median and interquartile.

(Figure 1). This means that the baseline workload, which was only possible to be achieved with a large contribution of anaerobic metabolism (RCP), was reached almost exclusively by the aerobic metabolism (VT) after 12 weeks of training.

The benefits observed in the cardiopulmonary tests were also seen in the functional capacity tests. Indeed, after 12 weeks, the patients increased on average 9.2% in the distance walked in the six-minute walk test. It is of note that the distance value achieved after the period of training was similar to that observed in sedentary healthy individuals.^{39,40} Improvement of functional capacity tests, particularly in the six-minute walk test, has also been observed in patients on dialysis, independently of the type of exercise employed.^{41,42} An important result of our study was found in the two-minute step test as well. The increase in the number of steps was on average 20.3%. There was also

improvement of anaerobic characteristic tests, such as sit and stand test (35.7%), arm curl test (16.3%) and time up and go test (15.3%). Although the reason for this finding is not clear, since the training was aerobic, it could be attributed to psychological aspects, as motivation, better self-esteem and sense of well-being. A more efficient neuromuscular interaction could also be speculated.⁴³

The improvement in the cardiopulmonary and functional capacities of patients was also perceived by a trend towards an increase in general health perception score and a significant increase in the functional domain according to SF-36 questionnaire. Apart from the type of training, similar results have been found in several studies with patients undergoing hemodialysis.^{24,44,45}

Of clinical importance, the 12-week training resulted in a significant reduction of both systolic and

TABLE 4 CLINICAL AND LABORATORIAL PARAMETERS BEFORE AND AFTER 12 WEEKS OF TRAINING (n = 10)

Variables	Baseline	12 weeks	p-value
Body weight (kg)	83.1 ± 12.7	83.5 ± 14.3	0.77
Serum creatinine (mg/dL)	3.1 ± 0.8	2.9 ± 0.7	0.32
Creatinine clearance (mL/min/1.73m ²)	39.4 ± 9.8	40.1 ± 15.0	0.39
Urea (mg/dL)	108.9 ± 43.6	90.0 ± 39.7	0.008
Glucose (mg/dL)	94.0 ± 17.8	90.4 ± 14.6	0.24
Glycate hemoglobin (%)	5.83 ± 0.8	5.79 ± 0.4	0.89
pH	7.28 ± 0.5	7.28 ± 0.3	0.93
Bicarbonate (mmol/L)	18.3 (16.5 – 22.3)	22.7 (17.7 – 25.4)	0.06
Hemoglobin (g/dL)	13.9 (11.4 – 15.0)	14.2 (13.0 – 15.1)	0.88
Albumin (g/dL)	4.4 (4.2 – 4.5)	4.2 (4.1 – 4.3)	0.21
Calcium (mmol/L)	1.3 ± 0.05	1.3 ± 0.07	0.54
Phosphorus (mg/dL)	3.5 ± 0.7	3.6 ± 0.9	0.31
Serum sodium (mEq/L)	139.7 ± 1.3	142.4 ± 9.3	0.36
Potassium (mEq/L)	4.4 ± 0.4	4.5 ± 0.6	0.66
Urinary sodium (mEq/24hs)	232.3 ± 64.5	258.9 ± 112.5	0.31
PNA (g/dia)	82.0 ± 18.8	73.1 ± 19.6	0.035
CRP (mg/dL)	0,24 (0,11 – 1,1)	0,22 (0,13 – 0,4)	0,953
Systolic blood pressure (mmHg)	126.0 ± 8.4	112.5 ± 8.6	0.002
Diastolic blood pressure (mmHg)	80.0 ± 4.7	73.0 ± 6.7	0.02
Mean blood pressure (mmHg)	96.7 (93.3 – 97.5)	85.0 (82.9 – 90.8)	0.008
Resting heart rate (bpm)	77.0 ± 10.9	70.3 ± 8.7	0.06

Data are presented as mean ± standard deviation or median and interquartile. PNA: protein equivalent of total nitrogen appearance; CRP: c-reactive protein.

diastolic blood pressures of the patients. The decrease in blood pressure due to mild/moderate aerobic exercise has been well established both in normotensive and hypertensive individuals,^{46,47} as well as in CKD patients.^{28,48} Aerobic training lowers blood pressure by reducing peripheral vascular resistance due to the improvement of endothelium-mediated vasodilatation, attenuation of increased sympathetic nervous system activity and vascular remodeling.⁴⁶ Most important, the blood pressure reduction occurred in face of no modifications in the antihypertensive medication, sodium intake (estimated by the 24-h urinary sodium excretion) and body weight. It is of note that no specific dietary intervention aiming at body weight reduction was employed in the current study. Thus, it is possible to conclude that the benefits achieved herein may be attributed primarily to the exercise.

The reason for the tendency to increase serum bicarbonate after the 12 weeks of training is not clear. We could speculate that the patients were more

compliant to the medication (sodium bicarbonate) since in each monthly visit the adequate use of medication was reinforced. It is also possible that the decrease in protein intake estimated by PNA could have contributed to the decrease of the acid load.

