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Effectiveness of a cardiorespiratory, muscular and ventilatory training program in the aerobic performance of hemodialysis patients

Efectividad de un entrenamiento cardiorrespiratorio, muscular y ventilatorio en el rendimiento aeróbico de pacientes hemodializados

Paula Moscoso Aguayo[1], Catalina Arismendi Newmann[1], Rocío Bahamondes Lobo[1], Rosa Soto Cárdenas[1], Luis Ojeda Silva[2]

[1]School of Kinesiology, School of Medicine, Universidad Austral de Chile. Dialysis Unit, Hospital Base Valdivia, Valdivia, Chile.
[2]Institute o Statistics, Faculty of Economic and Administrative Sciences, Universidad Austral de Chile, Valdivia, Chile.

Abstract

Introduction: End stage kidney disease causes fatigue and progressive muscle weakness, which affects not only the muscles of the extremities, but also the respiratory. There are several studies of combined training in dialysis patients, but not including respiratory work. Therefore, the present study aims to determine the effectiveness of an aerobic, lower limb resistance and inspiratory muscle resistance combined training in the generation of changes in aerobic performance of patients undergoing hemodialysis.
Material and methods: Randomized controlled trial which included 11 hemodialysis patients from Valdivia's Central Hospital. The sample was divided into two groups, the first one included: an aerobic, lower limbs and inspiratory muscle training (ARM+V) (n=6) and the second one included an aerobic and lower limbs muscle training (ARM) (n=5). The training was performed during 8 weeks and three variables were measured in both groups pre and post intervention, inspiratory muscle strength (Carefore Airlift NIF-gauge ®), aerobic endurance (6MWT) and pulmonary function (Sibelmed Datospir Micro Spirometer 120D ®).
Results: ARM+V group obtained significant improvements (p<0.05) in 6MWT performance (p=0.027) and MIP (p=0,001). Likewise, performance improved in 6MWT (p=0.022) and MIP (p=0.002) at ARM group, but decreased in spirometry values: FEV1 (p=0.004), FVC (p=0.005) and FEV1/FVC (p=0,038).
Conclusion: Both training protocols were effective in the aerobic endurance improvement, however the patients in the ARM+V group presented better changes than the ARM group. Neither of the two training programs improved pulmonary function.
Key words: Renal dialysis, exercise therapy, respiratory muscles.

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Resumen

Introducción: la enfermedad renal crónica terminal provoca fatiga y debilidad muscular progresiva, que afecta no solo la musculatura de extremidades, sino también la respiratoria. Existen diversos estudios de entrenamiento combinado en pacientes dializados, pero sin incluir trabajo respiratorio. Por esto, el presente estudio pretende determinar la efectividad de un entrenamiento combinado aeróbico, de resistencia de miembro inferior y de resistencia muscular inspiratoria, en el rendimiento aeróbico de pacientes hemodializados.
Materiales y métodos: ensayo clínico aleatorizado que incluyó 11 pacientes hemodializados del Hospital Base Valdivia. Fueron divididos en dos grupos, uno sometido a un programa de entrenamiento con ejercicio aeróbico, de resistencia muscular de miembros inferiores y de musculatura inspiratoria (ARM+V) (n=6), y el otro, a un programa de entrenamiento con ejercicio aeróbico y de resistencia muscular de miembros inferiores (ARM) (n=5). La intervención fue realizada durante 8 semanas evaluando el rendimiento pre y post intervención de capacidad aeróbica (TM6M), fuerza inspiratoria máxima (Carefore Airlift NIF-gauge®) y función pulmonar (Sibelmed Datospir Micro Spirometer 120D®) en ambos grupos.
Resultados: el grupo ARM+V obtuvo mejoras significativas (p<0,05) en el rendimiento del TM6M (p=0,027) y PIM (p=0,001); así mismo el grupo ARM mejoró en el TM6M (p=0,022) y PIM (p=0,002) y en la espirometría se mostró una disminución significativa en VEF1 (p=0,004), CVF (p=0,005) y VEF1/CVF (p=0,038).
Conclusión: ambos entrenamientos fueron efectivos en la mejora del rendimiento aeróbico, pero el grupo ARM+V obtuvo mejoras significativamente superiores en este ítem. Ninguno de los dos entrenamientos obtuvo mejoras en los valores espirométricos.
Palabras clave: diálisis renal, terapia por ejercicio, músculos respiratorios.

