Effects of aerobic training during hemodialysis on heart rate variability and left ventricular function in end-stage renal disease patients

Authors

Maycon de Moura Reboredo[1]
Bruno do Valle Pinheiro[2]
José Alberto Neder[3]
Maria Priscila Wermelinger Ávila[4]
Maria Lídia de Borges Araujo e Ribeiro[5]
Adriano Fernandes de Mendonça[4]
Mariane Vaz de Mello[4]
Ana Clara Cattete Bainha[4]
José Dondici Filho[2]
Rogério Baumgratz de Paula[2]

[1] Federal Institute of Education, Science and Technology of Southeast of Minas Gerais (Instituto Federal de Educação, Ciência e Tecnologia do Sudeste de Minas Gerais from Portuguese)
[2] Department of Internal Medicine of the Universidade Federal de Juiz de Fora – UFJF
[3] Escola Paulista de Medicina of the Universidade Federal de São Paulo
[4] Physical therapy of the UFJF
[5] Medical School of the UFJF

This study was conducted at the Universidade Federal de Juiz de Fora - Interdisciplinary Nucleus of Study and Research in Nephrology (NIEPEN).

Submitted: 07/12/2010
Accepted: 08/22/2010

Corresponding author:
Dr. Maycon de Moura Reboredo
Rua José Lourenço Khelmer, 1300 - sobreloja, Bairro São Pedro, Juiz de Fora – Minas Gerais – Brasil.
CEP: 36036-330
E-mail: mayconreboredo@yahoo.com.br

Financial support:
Fundação de Amparo à Pesquisa do Estado de Minas Gerais - FAPEMIG (APQ-02452-09), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – CAPES, and Fundação IMEPEN (Instituto Mineiro de Estudos e Pesquisas em Nefrologia).

Abstract

Introduction: Decreased heart rate variability (HRV) in patients with end stage renal disease (ESRD) undergoing hemodialysis is predictive of cardiac death, especially due to sudden death. **Objective:** To evaluate the effects of aerobic training during hemodialysis on HRV and left ventricular function in ESRD patients. **Methods:** Twenty two patients were randomized into two groups: exercise (n = 11; 49.6 ± 10.6 years; 4 men) and control (n = 11; 43.5 ± 12.8; 4 men). Patients assigned to the exercise group were submitted to aerobic training, performed during the first two hours of hemodialysis, three times weekly, for 12 weeks. HRV and left ventricular function were assessed by 24 hours Holter monitoring and echocardiography, respectively. **Results:** After 12 weeks of protocol, no significant differences were observed in time and frequency domains measures of HRV in both groups. The ejection fraction improved non-significantly in exercise group (67.5 ± 12.6% *vs.* 70.4 ± 12%) and decreased non-significantly in control group (73.6 ± 8.4% *vs.* 71.4 ± 7.6%). **Conclusion:** A 12-week aerobic training program performed during hemodialysis did not modify HRV and did not significantly improve the left ventricular function.

Keywords: exercise, renal dialysis, heart rate, ventricular function, left.

[J Bras Nefrol 2010;32(4): 367-373]©Elsevier Editora Ltda.

Introduction

The high mortality rate among patients with chronic kidney disease (CKD) undergoing hemodialysis is mainly associated with a high prevalence of cardiovascular diseases, such as coronary artery disease, arterial hypertension, left ventricular hypertrophy, and heart failure.[1] Another relevant cardiovascular event in those patients is the occurrence of cardiac arrhythmias, which represent the major cause of sudden death.[2]

The development of cardiac arrhythmias in patients with CKD is associated with autonomic dysfunction evidenced by the reduction in heart rate variability (HRV).[3] In addition, the reduction in HRV represents an independent risk factor for cardiac mortality in those patients.[4,5]

Thus, strategies, such as exercise training, have been implemented aiming at reducing cardiovascular mortality due to an increase in HRV and improvement of the left ventricular function, specially in the population with heart disease.[6,7] However, only a few studies have assessed the effect of an exercise training program on those cardiovascular parameters in patients with CKD undergoing hemodialysis.[8-11]

This study aimed at assessing the effects of guided aerobic training during hemodialysis sessions on HRV and left ventricular function of patients with CKD.

