Beneficial effects of intradialytic cardiopulmonary rehabilitation

Efeitos benéficos da reabilitação cardiopulmonar intradialítica

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ABSTRACT

Introduction: Patients on hemodialysis (HD) present high mortality from cardiovascular complications and high morbidity, including decreasing functional capacity and quality of life. **Objective:** To analyze clinical and laboratory responses of patients in HD to intradialytic cardiopulmonary rehabilitation on an outpatient basis. **Methods:** We evaluated 14 patients in a prospective study for 8 months using cardiopulmonary rehabilitation protocol (CRehab) consisted of intradialytic aerobic exercise with a cycle ergometer. We analyzed heart rate (HR), systolic (SBP) and diastolic blood pressure (DBP), peripheral oxygen saturation (SpO_2) and modified Borg scale. We evaluated cardiac function by echocardiogram, functional capacity by six minutes walk test (6MWT), and quality of life by SF-36 survey, before and after CRehab. Biochemical data and KT/Vsp were collected form medical records. **Results:** During CRehab, the results of HR, SBP, DBP, SpO_2 and Borg scale showed no significant changes. 6MWT test showed progressive increase in the distance covered ($p < 0.001$) as well as a reduction in the scale of Borg post-6MWT ($p = 0.009$). There was no significant change in any biochemical data or in KT/Vsp. There was increase in left ventricular ejection from 65.7 ± 10.2% to 73.6 ± 10.1% ($p = 0.028$) and in left ventricular diastolic diameter ($p = 0.027$). According to SF-36 survey, patients showed improvement in three areas: physical role functioning ($p = 0.012$), bodily pain ($p = 0.007$) and vitality ($p = 0.009$). **Conclusion:** The intradialytic CRehab applied in this population was safe and allowed objective improvement of functional capacity and exercise tolerance, subjective improvement in the perception of effort, significant increase in cardiac function and better quality of life in different domains.

Keywords: renal insufficiency, chronic; renal dialysis; quality of life; exercise.

RESUMO

Introdução: Pacientes em hemodiálise (HD) têm alta mortalidade e morbidade por complicações cardiovasculares, inclusive por redução da capacidade funcional e qualidade de vida. **Objetivo:** Analisar a evolução clínica e laboratorial de pacientes em HD ambulatorial submetidos à reabilitação cardiopulmonar (RCP) intradialítica. **Métodos:** Avaliamos 14 pacientes em um estudo prospectivo por 8 meses, utilizando protocolo de RCP com exercícios aeróbicos intradialíticos. Analisamos frequência cardíaca (FC), pressão arterial sistólica (PAS) e diastólica (PAD), saturação periférica de oxigênio (SpO_2) e escala de Borg modificada em todas as sessões de HD. Avaliamos função cardíaca por ecocardiograma, capacidade funcional (CF) pelo teste de caminhada de seis minutos (TC6M), e qualidade de vida pelo Questionário SF-36, antes e depois da RCP. Dados bioquímicos e de Kt/Vsp foram coletados dos prontuários. **Resultados:** Durante a RCP, os resultados de FC, PAS, PAD, SpO_2 e escala de Borg não mostraram alterações significativas. No TC6M observamos aumento progressivo da distância percorrida ($p < 0,001$) e redução na escala de Borg pós-TC6M entre D0-D180 ($p = 0,009$). Não houve alteração significativa nos testes bioquímicos e no KT/Vsp. Houve aumento na fração de ejeção de 65,7 ± 10,2 para 73,6 ± 10,1% ($p = 0,028$) e no diâmetro diastólico do ventrículo esquerdo ($p = 0,027$). No questionário SF-36, houve melhora significativa nos domínios: limitação física ($p = 0,012$), dor ($p = 0,007$) e vitalidade ($p = 0,009$). **Conclusão:** A RCP intradialítica nesta população foi segura e permitiu melhora objetiva da CF e tolerância ao exercício, melhora subjetiva na percepção do esforço, aumento significativo da função cardíaca, bem como melhoria na qualidade de vida em diferentes domínios.