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Correspondence: Paula Moscoso Aguayo, paula.moscoso@uach.cl
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Introduction

Chronic kidney disease (CKD) is a general term for heterogeneous disorders that affect the kidney structure and function.[1] The CKD has different stages, of which stage 5 corresponds to the progressive and permanent loss of kidney function, where the only treatment available is exposure to hemodialysis (HD) or finally, kidney transplantation.[2] It is currently a serious public health problem, since only in Chile in the year 2017, HD reached a prevalence of 1208 people per million.[3]

HD treatment causes a series of consequences in all systems, of which the most affected are the cardiovascular and musculoskeletal, causing fatigue and muscle weakness[4]; this subsequently leads to a progressive loss of muscle mass.[5]

These are reasons that give importance to physical exercise in this type of patients, for whom intradialysis physical training programs which use aerobic and resistance exercises of the lower limbs (LL)[4,6,7]; in this way, positive results are obtained, which are reflected not only in the increase in the aerobic capacity and muscle strength in these patients, but also in the improvement of the effectiveness of HD and a significant decrease in the level of disability.[6]

On the other hand, the respiratory system is highly affected in these patients, since degenerative muscle changes occur by the decrease of contractile tissue due to uremic toxins, leading to a decreased strength of the ventilatory muscles.[8,9] This also brings consequences in the decrease of the forced expiratory volume in the first second (FEV1) and the forced vital capacity (FVC) values, reflecting a deterioration in the lung capacity of patients undergoing HD.[10]

In 2010, Silva *et al*.[11] carried out a protocol of ventilatory muscle strength exercises in patients under HD treatment, using an inspiratory threshold valve. After 8 weeks of training, a statistically significant improvement ($p<0.05$) in the aerobic capacity and in the maximum inspiratory pressure (MIP) was observed in the experimental group. This study proves the relationship between ventilatory training and aerobic capacity; however, there are no protocols that demonstrate whether the ventilatory work combined with an aerobic and/or LL resistance training has better results in the increase of the aerobic capacity in hemodialysis patients.

This is why the main objective of the present study is to determine the effectiveness of an aerobic, lower limb resistance and inspiratory muscle resistance training in generating changes in the aerobic performance of patients undergoing hemodialysis; and the hypothesis generated is that a training that combines aerobic, lower limb resistance exercise, and that also includes inspiratory muscular resistance training, is more effective in generating changes in aerobic performance in hemodialysis patients.

Materials and methods

Study design and population

The design of the present study is experimental, corresponding to a randomized clinical trial. We worked for 8 weeks with patients undergoing HD in the dialysis unit of the Hospital Base de Valdivia from October 2015 to February 2016, belonging to the three shifts of Mondays, Wednesdays and Fridays, and to the second and third shifts of Tuesdays, Thursdays and Saturdays.

Outpatients undergoing HD via arteriovenous fistula (AVF) with a treatment longer than three months and with a result equal to or higher than 24 points in the Mini-Mental Test were included. The exclusion criteria included the use of antihypertensive drugs in the hour preceding the HD, suffering from diabetes and uncontrolled hypertension, mental confusion, lower limb amputation, acute cardiac syndrome, isolated patients, patients with an acute lung disease, and presenting class III or IV angina. Of the total population of 118 patients, 21 met the selection criteria; 15 of them agreed to be part of the study. Of the latter, 4 were excluded for the following causes: problems with the arteriovenous fistula, patients under cardiac study and presence of pulmonary edema. Given the above, the final sample included 11 patients (6 women and 5 men).

The 11 patients studied were randomly divided into two groups. Using a tombola, one person outside the study chose numbers from 1 to 11 corresponding to each patient and divided them interspersed in each group; one group (n=6) was assigned to an aerobic exercise training, of LL muscles resistance and inspiratory muscle training (ARM+V); and only aerobic exercises and of LL muscle resistance (ARM) were assigned to the other group (n=5). All the participants, both those in the ARM + V group and those in the ARM group, were blinded to the group assignment, since they were in different rooms and did not know what the intervention of the group was about. The evaluators and the treating team were not blinded, since they were the same researchers of the study who knew in advance the nature of each group.

Measurement of variables

Measurements were made in the two groups both at the beginning and at the end of the eight weeks of intervention. The measured parameters included aerobic capacity, pulmonary function and inspiratory muscle strength.