Methods

Patients

The sample comprised patients with CKD undergoing hemodialysis at the Nephrology Service of the Hospital Universitário of the Universidade Federal de Juiz de Fora, state of Minas Gerais, three times a week, in a total of 12 hours per week, for at least six months. During hemodialysis sessions, polysulfone membrane and bath with the following characteristics were used: sodium, 138.0 mEq/L; potassium, 2.0 mEq/L; calcium, 2.5 mEq/L; magnesium, 1.0 mEq/L; chloride, 108.5 mEq/L; acetate, 3.0 mEq/L; bicarbonate, 32.0 mEq/L. Adult patients, of both sexes, who did not exercise on a regular basis for at least six months were included.

The exclusion criteria were as follows: diabetes mellitus; unstable angina; uncontrolled arterial hypertension [systolic blood pressure (SBP) ≥ 200 mm Hg and/or diastolic blood pressure (DBP) ≥ 120 mm Hg]; use of antiarrhythmic drugs; severe pneumopathies; acute systemic infection; severe renal osteodystrophy; and disabling neurological and muscle-skeletal disorders.

The study project was approved by the Committee on Ethics in Research of the Universidade Federal de Juiz de Fora and all patients who agreed to participate in the study provided written informed consent.

Experimental procedure

Initially, the patients included in the study were randomized into an exercise and a control group. Patients in the exercise group underwent three sessions of aerobic exercise per week, performed during hemodialysis sessions, for 12 weeks, while patients in the control group remained in the usual dialytic treatment.

At baseline and after 12 weeks in the study, all patients underwent Holter monitoring and echocardiography, conducted by examiners who did not know about the groups. In addition, a blood sample was also collected.

Holter monitoring and heart rate variability assessment

Holter monitoring was performed for 24 hours, in the interdialytic period, by use of a digital Holter monitor (DMS 300-7, Compact Flash Card Holter Recorder, DMS, Nevada, USA). The data stored were processed by use of the Cardio Scan 8.0 software to assess HRV. Abnormal beats and artifact areas were automatically and manually identified and excluded from analysis. Heart rate variability was assessed in the time and frequency domains.

For analysis in the time domain, normal R-R intervals were called iNN. To assess HRV in the time domain and based on iNN, the following parameters were obtained by use of statistical methods: mean of the standard deviations of iNN every five minutes (SDNN index); root of the mean squared difference of successive iNN (RMSSD); and percentage of successive iNN with a difference in duration greater than 50 ms (pNN50).[12]

When assessing HRV in the frequency domain, a low frequency (LF) band (between 0.04 and 0.15 Hz) and a high frequency (HF) band (between 0.15 and 0.40 Hz) were used. The LF/HF ratio was obtained.[12]

Beta-blockers were suspended four days before Holter monitoring.

Echocardiography

M mode and two-dimensional echocardiography was performed in the interdialytic period by a single cardiologist, with the Doppler technique (VIVID 3 - GE Healthcare, Milwaukee, Wisconsin, USA). Anatomical and functional data were obtained at rest by use of a 3.5-MHz linear transducer, placed on the third or fourth left intercostal space. Measures were obtained and analyzed according to the guidelines of the American Society of Echocardiography.[13]

Left ventricular mass index was obtained by correcting left ventricular mass to body surface.[14,15] The geometrical classification of the left ventricle was based on the assessment of left ventricular mass and relative wall thickness.[15] The following indices were measured for assessing left ventricular function: end diastolic volume; end systolic volume; systolic volume; and ejection fraction.

Laboratory data

The following values were assessed: hemoglobin (g/dL); hemodialysis efficiency index (Kt/V); creatinine (mg/dL); phosphorus (mg/dL); potassium (mEq/L); calcium (mg/dL); and albumin (g/dL). Blood samples were collected before the hemodialysis session, with no indication of fasting.

Aerobic exercise

Supervised aerobic training was performed within the first two hours of hemodialysis, and lasted, on average, one hour. The training comprised three steps: warm up; conditioning; and cool down. A horizontal electromagnetic cycle ergometer (Movement, BM 4000, Brudden Equipamentos Ltda, São Paulo, Brazil) was used for aerobic exercise training.