Although the present investigation has limitations, such as the small sample size and lack of a control group, some strengths deserve to be mentioned. First, we used an objective and reliable method for measuring cardiopulmonary capacity. Second, the benefits on physical capacity and clinical aspects were clearly evidenced by a set of markers of cardiopulmonary and functioning capacities.

Aerobic exercise performed at VT intensity improved cardiopulmonary and functional capacities of overweight CKD patients with no adverse effect. Additional benefit on blood pressure was observed. These results suggest that VT can be effectively applied for prescribing exercise intensity in this particular group of patients.

ACKNOWLEDGMENTS

This study was supported by Fundação de Amparo à Pesquisa do Estado de São Paulo – Fapesp (2009/14786-0), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Oswaldo Ramos Foundation and CEPE/AFIP.

REFERENCES

- Hsieh RL, Lee WC, Huang HY, Chang CH. Quality of life and its correlates in ambulatory hemodialysis patients. *J Nephrol* 2007;20:731-8.
- Kouidi EJ. Central and peripheral adaptations to physical training in patients with end-stage renal disease. *Sports Med* 2001;31:651-65.
- Hsieh RL, Lee WC, Chang CH. Maximal cardiovascular fitness and its correlates in ambulatory hemodialysis patients. *Am J Kidney Dis* 2006;48:21-7.
- Adams GR, Vaziri ND. Skeletal muscle dysfunction in chronic renal failure: effects of exercise. *Am J Physiol Renal Physiol* 2006;290:F753-61.
- Mustata S, Chan C, Lai V, Miller JA. Impact of an exercise program on arterial stiffness and insulin resistance in hemodialysis patients. *J Am Soc Nephrol* 2004;15:2713-8.
- Johansen KL, Young B, Kaysen GA, Chertow GM. Association of body size with outcomes among patients beginning dialysis. *Am J Clin Nutr* 2004;80:324-32.
- Sietsema KE, Amato A, Adler SG, Brass EP. Exercise capacity as a predictor of survival among ambulatory patients with end-stage renal disease. *Kidney Int* 2004;65:719-24.
- Knight EL, Ofsthun N, Teng M, Lazarus JM, Curhan GC. The association between mental health, physical function, and hemodialysis mortality. *Kidney Int* 2003;63:1843-51.
- Painter P. Physical functioning in end-stage renal disease patients: update 2005. *Hemodial Int* 2005;9:218-35.
- da Cunha FA, Farinatti Pde T, Midgley AW. Methodological and practical application issues in exercise prescription using the heart rate reserve and oxygen uptake reserve methods. *J Sci Med Sport* 2011;14:46-57.
- Kesaniemi YK, Danforth E, Jr., Jensen MD, Kopelman PG, Lefèbvre P, Reeder BA. Dose-response issues concerning physical activity and health: an evidence-based symposium. *Med Sci Sports Exerc* 2001;33:S351-8.
- American College of Sports Medicine Position Stand. The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults. *Med Sci Sports Exerc* 1998;30:975-91.
- Wasserman K. Determinants and detection of anaerobic threshold and consequences of exercise above it. *Circulation* 1987;76:VI29-39.
- Mader A, Heck H. A theory of the metabolic origin of “anaerobic threshold”. *Int J Sports Med* 1986;Suppl 1:45-65.
- Gitt AK, Wasserman K, Kilkowski C, *et al.* Exercise anaerobic threshold and ventilatory efficiency identify heart failure patients for high risk of early death. *Circulation* 2002;106:3079-84.
- Sullivan MJ, Higginbotham MB, Cobb FR. Exercise training in patients with chronic heart failure delays ventilatory anaerobic threshold and improves submaximal exercise performance. *Circulation* 1989;79:324-9.
- Koufaki P, Mercer TH, Naish PF. Effects of exercise training on aerobic and functional capacity of end-stage renal disease patients. *Clin Physiol Funct Imaging* 2002;22:115-24.
- Sakkas GK, Sargeant AJ, Mercer TH, *et al.* Changes in muscle morphology in dialysis patients after 6 months of aerobic exercise training. *Nephrol Dial Transplant* 2003;18:1854-61.
- Bhambhani Y, Singh M. Ventilatory thresholds during a graded exercise test. *Respiration* 1985;47:120-8.
- Zhang JG, Ohta T, Ishikawa-Takata K, Tabata I, Miyashita M. Effects of daily activity recorded by pedometer on peak oxygen consumption (VO_{2peak}), ventilatory threshold and leg extension power in 30- to 69-year-old Japanese without exercise habit. *Eur J Appl Physiol* 2003;90:109-13.
- Stringer WW, Wasserman K. Statement on exercise: American College of Chest Physicians/American Thoracic Society--exercise for fun or profit? *Chest* 2005;127:1072-3; author reply 3-4.
- Okin PM, Ameisen O, Kligfield P. A modified treadmill exercise protocol for computer-assisted analysis of the ST segment/heart rate slope: methods and reproducibility. *J Electrocardiol* 1986;19:311-8.
- Rikli RE JC. Development and validation of functional fitness test for community-residing older adults. *J Aging Phys Activity* 1999;7:129-61.
- Painter P, Carlson L, Carey S, Paul SM, Myll J. Physical functioning and health-related quality-of-life changes with exercise training in hemodialysis patients. *Am J Kidney Dis* 2000;35:482-92.
- Sargent JA, Gotch FA. Mass balance: a quantitative guide to clinical nutritional therapy. I. The predialysis patient with renal disease. *J Am Diet Assoc* 1979;75:547-51.
- Eidemak I, Haaber AB, Feldt-Rasmussen B, Kanstrup IL, Strandgaard S. Exercise training and the progression of chronic renal failure. *Nephron* 1997;75:36-40.
- Clyne N, Ekholm J, Jogestrand T, Lins LE, Pehrsson SK. Effects of exercise training in predialytic uremic patients. *Nephron* 1991;59:84-9.
- Boyce ML, Robergs RA, Avasthi PS, *et al.* Exercise training by individuals with predialysis renal failure: cardiorespiratory endurance, hypertension, and renal function. *Am J Kidney Dis* 1997;30:180-92.
- Fried LF, Katz R, Cushman M, *et al.* Change in cardiovascular risk factors with progression of kidney disease. *Am J Nephrol* 2009;29:334-41.
- Mecca GC, Jeanty SR, Prado LFAE. [The adverse effects of exercise]. *Nefrologia* 2009;29:365.
- Goldberg AP, Geltman EM, Hagberg JM, *et al.* Therapeutic benefits of exercise training for hemodialysis patients. *Kidney Int Suppl* 1983;16:S303-9.
- Goldberg AP, Geltman EM, Gavin JR 3rd, *et al.* Exercise training reduces coronary risk and effectively rehabilitates hemodialysis patients. *Nephron* 1986;42:311-6.