The aerobic capacity was determined by the distant covered in the six minute walking test (6MWT) which was obtained by counting the number of laps fully covered plus the final meters where the patient stopped at the end of the 6 minutes.[12] The test was carried out using the protocol and recommendations of the ATS.[13]

The lung function was measured with the spirometry test, using a Datospir Micro® Sibelmed spirometer. The forced expiratory volume in one second (FEV1), Tyffenau index (FEV1/FVC) and forced vital capacity (FVC) values were measured. This evaluation was conducted according to the protocol of the Chilean Society of Respiratory Diseases.[14]

Ventilatory muscle strength was determined by evaluating the maximum inspiratory pressure (MIP), based on the pimometry technique described by Black and Hyatt.[15] A Carefore Airlift® aneroid manometer, calibrated in cmH2O, was used for this technique.

Exercise protocol

The patients were trained with a frequency of three times per week divided into Monday, Wednesday and Friday, and Tuesday, Thursday and Saturday. The trainings were conducted during the first two hours of HD to avoid any adverse effect. It was applied an 8-week training program in which the ARM+V group performed aerobic, LL muscle resistance and inspiratory muscle resistance exercises, while the ARM group only performed aerobic and LL muscle resistance exercises. Each session lasted 45 to 60 minutes. The eleven patients worked uninterruptedly for the eight weeks; only the assigned protocol was applied to each group.

Aerobic training protocol

The training consisted in performing exercises, during 25 to 30 minutes for both groups, in a static pedal, involving only the lower limbs; the work intensity (pedal load) was measured and controlled through the heart rate reserve (HRR). They worked at moderate intensities between 40 and 60% of the HHR (calculated with the formula proposed by Karvonen). In addition, the parameters were controlled to monitor the condition of the patients and their perception of effort associated with exercise during the beginning, the middle and the end of training. These parameters were HHR, oxygen saturation, blood pressure and the subjective sensation of effort; the latter was measured using the modified Borg scale.[16,17]

Lower limb strength training protocol

Isotonic exercises were performed using free weights, with a duration of 10 to 15 minutes per session for both groups. These exercises consisted in knee extensions from 90 to 0°, where the weight was located at the distal end of the leg segment, allowing full movement of the involved joint.[7] The amount of weight used and the subsequent progression were established according to the motor performance of each patient and the perception of effort in relation to the LL strength, measured by the OMNI-RES scale.

Inspiratory muscle training protocol

The ventilatory training protocol was applied only to the ARM+V group and consisted in inspiratory muscle resistance work. This training was performed using a Phillips Respironics® Threshold IMT loading valve; the patient was sitting and with the valve regulated at 40% of the MIP[11]; he exercise consisted in inspiratory maneuvers applied in series of five repetitions with one minute of rest between them, with a total duration of 15 minutes. Progression was made one month after starting training, when the MIP was evaluated again in order to continue maintaining the ventilatory work at 40% of the MIP.

Data analysis

For the statistical analysis, specialized tests were used in small samples to disprove the null hypothesis (Ho). The normality of the variables was determined using the ShapiroWilk test, so that the variables with normal distribution were expressed as mean ± standard deviation. The t test for related samples was used to establish significant differences between initial and final data. The SPSS software (Statistical Package for Social Sciences) version 20.0 for Windows was used for data analysis. A p-value <0.05 was considered statistically significant.

Ethical responsibilities

The present study was approved by the ethics committee of the Valdivia Health Service and was carried out under the ethical standards of the World Medical Association and the Declaration of Helsinki.

The confidentiality of the data of the people intervened was maintained and under no circumstances names, initials or numbers of clinical records have been used to identify the patients of this trial.

Furthermore, prior to any evaluation and/or intervention, written informed consent was obtained from all participating patients and/or subjects referred to in the article.

Results

The final sample of the study included 11 patients with CKD belonging to the Dialysis Unit of the Hospital Base de Valdivia (women 54.5% and men 45.5%, with an average age of 50.8 ± 18.3 years) who were under HD treatment three times per week for 35.7 ± 32.7 months. The patients were divided into two groups, where six made up the group with aerobic, LL resistance and ventilatory training (ARMV), while five belonged to the group with aerobic and LL resistance training (ARM). Table 1 shows the characteristics of each group. The evolution in the performance of the 6MWT pre- and post-intervention of both groups is reflected in Table 2.

There are significant changes ($p<0.05$) between the averages of the final and initial results both in the patients belonging to the ARM ($p=0.022$) and in those of the ARM+V group ($p=0.027$); however, the patients belonging to the ARM+V group achieved significantly higher deltas ($p=0.024$) regarding the meters covered pre- and post-intervention than those of the ARM group (Figure 1).