Palavras-chave: doença renal crônica; diálise renal; qualidade de vida; exercício.

Introduction

Malnutrition and chronic inflammation of chronic kidney disease (CKD) patients on hemodialysis are closely related to muscle mass loss, with resulting decrease in the ability of routine daily activities.[1] As a consequence, in the last decade the use of CRehab in HD patients has been increasily considered.[2] However, although the majority of CRehab programs have been applied in the periods between dialysis (interdialytic period),[3] exercise during HD (intradialytic program) may be of significant impact.[2]

In general, intradialytic exercise is recommended for the first two hours of HD as cardiovascular instability with nausea and vomiting may occur beyond the third hour, which may affect the regularity of training. Despite evidences pointing to clear benefits of aerobic exercises for HD patients, this practice is not routinely employed in this population, differently from what is applied to chronic pulmonary obstructive disease and heart failure.[3] Therefore, the present study attempted to evaluate the impact of a medium term aerobic intradialytic program, on the functional capacity, quality of life, exercise tolerance and heart function of stable renal patients on a regular HD program,

Methods

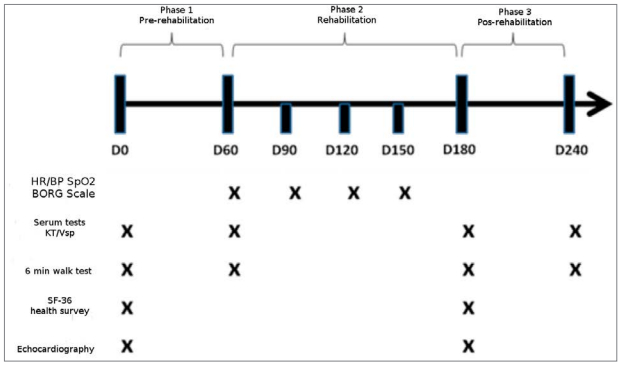
This is a prospective, non-randomized study, involving stage 5D CKD patients on a regular HD program. Patients above 18 years old, on HD (4 hours, 3 times a week) for at least 6 months, and using arteriovenous fistula were included. Patients with cardiovascular disease, neurological, musculoskeletal and any other disability that would preclude the use of cycle ergometer or active inflammatory/infectious disease in the last 6 months, and patients becoming acutely sick needing hospitalization, were all excluded.

The initial population was composed by 24 eligible patients followed between 2011 and 2015. From these selected patients, 4 patients needed hospitalization, 1 was transplanted, 1 was transferred to another unit, 1 relapsed systemic erythematous lupus and 3 dropped out for particular reasons, with 14 patients remaining for the entire study period.

Study design

Patients were evaluated during 3 phases with total length of 240 days. All were submitted to transthoracic echocardiography, functional capacity evaluation by walk test of six minutes (6MWT, m)[4] and SF-36 quality of life Survey (SF-36).[5] Laboratory data were collected from medical records. The 3 phases are described in Figure 1.

Figure 1. Study design. D = day; HR = heart rate; BP = blood pressure; SpO_2 = peripheral oxygen saturation.



Phase I: Total of 60 days without intradialytic CRehab. Patients were regularly dialyzed and submitted to routine Lab tests, echocardiography and SF-36. The 6MWT was performed at baseline and day 60.

Phase II: Total of 120 days with intradialytic CRehab in all HD sessions. The CRehab was performed, beginning after the first hour of HD. During the procedure the patients were monitored for arterial systolic (SBP) and diastolic (DBP) blood pressure, heart rate (HR), peripheral oxygen saturation (SpO_2) measured by usual oxymeter (Octivetech 300C, Clinical Guard, Atlanta, USA) and modified Borg scale,[6] all in 4 moments (0, 10, 20 and 30 min). The 6MWT was performed at day 180.