Warm up comprised stretching the lower limbs for approximately 10 minutes, and aerobic exercise training with low load (4.9 N·m) and at low rotation (up to 35 rpm) for five minutes. Conditioning consisted of aerobic exercise training for up to 35 minutes. The duration of exercise training was individualized according to the response of the patients: they started training for a period of time with which they felt comfortable and were encouraged to increase the length of training session to complete 35 minutes. Load was assigned according to the tolerance of each patient, who was instructed to maintain a constant rotation throughout the entire aerobic exercise training. The intensity of the training was determined by the Borg-modified scale, in which patients had to remain between four and six.[16] Cool down consisted in one to three minutes of aerobic exercise with a 4.9 N·m load and at low rotation.

Arterial blood pressure was monitored at rest, every five minutes during conditioning, and after cool down. Heart rate was continuously monitored by use of a cardiofrequencemetre (Polar F1, Polar Electro Oy, Kempele, Finland).

The criteria for interrupting aerobic exercise included intense physical fatigue, chest pain, dizziness, paleness, lipothymia, tachycardia, hypotension, and lower limb fatigue.

When patients had a change in blood pressure (SBP > 180 mm Hg and/or DBP > 110 mm Hg), interdialytic weight gain greater than 5 kg, difficulty in vascular access, or any significant complain (pain, dyspnea) before exercise training, they could not exercise on that day or while such changes persisted.

Statistical analysis

Data were expressed as mean ± standard deviation or median (interquartile range), when appropriate. For comparing initial and final values in each group, paired *t* test and Wilcoxon test were used for parametric and nonparametric data, respectively. For comparing the groups, non-paired *t* test or Mann-Whitney test were used, when appropriate.

Difference was considered statistically significant when p value was lower than 0.05. All analyses were performed in the SPSS 13.0 for Windows program (SPSS Inc, Chicago, USA).

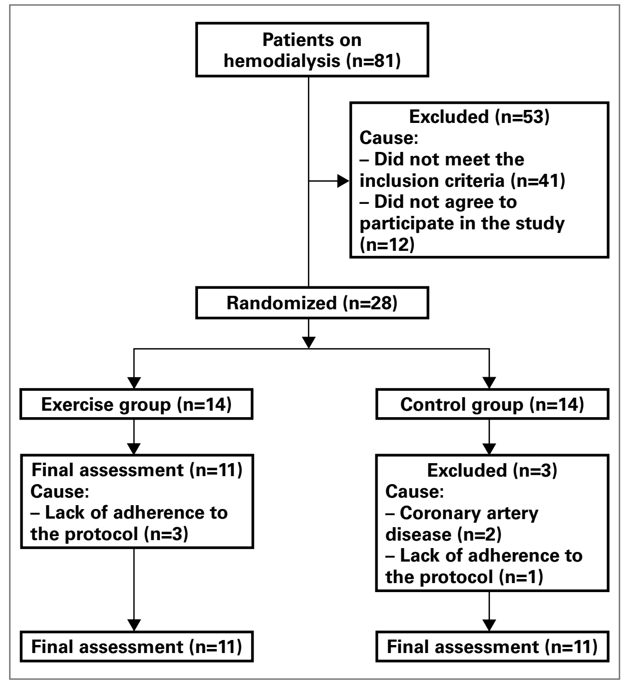
Results

Characteristics of the patients

Of the 81 patients on chronic hemodialysis, 28 met the inclusion criteria and agreed to participate in the study. Of those, 22 patients completed the study, 11 in each group (Figure 1). As shown in Table 1, no significant difference was observed in the clinical and demographic characteristics and medications between the groups assessed.

After 12 weeks following the protocol, a significant difference was observed in neither dry weight (exercise group: 59 ± 4.6 kg *vs*. 59.1 ± 4.4 kg; control group 59.7 ± 15.3 kg *vs*. 59.6 ± 15.4 kg) nor interdialytic weight gain (exercise group: 1.9 ± 0.8 kg *vs*. 2.2 ± 0.9 kg; control group 1.7 ± 0.6 kg *vs*. 1.6 ± 0.8 kg). Similarly, the anti-hypertensive drugs and phosphorus binders were maintained in both groups.

Figure 1. Flowchart of patients throughout the protocol.



Aerobic exercise

Adherence to exercise training during the 12 weeks was 75.3 ± 15.2%, and no significant clinical complication was observed during training. The major causes for skipping training were report of pain and fatigue, in addition to pre-dialysis arterial hypotension.