The changes in the initial and final pimometry for both groups are shown in Table 3, where we can see that in both groups the pre and post-intervention evolution deltas were statistically significant ($p<0.05$).

Although the differences in the cmH2O obtained pre- and post-intervention of the ARM+V group were significantly greater ($p=0.01$) than those of the ARM group (Figure 2).

As for the results of the spirometric values reflected in Table 4, statistically significant values were found in the ARM ($p<0.05$) for the FEV1, FVC and FEV1/FVC functions, where there was a decrease in their post-intervention values. On the other hand, in the ARM+V group no significant differences were found ($p> 0.05$) for any of the pulmonary function parameters, despite the fact that

Table 1. Characteristics of the population.

	Characteristics of the sample	
	ARM (n=5)	
Age (years)*	51.6 ± 22.39	**Age (years)***
Number of women (%)	4 (80%)	**Number of women (%)**
Number of men (%)	1 (20%)	**Number of men (%)**
HD time (months)*	31.8 ± 33.8	**HD time (months)***
Diabetes *mellitus*	4 (80%)	**Diabetes *mellitus***
Weight (kg)*	82.4±8.5	**Weight (kg)***
Height (cm)*	157.2±5.4	**Height (cm)***
Arterial hypertension	2(40%)	**Arterial hypertension**

HD: Hemodialysis, *data shown as mean ± standard deviation. ARM: aerobic and LL resistance training. ARM+V: aerobic, LL resistance and inspiratory muscle training.

Table 2. Pre- and post-intervention 6MWT results.

	Pre-intervention	Post-intervention	p*	Control delta-experimental delta**
ARM (n=5)	412.6 ± 143.94	434 ± 182.29	0.022	0.024

The variables are shown in meters as mean ± standard deviation; *paired T test for normal distribution of samples.
**T test for independent samples. Statistically significant test when p<0.05. ARM: aerobic and LL resistance training. ARM+V: aerobic, LL resistance and inspiratory muscle training.

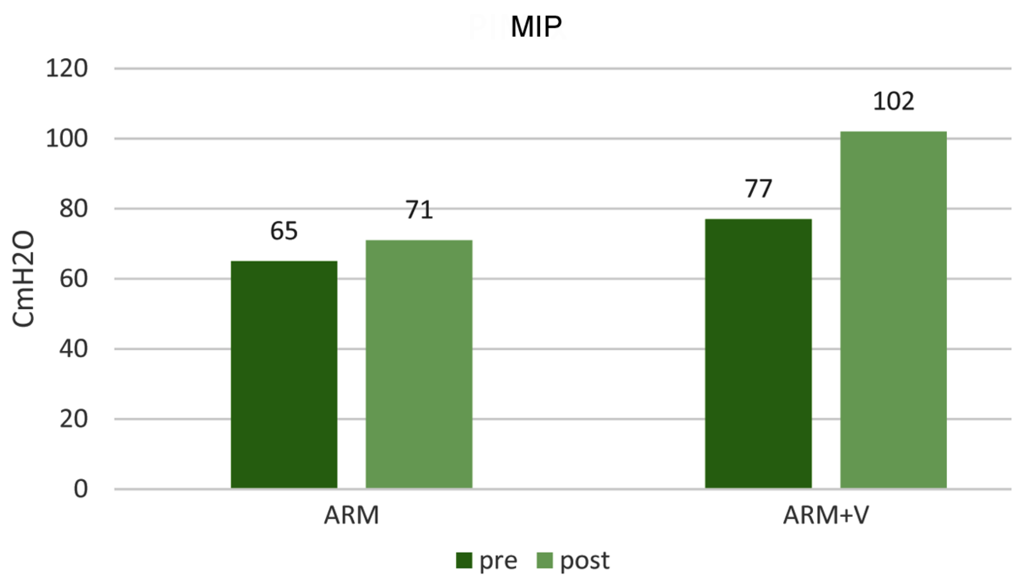

Figure 1. Comparison of the mean number of meters covered in 6MWT post- and pre-intervention between the ARM group and the ARM+V group. * Delta ARM group: 22 m. ** Delta ARM+V group; 130 m. ARM: aerobic and LL resistance training. ARM+V: aerobic, LL resistance and inspiratory muscle training.

Table 3. Results of MIP pre- and post-intervention.