Phase III: Total of 60 days without intradialytic CRehab. Patients were regularly dialyzed and submitted to routine Lab tests, ECHO and SF-36. The 6MWT was performed at day 240.

Intradialytic crehab protocol

According to National[7] and International[8,9] guidelines for CRehab, the patients were submitted to aerobic exercise in lower limbs for 30 minutes. The use of the cycle ergometer (Original Pedlar, Battle Creek, Fremont, USA) for CRehab was always initiated after the first 60 minutes of HD. On some patients with lower functional capacity according to 6MWT, the weekly progression of time was introduced until reaching the total time of 30 minutes. In order to define the dose of the exercise, the Karvonen formula was applied to calculate the training heart rate (THR),

through a maximal heart rate (MHR)[10] and using 50-80% of reserve heart rate (RHR).[11] In addition, to assure patient safety during the procedures, the modified Borg scale was used each 10 minutes for measuring the effort perception.

Functional capacity (FC) test

The evaluation of functional capacity was performed using 6MWT in the interdialytic period according to the American Thoracic Society and European Respiratory Society Recommendations.[4] The test could be stopped in case of thoracic pain, shortness of breath, cramps, paleness or dizziness. Before and after the procedure, vital signs, Borg scale and SpO_2 were examined. In case the patients presented high levels of SBP (> 180 mmHg) and or DBP (> 110 mmHg), the test would not be done.

Laboratory tests, cardiac function and quality of life

Data for serum biochemistry, hemoglobin, electrolytes and C-reactive protein (CRP) were obtained from routine Lab tests. The values for KT/V were calculated from usual formula[12] for days 0, 60, 180 and 240. The evaluation of cardiac function was done using thoracic bidimensional echocardiography (Acuson X300, Siemens, München, Germany). The following parameters were described: left ventricle systolic (LVSD) and diastolic (LVDD) diameter; left ventricle posterior wall (LVPW); ejection fraction (EF). The SF-36[5] was used for quality of life evaluation.

Statistical analysis

All the values obtained were presented as mean ± standard deviation (SD) or median (interquartile interval: 25%, 75%) according to symmetric or asymmetric distribution of variables. The values were analyzed by Student`s t test (paired and non-paired) for quantitative symmetric distribution, and Mann-Whitney and Wilcoxon for asymmetric distribution variables. Such tests were used for 2-groups comparison. For comparative analysis of 3 or more groups, one-way ANOVA repeated measures was used for symmetric distribution and Friedman test for asymmetric distribution variables. Holm-Sidak was used for comparison between pairs of groups as post-test. Results were considered significant when $p < 0.05$.

Results

A total of fourteen patients, being 8 women and 6 men, were evaluated. Mean age was 50.2 ± 15.2. The patients were ethnically diverse with 3 white, 8 black and 3 brown or mulattos. The causes of renal diseases were as follows: arterial hypertension (6), diabetes *mellitus* (4), chronic glomerulonephritis (2), unknown (2). Mean time on HD was 23 ± 10 months. Body weight (kg) and BMI (kg/m^2) were not significantly different comparing before and after the study (67 ± 22 and 66 ± 18 kg, 22 ± 12 and 21 ± 10, respectively). The results from blood tests and KT/Vsp values are expressed in Table 1 for the periods D0, D60, D180 and D240. There was no significant difference among all these parameters.

Table 2 depicts all vital signs, modified Borg scale and SpO_2 with data from all HD sessions at each 10 minutes during intradialytic CRehab. There was no significant alteration observed in all parameters analyzed. Figure 2 describes the results for FC test as analyzed by the distances covered during 6MWT. It was observed a significant increase of the covered distance in the CRehab period.

On the other hand, after CRehab interruption (D180 to D240), there was a significant decrease of covered distance. It is noteworthy that at day 240, the patients were still able to walk for longer distance when compared with moments D0 and D60. Table 3 shows comparative analysis of HR, SpO_2 and Borg scale at pre and post 6MWT on periods D0, D60, D180 and D240. Values of HR showed significant increase between pre and post 6MWT, at all moments, except on D60.