Heart rate variability

After 12 weeks following the protocol, no significant difference was observed in the HRV parameters in the time and frequency domains in both groups (Table 2).

Echocardiographic data

At baseline and at the end of 12 weeks of training, no significant difference was observed in the echocardiographic variables between the exercise and control groups. Most patients had concentric left ventricular hypertrophy (seven in the exercise group and eight in the control group), while concentric remodeling was identified in the others.

Table 1 CLINICAL AND DEMOGRAPHIC CHARACTERISTICS OF THE EXERCISE AND CONTROL GROUPS

Characteristics	Exercise group (n = 11)	Control group (n = 11)	p
Age (years)	49.6 ± 10.6	43.5 ± 12.8	0.23
Sex (men/women)	4/7	4/7	
Dialysis time (months)	41.9 ± 42.4	60.1 ± 54.4	0.39
Dry weight (kg)	59 ± 4.6	59.7 ± 15.3	0.88
BMI (kg/m²)	22.6 ± 2.3	22.9 ± 4.1	0.82
Etiology of CKD (patients, %):			
Chronic glomerulonephritis	5 (45.5%)	7 (63.6%)	
Arterial hypertension	2 (18.2%)	1 (9.1%)	
Renal amyloidosis	2 (18.2%)	0	
Hemolytic uremic syndrome	1 (9.1%)	0	
Obstructive uropathy	0	1 (9.1%)	
Systemic lupus erythematosus	0	2 (18.2%)	
Undefined	1 (9.1%)	0	
Anti-hypertensive drugs (patients, %):			
Calcium channel blockers	6 (54.5%)	5 (45.5%)	
Beta-blockers	5 (45.5%)	4 (36.4%)	
ACEI	6 (54.5%)	4 (36.4%)	
Central action blockers	2 (18.2%)	3 (27.3%)	
Diuretics	4 (36.4%)	3 (27.3%)	
AT1 receptor blocker	1 (9.1%)	3 (27.3%)	
Phosphorus binders			
Calcium acetate	7 (63.6%)	7 (63.6%)	
Calcium carbonate	3 (27.3%)	1 (9.1%)	
Sevelamer	1 (9.1%)	3 (27.3%)	

BMI: body mass index; CKD: chronic kidney disease; ACEI: angiotensin-converting enzyme inhibitors

Table 2 PARAMETERS OF HEART RATE VARIABILITY IN THE TIME AND FREQUENCY DOMAINS AT BASELINE AND END OF 12 WEEKS IN THE EXERCISE AND CONTROL GROUPS

	Exercise group (n = 11)		Control group (n = 11)	
	Baseline	Week 12	Baseline	Week 12
Time Domain				
SDNN index (ms)	34.6 ± 10.6	32.6 ± 9.7	39.1 ± 10.2	40.4 ± 12.7
RMSSD (ms)	19.9 ± 10.1	21.4 ± 9.7	22.6 ± 8	24 ± 6.9
pNN50 (%)	1 (3)	1 (8)	2 (6)	4 (7)
Frequency domain				
LF (ms²)	297.3 ± 163.7	302.1 ± 191.5	328.3 ± 139.6	416.7 ± 305.8
HF (ms²)	73.7 (87.9)	81.4 (58.3)	118.1 (66.8)	108.2 (90.1)
LF/HF	3.7 (1.1)	4 (3.4)	3.2 (2.3)	3.3 (2.1)

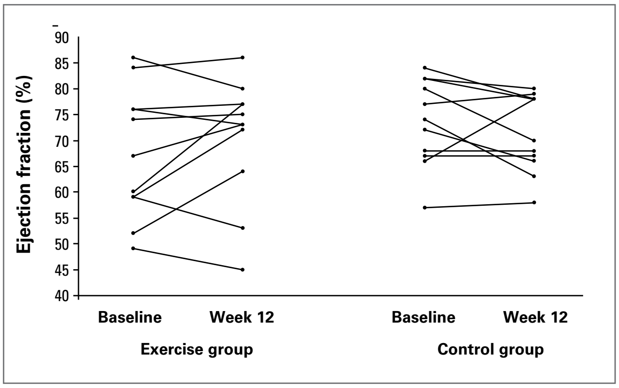
Values expressed as mean ± standard deviation or median (interquartile range). LF: low frequency; HF: high frequency.