	Pre-intervention	Post-intervention	p*	Control delta-experimental delta**
ARM (n=5)	65 ± 22.36	71 ± 20.54	0.002	0.001
ARM +V(n=6)	77.5 ± 12.9	102.5 ± 11.02	0.001	

The variables are shown in cm H2O as mean ± standard deviation; * Paired t test for normal distribution of samples. ** T test for independent samples. Statistically significant test when p<0.05. ARM: aerobic and LL resistance training. ARM+V: aerobic, LL resistance and inspiratory muscle training.

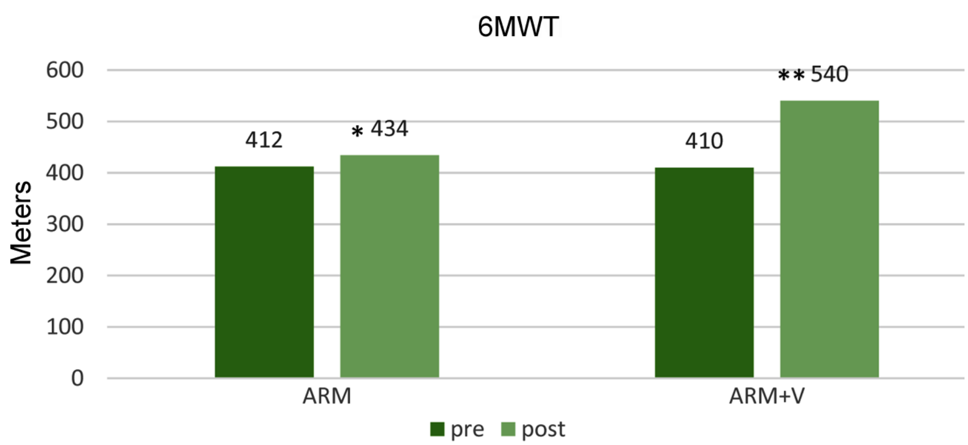

Figure 2. Comparison of the average of $_2$cmH O obtained in the post- and pre-intervention MIP between the ARM and ARM+V groups. * Delta ARM group: 8 cmH O. ** Delta ARM+V group: 25 cm. ARM: aerobic and LL resistance training. ARM+V: aerobic, LL resistance and inspiratory muscle training.

Table 4. Results of spirometry values pre- and post-intervention.

	Group	Pre-intervention	Post-intervention	p-value*
FEV1 (L)	ARM	1,97 ± 0.38	1.86 ± 0.46	0.004
	ARM+V	2.42 ± 0.54	2.40 ± 0.97	0.116
FVC (L)	ARM	2.19 ± 0.43	2.22 ± 0.49	0.005
	ARM+V	3.04 ± 0.72	3.12 ± 0.80	0.062
FEV1/FVC (%)	ARM	87.84 ± 3.57	83.53 ± 7.06	0.038
	ARM+V	79.82 ± 5.35	79.03 ± 3.66	0.396

The variables are shown as mean ± standard deviation. *Paired T test for normal distribution of samples. Statistically significant test when p<0.05. FEV1: forced expiratory volume in one second; FVC: forced vital capacity; FEV1/CVF (%): Tiffeneau index. ARM: aerobic and LL resistance training. ARM+V: aerobic, LL resistance and inspiratory muscle training.

the values of all these variables were maintained or increased.

The variables are shown as mean ± standard deviation. *Paired T test for normal distribution of samples. Statistically significant test when $p < 0.05$. FEV1: forced expiratory volume in one second; FVC: forced vital capacity; FEV1/FVC (%): Tiffeneau index. ARM: aerobic and LL resistance training. ARM+V: aerobic, LL resistance and inspiratory muscle training.

Discussion

The eight-week training in hemodialysis patients was effective in generating changes in aerobic capacity (6MWT), both in the group that maintained an aerobic and LL resistance training (ARM), and in the group that had an aerobic, LL muscle resistance and ventilatory resistance (ARM+V) training. Nevertheless, this improvement is significantly greater in the group with ventilatory training that obtained an increase of 31.7% in meters covered in the 6MWT compared with 5.2% in the group without ventilatory training.

This increase of 32% in the performance obtained in the 6MWT in the ARM+V group, compared with the 5% of the ARM group, is not related to the learning effect, because the test was applied to each subject only once during the beginning and the end, since the learning effect has been demonstrated mainly in repeated measurements at more than three consecutive times.[13]

The results obtained in our study in the 6MWT performance were higher than those of Oliveros *et al.*,[7] who implemented an aerobic and lower-limb resistance training in 15 patients on HD treatment for 16 weeks, resulting in an improvement of 5.7% in the performance of the 6MWT; despite our intervention lasted 8 weeks and the group with ARM training had similar results, the group with ARM+V training obtained a notably greater increase in the meters covered in the 6MWT. On the other hand, the results of the ARM+V training are higher than those presented by Silva et al.,[11] in which 15 hemodialysis patients performed an intradialysis inspiratory muscle training for 8 weeks, increasing by 22% the distance covered in the 6MWT; this difference alludes to the fact that ventilatory training combined with aerobic and muscular resistance training is more effective than ventilatory training alone.