However, when analyzing pre-test moments, a significant decrease was observed between moments D0 and D240 ($p = 0.009$) and between D60 and D240 ($p = 0.01$). Values for modified Borg scale were all different when comparing pre and post 6MWT. The comparison between moments pre-test revealed that the values were not significantly different, whereas on moments post-test there was a significant reduction between moments D0 and D180 ($p = 0.009$).

The values for SpO_2 did not show significant difference between values pre and post in all moments. However, when comparing pre-test values, we observed significant increase between moments D60 and D240 ($p = 0.009$). The post-test values were different

Table 1 Laboratory parameters and HD dose (Kt/Vsp) at different times of the study (baseline, 60 days, 180 days, 240 days)

	D0	D60	D180	D240	*p* value
Hb (g/dl)	11.2 (9.6;11.9)	11.0 (10.0;11.4)	11.5 (9.5; 12.1)	11.4 (10.9;12.3)	0.512
K (mEq/l)	4.9 (4.6;5.2)	5.0 (4.7;5.2)	5.1 (4.7;6.0)	5.1 (4.5;6.1)	0.509
Ca (mg/dl)	9.3 ± 1.2	9.6 ± 1.2	9.3 ± 0.9	9.2 ± 1.3	0.702
P (mg/dl)	5.3 (4.5;6.5)	4.3 (3.7;5.2)	4.4 (3.7;5.2)	4.7 (2.9;5.3)	0.197
C- reactive protein (mg/dl)	8.6 (4.2;13.8)	10.6 (7.3;19.1)	7.1 (4.4;9.5)	8.5 (8.1;21.1)	0.395
KT/Vsp	1.5 (1.3;1.6)	1.3 (1.2;1.4)	1.4 (1.2;1.6)	1.4 (0.9;1.6)	0.113

Values are median (interquartile interval: 25%, 75%).