After the aerobic training period, no echocardiographic parameter showed a significant increase (Table 3). The ejection fraction increased in seven of the 11 patients of the exercise group and decreased in most patients of the control group (Figure 2).

LABORATORY DATA

After 12 weeks following the protocol, a significant increase in potassium was observed in both groups, and in creatinine and albumin in the control group (Table 4).

Figure 2. Individual data of ejection fraction obtained on echocardiography at baseline and end of the 12 weeks in the exercise and control groups.



Discussion

The present study showed that 12 weeks of supervised aerobic training during hemodialysis sessions neither modified HRV nor significantly improved left ventricular function.

The HRV analysis is a non-invasive investigative method to assess the autonomic modulation exerted on the sinus node and has been described as one of the most sensitive techniques for diagnosing autonomic dysfunction.[3,12,17,18] The HRV reduction in patients with CKD is considered a risk factor for the occurrence of cardiac arrhythmias, and is associated with a higher cardiovascular mortality.[4,5] Cashion *et al.*[19], assessing hemodialysis patients by use of 24-hour Holter to study HRV in the time and frequency domains for a period of two years, have reported that the reduction in the SDNN, LF, and LF/HF parameters predicted cardiovascular death, especially sudden death. In that population, the reduction in HRV associated with injury to the parasympathetic system due to the structural impairment of arteries or the functional alterations of the autonomic nervous system secondary to uremic toxins.[18-20]

The increase in HRV in patients with CKD has been observed with kidney transplantation and the practice of exercise programs.[10,11,21,22] The present study did not show an increase in the HRV assessed in the time and frequency domains after 12 weeks of aerobic training. That finding is likely to be associated with the exercise training period. Contrarily, Deligiannis *et al.*[10], submitting 30 patients with CKD undergoing hemodialysis to 24 weeks of exercise

Table 3 Variables obtained on echocardiography at baseline and end of 12 weeks in the exercise and control groups

	Exercise group (n = 11)		Control group (n = 11)	
	Baseline	Week 12	Baseline	Week 12
LVMI (g/m2)	118.7 ± 25.7	120.9 ± 26.6	132.6 ± 49.1	131.3 ± 48.4
EDV (mL)	113 ± 50.7	133 ± 31.1	116.6 ± 36.5	117 ± 40.5
ESV (mL)	42.2 ± 29.3	44.6 ± 27.1	32.4 ± 20.4	35 ± 18.4
EF (%)	67.5 ± 12.6	70.4 ± 12	73.6 ± 8.4	71.4 ± 7.6
SV (mL)	74.9 ± 24.4	88.8 ± 15.8	84.2 ± 20.6	82 ± 27.1

Values expressed as mean ± standard deviation. LVMI: left ventricular mass index; EDV: end-diastolic volume; ESV: end-systolic volume; EF: ejection fraction; SV: systolic volume.

Table 4 Laboratory findings at baseline and end of 12 weeks in the exercise and control groups

	Control group (n = 11)		Control group (n = 11)	
	Baseline	Week 12	Baseline	Week 12
Hemoglobin (g/dL)	10.6 ± 2.9	10.9 ± 2.8	11.4 ± 2	11.3 ± 2.6
Kt/V	1.6 ± 0.2	2.0 ± 0.8	1.6 ± 0.3	1.8 ± 0.7
Creatinine (mg/dL)	11.9 (4.3)	12.6 (4.7)	9.3 (3)	10.5 (3.3)*
Phosphorus (mg/dL)	5.5 ± 2.1	4.9 ± 1.7	6.3 ± 1.2	5.9 ± 1.9
Potassium (mEq/L)	4.5 (0.6)	5.3 (1)*	4.7 (0.9)	5.2 (2)*
Calcium (mg/dL)	9.8 (1.2)	9.8 (1.6)	10 (1.4)	10.2 (1)
Albumin (g/dL)	3.9 ± 0.3	3.9 ± 0.3	3.9 ± 0.4	4.1 ± 0.5*

Values expressed as mean ± standard deviation or median (interquartile range). *$p < 0.05$, baseline; Kt/V: hemodialysis efficiency index.

during the interdialytic period, have reported a significant increase in HRV assessed on 24-hour Holter. In another study, those same authors applied 40 weeks of aerobic exercise and strength training during hemodialysis sessions and have also reported an improvement in HRV.[11] However, the training time seems to relate to an improvement in HRV in patients with CKD.