33. Akiba T, Matsui N, Shinohara S, Fujiwara H, Nomura T, Marumo F. Effects of recombinant human erythropoietin and exercise training on exercise capacity in hemodialysis patients. *Artif Organs* 1995;19:1262-8.
34. Harter HR, Goldberg AP. Endurance exercise training. An effective therapeutic modality for hemodialysis patients. *Med Clin North Am* 1985;69:159-75.
35. Konstantinidou E, Koukouvou G, Kouidi E, Deligiannis A, Tourkantonis A. Exercise training in patients with end-stage renal disease on hemodialysis: comparison of three rehabilitation programs. *J Rehabil Med* 2002;34:40-5.
36. Deligiannis A, Kouidi E, Tassoulas E, Gigis P, Tourkantonis A, Coats A. Cardiac effects of exercise rehabilitation in hemodialysis patients. *Int J Cardiol* 1999;70:253-66.
37. Kouidi E, Albani M, Natsis K, *et al.* The effects of exercise training on muscle atrophy in haemodialysis patients. *Nephrol Dial Transplant* 1998;13:685-99.
38. Kouidi E, Iacovides A, Iordanidis P, *et al.* Exercise renal rehabilitation program: psychosocial effects. *Nephron* 1997;77:152-8.
39. Camarri B, Eastwood PR, Cecins NM, Thompson PJ, Jenkins S. Six minute walk distance in healthy subjects aged 55-75 years. *Respir Med* 2006;100:658-65.
40. Chetta A, Zanini A, Pisi G, *et al.* Reference values for the 6-min walk test in healthy subjects 20-50 years old. *Respir Med* 2006;100:1573-8.
41. Koh KP, Fassett RG, Sharman JE, Coombes JS, Williams AD. Effect of intradialytic versus home-based aerobic exercise training on physical function and vascular parameters in hemodialysis patients: a randomized pilot study. *Am J Kidney Dis* 2010;55:88-99.
42. Headley S, Germain M, Mailloux P, *et al.* Resistance training improves strength and functional measures in patients with end-stage renal disease. *Am J Kidney Dis* 2002;40:355-64.
43. Lucia A, Hoyos J, Pardo J, Chicharro JL. Metabolic and neuromuscular adaptations to endurance training in professional cyclists: a longitudinal study. *Jpn J Physiol* 2000;50:381-8.
44. Johansen KL, Kaysen GA, Young BS, Hung AM, da Silva M, Chertow GM. Longitudinal study of nutritional status, body composition, and physical function in hemodialysis patients. *Am J Clin Nutr* 2003;77:842-6.
45. Painter P, Carlson L, Carey S, Paul SM, Myll J. Low-functioning hemodialysis patients improve with exercise training. *Am J Kidney Dis* 2000;36:600-8.
46. Pescatello LS, Franklin BA, Fagard R, Farquhar WB, Kelley GA, Ray CA. American College of Sports Medicine position stand. Exercise and hypertension. *Med Sci Sports Exerc* 2004;36:533-53.
47. Nybo L, Sundstrup E, Jakobsen MD, *et al.* High-intensity training versus traditional exercise interventions for promoting health. *Med Sci Sports Exerc* 2010;42:1951-8.
48. Pechter U, Maarros J, Mesikepp S, Veraksits A, Ots M. Regular low-intensity aquatic exercise improves cardio-respiratory functional capacity and reduces proteinuria in chronic renal failure patients. *Nephrol Dial Transplant* 2003;18:624-5.