Table 2 Clinical parameters

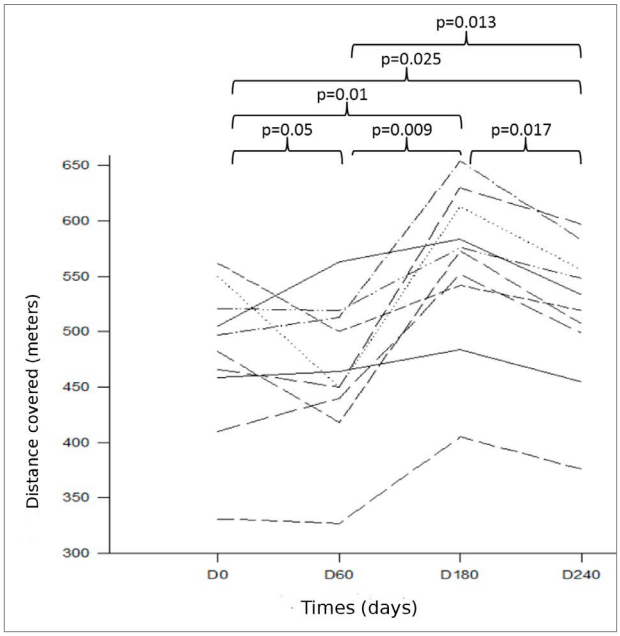
	D60-90	D90-120	D120-150	D150-180	*p* value
FC R	81.4 ± 8.1	81.5 ± 6.0	82.6 ± 10.6	82.6 ± 6.2	0.966
FC10	97.4 ± 9.2	103.2 ± 8.2	101.1 ± 13.6	96.4 ± 11.0	0.244
FC20	104.1 ± 13.8	110.0 ± 12.2	106.5 ± 16.4	102.0 ± 11.5	0.365
FC30	105.0 ± 13.2	111.9 ± 11.8	113.1 ± 13.4	104.4 ± 10.4	0.278
PAS R	136.3 ± 12.1	136,6 ± 12,8	138,9 ± 19,6	138,4 ± 9,2	0,951
PAS 10	144.5 ± 13.0	144.5 ± 12.1	149.5 ± 5.4	148.1 ± 7.3	0.573
PAS 20	147.7 ± 13.0	146.1 ± 12.2	148.8 ± 10.3	146.4 ± 7.7	0.926
PAS 30	156.8 ± 14.5	148.0 ± 13.1	139.5 ± 22.2	144.0 ± 8.7	0.574
PAD R	86.8 ± 9.9	85.9 ± 7.4	89.3 ± 7.3	90.9 ± 7.1	0.328
PAD 10	91.6 ± 5.8	88.1 ± 5.8	92.9 ± 5.6	89.8 ± 5.6	0.204
PAD 20	91.2 ± 7.4	89.6 ± 4.3	92.4 ± 6.5	89.1 ± 3.6	0.416
PAD 30	91.0 (87.7;96.4)	90.0 (87.0;92.1)	89.7 (87.4;97.8)	87.8 (83.7;89.4)	0.084
SpO_2 R	96.8 ± 1.0	97.4 ± 0.6	96.5 ± 0.9	97.2 ± 0.8	0.050
SpO_2 10	97.5 (96.0;98.0)	97.4 (96.8;97.8)	97.2 (96.9;97.2)	97.6 (97.1;97.8)	0.901
SpO_2 20	97.8 (98.6;95.0)	97.6 (97.0;97.9)	97.0 (96.6;97.8)	97.1 (96.1;97.6)	0.580
SpO_2 30	97.6 (95.5;97.9)	97.4 (96.7;97.6)	97.5 (97.0;97.8)	97.3 (96.3;97.4)	0.479
BORG R	0.2 ± 0.3	0.1 ± 0.2	0.2 ± 0.3	0.1 ± 0.3	0.607
BORG 10	0.6 ± 0.5	0.6 ± 0.7	0.7 ± 0.9	0.7 ± 0.5	0.956
BORG 20	0.9 ± 0.6	1.1 ± 0.7	1.0 ± 1.0	1.0 ± 0.6	0.965
BORG 30	1.4 ± 0.9	1.4 ± 0.9	1.1 ± 1.1	1.2 ± 0.8	0.818

R = baseline; HR = heart rate; SBP = systolic blood pressure (mmHg); DBP = diastolyc blood pressure (mmHg); SpO2 = peripheral oxygen saturation (%). Results expressed in mean ± standard deviation or median (25%;75%) according to symmetric or asymmetric distribution of variables. Statistical analyses were performed by Repeated measures ANOVA.

when moments D0 and D180 were compared ($p < 0.05$). The results pointed to a progressive decrease in the values of HR and Borg scale pre 6MWT on the periods examined.

The echocardiographic data revealed significant increase in left ventricular diastolic diameter (LVDD) and ejection fraction (EF) when comparing pre and post CRehab moments (D0 and D180). Results from SF-36 survey also demonstrated increased domains for physical role functioning, bodily pain and vitality. Results of cardiac function from ECHO and SF-36 are depicted on Table 4.

Figure 2. Comparison of distance covered during the 6min Walk Test in different moments of rehabilitation (baseline, 60 days, 180 days and 240 days). Statistical analyses were performed by Holm-Sidak test pos-repeated measured ANOVA.



Discussion

Chronic renal patients on HD present considerable less functional capacity when compared to normal subjects, which directly impacts on morbidity and mortality.[13,14] In addition, the sedentary behavior, normally adopted by renal patients on dialysis, may contribute to the decline on physical activity, generating functional incapacity and inactivity.[15] The present study attempted to apply an intradialysis CRehab program in order to examine the effect of the proposed procedure on physical conditioning, including cardiac function and psychosocial aspects linked to the quality of life.