The choice of the 12-week training period of this study was due to the benefits observed in previous protocols developed in our center. One of such studies has assessed the effect of a 12-week intradialytic aerobic training in 14 patients with CKD. After the training period, the following was observed: a reduction in blood pressure assessed by use of 24-hour ambulatory blood pressure monitoring; improvement in the quality of life assessed by use of the SF-36 questionnaire; an increase in functional capacity assessed by use of the six-minute walking test; and improvement of anemia and Kt/V[23]. The present study has not shown a significant increase in hemoglobin and Kt/V after 12 weeks of aerobic training. The significant increase in potassium in both groups and in creatinine and albumin in the control group was not clinically relevant.

In addition to HRV, left ventricular function has also been assessed by use of resting echocardiography. Although no significant improvement has been observed in the ejection fraction after the training period, that parameter increased in seven of the 11 patients in the exercise group. The duration of training also seems to have influenced the improvement in left ventricular function. In accordance, Shalom *et al.*[8] have reported that 12 weeks of exercise training were not accompanied by a significant improvement in left ventricular function. On the other hand, other protocols with longer training have shown a significant increase in ejection fraction.[9,11] In one of such studies, the authors have assessed left ventricular function by use of resting and stress echocardiography of 16 hemodialysis patients with CKD undergoing a 24-week aerobic and strength training in the interdialytic period. After the training period, significant gains in the ejection fraction and systolic volume were observed on resting echocardiography; however, on stress echocardiography, significant increases were observed in the ejection fraction, systolic volume, and cardiac output.[9] That result has also been confirmed after 40 weeks of aerobic and strength training during hemodialysis sessions.[11]

The aerobic training applied during hemodialysis sessions for 12 weeks in this study did not cause a significant improvement in the cardiovascular parameters assessed. Patients with CKD undergoing an exercise program have shown central adaptations, such as improvement of the cardiac performance, and mainly an improvement in peripheral mechanisms, represented by strength and muscle resistance gains, in addition to neural adjustments evidenced by an increase in the nervous conduction velocity.[24,25] Those data have been recently confirmed in a study developed by our group, in which, after 12 weeks of intradialytic aerobic training, a significant increase was observed in the kinetics of oxygen consumption.[26] Thus, our data allow the speculation that the time of training used in the present study provided an improvement in peripheral mechanisms, although consistent benefits regarding central mechanisms have not been observed. The discrepancy between our findings and those in the literature allows suggesting that aerobic exercises for patients with CKD aiming at assessing HRV should be prescribed for periods longer than 12 weeks.

Conclusion

Twelve weeks of supervised aerobic training during hemodialysis sessions have not modified HRV and have not promoted a significant improvement of left ventricular function. New protocols with longer training periods are required for assessing the effects of aerobic exercise in those cardiovascular parameters.

Acknowledgments

We thank the Fundação de Amparo à Pesquisa do Estado de Minas Gerais – FAPEMIG (APQ-02452-09), the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – CAPES, and the Fundação IMEPEN (Instituto Mineiro de Estudos e Pesquisas em Nefrologia) for financial support. We thank the cardiologist Paulo César Tostes for his support in Holter monitoring. We also thank the nephrologists, nurse team, and staff of the Hemodialysis Service of the HU-UFJF and Fundação IMEPEN for support during the study.

References

1. Sarnak MJ, Levey AS. Epidemiology of cardiac disease in dialysis patients. Semin Dial 1999; 12:69-76.
2. Meiera P, Vogtb P, Blanca E. Ventricular arrhythmias and sudden cardiac death in end-stage renal disease patients on chronic hemodialysis. Nephron 2001; 87:199-214.
3. Reed MJ, Robertson CE, Addison PS. Heart rate variability measurements and the prediction of ventricular arrhythmias. QJM 2005; 98:87-95.