Most of the interventions of the studies were carried out during 12 weeks,[18-20] but it has been demonstrated that during 8 weeks of intervention a significant difference is achieved in terms of the meters covered in the 6MWT,[7] as shown in our study, where a training program of only eight weeks was sufficient to induce a clinically significant improvement, since according to Puhan *et al*.[21] a difference of 25 to 35 meters in the performance of the 6MWT already generates functional improvements in the patients. It should be noted that studies that positively associate the performance of exercise with the quality of life in patients undergoing HD have been conducted,[22,23] in such a way that physical inactivity in hemodialysis patients has been associated with an increase in their mortality[24]; hence the importance of physical training in these patients, even more so when its simplicity and adherence make it feasible in any environment in which patients undergo dialysis sessions.[25]

In the present study, lung function did not show statistically significant differences when comparing the values of spirometries performed before training with those performed after 8 weeks of training for the ARM+V group, which is probably due to the fact that the threshold loading valve is aimed at improving inspiratory force and not lung volumes or capacities[11]; however, this training indeed contributed to the fact that at the end of the training they maintained the values obtained in the initial spirometries and did not have a significant loss of the parameters, as happened in the case of the ARM group which obtained a loss of 5.5% in the FEV1, of 1.3% in the FVC and of 4.31% in the FEV1/FVC.

As for pimometry, there were significant changes in both groups; however, the greatest increase was in the ARM+V group with 32.2%. This increase has not been previously found in studies carried out in hemodialysis patients, as in the case of Silva *et al.*,[12] where no significant changes were found in the final values of pimometries after eight weeks of training at 40% of the MIP three times per week. On the other hand, the ARM group achieved an increase of 9.2%. Although this percentage is much lower than that of the ARM+V group, it is a statistically significant increase and responds to the fact that although this group did not train said musculature, the muscles involved in inspiration are skeletal muscles and, therefore, can generate a decrease in the muscle strength and endurance due to the uremic myopathy[26]; that is why aerobic and muscle resistance exercises during dialysis have been shown to increase blood flow in the muscle, which dynamizes the flow of urea and toxins from the tissues to the vascular compartment, also favoring the ventilatory muscles,[6] so it can be inferred that both muscle resistance and aerobic training led to a better result in the MIP values; however, it was proven in this study that these values in pimometry are higher in those patients who perform training with the threshold load valve.

Conclusions

The combined modality of intradialysis training with aerobic, LL and inspiratory muscle resistance exercises, proved to be more effective than training without ventilatory muscles resistance exercises, since there was a greater increase in the meters covered in the 6MWT, an increase in the maximum inspiratory strength, and the spirometric values of the hemodialysis patients were also maintained. This suggests that inspiratory muscle strength contributes to exercise tolerance and functional capacity.

The study has some limitations such as the small study sample, which was mainly due to the inclusion and exclusion criteria, the health status of these patients and the refusal to participate. One of the biases found in the study is the interruption of training due to patient safety criteria, since a drop in blood pressure is very common and therefore the training could not be fully completed during the sessions.

It is necessary to conduct studies with a larger population, also including a variable of quality of life or level of disability, in order to better determine the effectiveness of each of the programs established for the different groups.

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Conflict of interest and funding

The authors declare that there is no conflict of interest.

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Ethical responsibilities

Protection of people and animals

The authors declare that no experiments were performed on human beings or animals for this research.

Data confidentiality

The authors declare that they have followed the protocols of their workplace on the publication of patient data.

Right of privacy and informed consent

The authors declare that patient data do not appear in this article.

Contribution of the authors

This research is original and unpublished. All authors have contributed significantly to the present study from conception to submission of the manuscript.

Paula Moscoso was the manager of the research idea, constant guide of the study, literature reviewer and organizer of the manuscript to be submitted to this scientific journal; Cathalina Arismendi, Rocío Bahamondes and Rosa Soto were the trainers of the hemodialysis patients, literature reviewers, and writers of the initial article. Luis Ojeda was the constant statistical study advisor.

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