Historically, the first CRehab for patients on dialysis was applied and described by Goldberg *et al.* in 1983[16] with beneficial results for arterial pressure control and serum hemoglobin levels. Ever since, several studies have been done using different modalities of exercises between sessions of HD, with interesting results on functional capacity, cardiac function and arterial pressure control, anemia and quality of life.[17,18]

In hemodialysis patients, the majority of CRehab programs have been applied in the interdialytic period. Nevertheless, it has been suggested that the intradialytic exercise can be more beneficial since it might promote better clearance of solutes due to increased blood flow systemically.[2,3,19,20] Our results on arterial pressure control revealed no change on regular levels previously recorded from the patients, although there was a tendency to decrease the levels. These results are in variance with previous studies that showed significant decrease on baseline SBP and DBP in protocols using 4 to 7 months of CRehab.[16,17,21,22] In only one study, however, the protocol was applied for a period of 3 months.[23]

The 6MWT used in our study to examine FC is accessible and cost-effective, given the possibility of correlation between covered distance and the peak VO_2.[17,24] Our study showed a significant improvement on functional capacity of HD patients, as seen by the increase of distance covered. These results are in agreement with previous studies where an improvement of FC was observed to be in the order of 9 to 25%.[23,25-28]

On the other hand, the study by Segura-Ortí *et al.*[27], was not able to show a better FC using the same test, albeit close assessment of supervision during CRehab by the physiotherapist. By contrast, in the studies by Koh *et al.*[28] and Fitts,[29] there could not be observed better FC, although supervision during CRehab did not occur. Other aspects on the evaluation of FC using 6MWT deal with SpO_2, HR and

Table 3 Comparison between clinical parameters HR (heart rate), SPO_2 (peripheral oxygen saturation) and Borg scale pre e post 6min walk test in different moments (baseline, 60 days, 180 days and 240 days)

	D0			D60			D120			D240		
	PRE	POST	*p* value	PRE	POST	*p* value	PRE	POST	*p* value	PRE	POST	*p* value
HR	86.4 ± 11.8	105.6 ± 9.2	< 0.001	83.5 (74.0;91.0)	107.0 (98.0;112.0)	0.084	75.9 ± 10.0	102.9 ± 4.8	< 0.001	72.8 ± 8.6	104.4 ± 12.9	< 0.001
SpO_2	98.0 (96.8;98.0)	96.0 (92.0;98.0)	0.074	97.5 (96.0;98.0)	96.5 (93.5;98.0)	0.063	98.0 (98.0;98.0)	98.0 (98.0;99.0)	0.375	98.0 (98.0;98.0)	98.0 (98.0;98.0)	0.313
BORG scale	0.0 (0;0.6)	3.0 (2.0;4.5)	< 0.001	0.4 ± 0.7	2.6 ± 1.8	0.002	0.00 (0;0)	1.0 (0.5;1.0)	0.008	0.0 ± 0.0	1.3 ± 1.1	0.009

Results expressed in mean ± standard deviation or median (25%;75%) according to symmetric or asymmetric distribution of variables. Statistical analyses were performed by paired *t*-test or Wilcoxon signed rank test.

Table 4 Parameters of echocardiogram and SF-36 survey befrore and after rehabilitation

	Pre-Rehabilitation	Post-Rehabilitation	*p* value
Echocardiogram			
LVDD (mm)	54.5 (49.0;56.0)	56.0 (53.0;58.0)	0.027
LVSD (mm)	32.4 ± 6.7	29.8 ± 4.6	0.259
LVPW (mm)	12.2 ± 1.8	13.3 ± 3.3	0.909
EF (%)	65.7 ± 10.2	73.6 ± 10.1	0.028
SF-36 Survey			
Physical functioning	59.1 ± 14.3	60.1 ± 26.3	0.877
Physical role functioning	20.5 ± 21.8	65.0 ± 37.6	0.012
Bodily pain	42.1 ± 22.1	71.3 ± 34.4	0.007
General health perceptions	49.9 ± 25.7	60.4 ± 25.2	0.111
Vitality	40.5 ± 21.6	64.5 ± 24.9	0.009
Social role function	60.9 ± 25.0	87.5 ± 19.5	0.087
Emotional role function	48.5 ± 40.5	70.7 ± 35.3	0.173
Mental health	62.5 ± 24.2	80.0 ± 27.6	0.234