4. Hayano J, Takahashi H, Toriyama T *et al*. Prognostic value of heart rate variability during long-term follow--up in chronic haemodialysis patients with end-stage renal disease. Nephrol Dial Transplant 1999; 14:1480-8.
5. Fukuta H, Hayano J, Ishihara S *et al*. Prognostic value of heart rate variability in patients with end-stage renal disease on chronic haemodialysis. Nephrol Dial Transplant 2003; 18:318-25.
6. Larsen AI, Gjesdal K, Hall C, Aukrust P, Aarsland T, Dickstein K. Effect of exercise training in patients with heart failure: a pilot study on autonomic balance assessed by heart rate variability. Eur J Cardiovasc Prev Rehabil 2004; 11:162-7.
7. Hagberg JM, Ehsani AA, Holloszy JO. Effect of 12 months of intense exercise training on stroke volume in patients with coronary artery disease. Circulation 1983; 67:1194-9.
8. Shalom R, Blumenthal JA, Williams RS, Mcmurray RG, Dennis VW. Feasibility and benefits of exercise training in patients on maintenance dialysis. Kidney Int 1984; 25:958-63.
9. 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.
10. Deligiannis A, Kouidi E, Tourkantonis A. Effects of physical training on heart rate variability in patients on hemodialysis. Am J Cardiol 1999; 84:197-202.
11. Kouidi EJ, Grekas DM, Deligiannis AP. Effects of exercise training on noninvasive cardiac measures in patients undergoing long-term hemodialysis: a randomized controlled trial. Am J Kidney Dis 2009; 54:511-21.
12. Task Force of the European Society of Cardiology and the North American Society of pacing and electrophysiology. Heart rate variability: standards of measurement, physiological interpretation and clinical use. Eur Heart J 1996; 17:354-81.
13. Gottdiener JS, Bednarz J, Devereux R *et al*. American Society of Echocardiography recommendations for use of echocardiography in clinical trials: A report from the American Society of Echocardiography guidelines and standards committee and the task force on echocardiography in clinical trials. J Am Soc Echocardiogr 2004; 17:1086-119.
14. Devereux RB, Alonso DR, Lutas EM *et al*. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. Am J Cardiol 1986; 57:450-8.
15. Camarozano A, Rabischoffsky A, Maciel BC *et al*. Sociedade Brasileira de Cardiologia. Diretrizes das indicações da ecocardiografia. Arq Bras Cardiol 2009; 93:e265-e302.
16. Borg G. Psychophysical scaling with applications in physical work and the perception of exertion. Scand J Work Environ Health 1990; 16(Suppl1):55-8.
17. Kleiger RE, Stein PK, Bigger Jr. JT. Heart rate variability: measurement and clinical utility. Ann Noninvasive Electrocardiol 2005; 10:88-101.
18. Tory K, Suveges Z, Horvath E *et al*. Autonomic dysfunction in uremia assessed by heart rate variability. Pediatr Nephrol 2003; 18:1167-71.
19. Cashion AK, Holmes SL, Arheart KL, Acchiardo SR, Hathaway DK. Heart rate variability and mortality in patients with end stage renal disease. Nephrol Nurs J 2005; 32:173-84.
20. Kotanko P. Cause and consequences of sympathetic hyperactivity in chronic kidney disease. Blood Purif 2006; 24:95-9.
21. Hathaway DK, Wicks MN, Cashion AK, Cowan PA, Milstead EJ, Gaber AO. Heart rate variability and quality of life following kidney and pancreas–kidney transplantation. Transplant Proc 1999; 31:643-4.
22. Rubinger D, Sapoznikov D, Pollak A, Popovtzer MM, Luria MH. Heart rate variability during chronic hemodialysis and after renal transplantation: studies in patients without and with systemic amyloidosis. J Am Soc Nephrol 1999; 10:1972-81.
23. Reboredo MM, Henrique DMN, Faria RS, Chaoubah A, Bastos MG, Paula RB. Exercise training during hemodialysis reduces blood pressure and increases physical functioning and quality of life. Artif Organs 2010; 34:586-93.
24. 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.
25. Kouidi EJ. Central and peripheral adaptations to physical training in patients with end-stage renal disease. Sports Med 2001; 31:651-65.
26. Reboredo MM, Neder JA, Henrique DMN *et al*. Effects of aerobic training on the oxygen uptake kinetics at the onset of dynamic exercise in hemodialysis patients. Am J Respir Crit Care Med 2010; 181:A5325.