LVDD = left ventricular diastolic diameter; LVSD = left ventricular systolic diameter; LVPW = left ventricular posterior wall diameter; EF = ejection fraction. results expressed in mean ± standard deviation or median (25%;75%) according to symmetric or asymmetric distribution of variables. statistical analyses were performed by paired *t*-test teste *t* or Wilcoxon signed rank test.

modified Borg scale. These parameters were only examined in the study by Reboredo *et al.*,[30] which was in agreement with our results showing reduction on modified Borg scale in the post-test moments.

The analysis of clinical laboratory data did not reveal significant findings when comparing all moments. In addition, data of KT/Vsp were not significantly different after CRehab, which opposes data from other studies showing increases from 11 to 38%.[17,23,30,31] The studies by Momeni *et al.*[32] and Musavian *et al.*[33] and showed significant reduction of serum potassium after 16 and 12 weeks of CRehab, respectively. Likewise, Goldberg *et al.*[16] observed a significant increase of 29% on serum hemoglobin, while in the study by Musavian *et al.*[33] the increase was up to 0.6 mmol/L.

Regarding the results on serum levels of calcium, phosphorus and sodium, to our knowledge, no study showed significant alterations. In addition, two recent studies have examined these electrolytes, with no relevant results.[34,35] Finally, the results on serum CRP levels were shown to decrease after an 8-week protocol in 21 patients.[36] Our results did not show this decrease on CRP and this cannot be explained at this moment. Nevertheless, one can consider that different results may be accounted by the different populations examined.

In the present study we documented a clear significant improvement on cardiac function as we could observe an increase in LVDD and EF after CRehab (Table 4). In fact, few studies have examined cardiac function using ECHO after this protocol. The previous study by Deligiannis *et al.*[21] applied intradialytic aerobic exercises during 3 months for 30 minutes with 60 to 70% MHR and observed increase of EF. In addition, Momeni *et al.*[32] used the same protocol of the group of Deligiannis *et al.*[21] observed increase of EF, systolic and diastolic VE function.

The explanation for these results may reside on better conditioning of the heart with adaptation to aerobic exercise, regularly observed in normal individuals. Moreover, the patients of this study presented arterial pressure in the normal range before the procedures (Table 2), and also EF levels on normal values (Table 4). All these results give support to the notion of preserved ventricular mass, still able to react as into Frank Starling mechanism of adaptation to the proposed exercise stress and aerobic demand.

Finally, the results on the evaluation of quality of life by SF-36 survey demonstrated that CRehab protocol was of great benefit as it promoted a significant improvement in three domains: physical role functioning, bodily pain and vitality (Table 4). Previous studies from other groups also encountered positive results with the same domains.[2,17,22,37] Among these studies, only two of them presented significant results on emotional role function and general health perception.[22,37] In fact, one can speculate about the

new feeling of well-being after the progress achieved on physical conditioning and true cardiac function improvement. Nevertheless, more specific studies are needed to address this issue.

In conclusion, the present study applying a proposed cardiopulmonary rehabilitation intradialytic protocol to patients on hemodialysis, with controlled supervised aerobic exercises, clearly demonstrated a beneficial effect on functional capacity, cardiac function with increase of EF and LVDD, and subjective signs of improvement on quality of life. These findings strongly suggest that a careful, supervised program of cardiopulmonary rehabilitation on renal patients on dialysis may be more intensively applied in order to decrease the incidence of cardiovascular morbidity and mortality, and to improve the quality of life of these patient population.

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