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Original Research

Is It Safe for Hemodialysis Patients to Seek Gains with Less Pain? Acute Hemodynamic Response to Intradialytic Blood Flow Restriction Training

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ABSTRACT

International Journal of Exercise Science 15(2): 434-441, 2022. Considering that the hemodynamic safety is a major concern about intradialytic exercise with blood flow restriction, this analysis was performed to compare the blood pressure (BP) behavior during the first two hours of hemodialysis (HD) between sessions with no exercise (control group, CG), low/moderate intensity aerobic exercise with blood flow restriction (BFRE) and conventional aerobic exercise (AE). Adult patients with chronic kidney disease on HD at a university hospital were randomly assigned and submitted to a 12-week intradialytic training with BFRE or AE compared with the CG group. The main outcomes of this report were the change in systolic (SBP) and diastolic (DBP) BP during HD and the frequency of low BP (LBP) and high BP (HBP) episodes. A total of 6,074 BP measurements of 58 patients were analyzed. There was a larger decrease in BP in the exercise sessions compared with the control sessions, but with a similar magnitude in the BFRE and AE groups (effect size 0.49). There was a higher number of LBP in the BFRE group. The frequency of HBP was similar between the BFRE and the CG groups and lower in the AE group. Despite a greater number of mild LBP in BFRE patients, the BP change during the first two hours of HD was similar to that of patients in AE. Intradialytic aerobic exercise with blood flow restriction does not seem to be associated with a higher hemodynamic burden than conventional aerobic exercise.

KEY WORDS: Chronic kidney disease, hemodialysis, exercise, blood pressure, post-exercise hypotension

INTRODUCTION

Chronic kidney disease (CKD) is a public health problem due to its high prevalence (about 10% of the adult world population), negative impact on survival and quality of life and high economic cost of its treatment (14). As disease progresses, patients become less and less

physically active. In the later stages of the disease, when patients need renal replacement therapy (usually hemodialysis) to survive, most of them are highly sedentary and sarcopenic. Previous studies have shown that the less physical activity and the more muscle atrophy the patients have, the lower their survival will be (9). Given these observations, efforts have been undertaken to make these people more active. However, frailty and lack of motivation, on top of time constraints, create huge barriers to success in mitigating the sedentary lifestyle of CKD patients.

Exercise during the hemodialysis session, when patients stand still for about four hours, is a promising strategy to overcome the problem. Several previous publications have assured the safety of physical exercise during the first two hours of hemodialysis (7). To face the sarcopenia issue in CKD, high intensity exercise should be addressed. However, the patient's frailty prevents training of greater intensity.

Blood flow restriction training was pioneered in the 1970s by the Japanese sports scientist Yoshiaki Sato (12). The method involves blood pooling in the capillary beds of the exercising muscle due to the application of an external constricting device to the proximal limb. In the last decades, the technique has had a revival, with an increased number of publications on the issue. The greatest gain in strength and muscle mass with less intense training is the main advantage attributed to the blood flow restriction exercise (13), which may be especially useful for frail, older or sick populations.

Despite initial auspicious findings, concern remains regarding the safety of blood flow restriction application in clinical patients (6). Thrombotic and hemodynamic events have been described. Athletes and healthy sedentary people have presented higher hypertensive responses during resistance training with blood flow restriction (1, 11), usually with post-training hypotensive episodes (8). These hemodynamic effects have postponed further evaluation and widespread implementation of the technique in clinical populations. The present analysis aims to compare blood pressure (BP) behavior during the first two hours of hemodialysis between sessions with blood flow restriction aerobic exercise, no exercise and conventional aerobic exercise.

METHODS

This is a retrospective analysis of blood pressure data recorded during a randomized controlled trial. The trial aimed to assess the effects of intradialytic aerobic training with blood flow restriction on inflammatory, functional and quality of life outcomes in CKD patients on hemodialysis (3, 4). Participants were randomly assigned into one of three groups: a) Exercise with BFR (BFRE), b) conventional aerobic exercise (AE), and c) no-exercise control group (CG).

Participants

The study included patients 18 years of age or older and on hemodialysis treatment for more than three months. Patients with active infection or cancer, admitted to the Critical Care Unit,

with either musculoskeletal disease precluding exercise or cognitive impairment preventing the understanding of the instructions, were excluded from the study. The randomization was performed through a computer-generated list of random numbers. The protocol was approved for the Institutional Review Board and the National Research Ethics Committee (IRB/CONEP), and it adheres to all ethical policies set by the IJES Editorial Board (10). The study protocol was registered in the Brazilian Registry of Clinical Trials (ReBEC) with the identification code RBR-8T2P2M.

A total of 66 patients were randomized, 22 in each study group. Fifty-eight patients completed the 12-week intervention protocol. The mean age was 52.4 ± 15.8 years, half of the sample was male and 64% was white. The mean weight, height and body mass index were, respectively, 71.6 ± 12.7 Kg, 1.63 ± 0.1 meters, and 26.3 ± 2.9 Kg/m2 in control group, 75.8 ± 15.0, 1.66 ± 0.1 meters and 27.1 ± 5.3 Kg/m2 in AE group, and 69.9 ± 10.8 Kg (p = 0.35), 1.64 ± 0.1m (p = 0.76) and 26.1 ± 3.5 Kg/m2 in BFRE group. There was no statistical difference in sample characteristics according to allocation groups (3).

Protocol

The exercise groups trained on a cycle ergometer (O'neal, TP320) for twenty minutes during the first two hours of the three weekly hemodialysis sessions for 12 weeks. The exercise intensity aimed around 60% of maximal heart rate in the first six weeks, what correspond to 10-11 on the subjective effort perception scale. After that, exercise intensity was increased aiming around 70% of maximal heart rate, or 12-13 on the subjective effort scale. The BFRE performed the same exercise intervention wearing a 6-cm wide band positioned in the proximal thighs (inflator Hokanson DS400 and cuff Hokanson SC5) inflated to attain a 50% restriction of the arterial blood flow, throughout the exercise session (3).

Blood pressure was monitored during exercise. The training was interrupted if the systolic and/or diastolic blood pressure fell below 90 / 60 mmHg or exceeded 200 / 120 mmHg, respectively. Systolic and diastolic blood pressures were also measured and recorded before and at 60-minute intervals during hemodialysis using an aneroid sphygmomanometer (Tycos, Welch Allyn, NY). Systolic or diastolic blood pressure below 100 and 60 mmHg, respectively, was considered as low blood pressure, and above 140 and 90 mmHg, respectively, as high blood pressure. Further details on protocol, intervention and outcomes were published elsewhere (3, 4).

Statistical Analysis

The statistical analysis of blood pressure behavior was performed using Stata 15.1 software. Descriptive statistics of the sample were performed using t-test for continuous parametrical variables and Mann Whitney ranksum for non-parametrical variables. Categorical variables were analyzed by the Chi-square test. Mixed models for repeated measures compared the change in systolic and diastolic pressures over times 0 / 60 / 120 min according to the allocation group. The assumption of normal distribution of residuals was tested by the IQR test. The effect size on the change in SBP and DPB of each type of exercise compared with the control group

was calculated. The occurrence of low and high blood pressure and the frequency of systolic pressure above 160 mmHg and 180 mmHg were compared between groups at each time point using the Chi-square test.

RESULTS

A total of 6,074 blood pressure measurements were recorded, about one third at each time (before, 60 min and 120 min of hemodialysis) of the fifty-eight patients who completed the 12-week intervention protocol. There was adherence to the intervention above 80% in both groups. The mean occlusion pressure applied in the BFRE was 109.55 ± 13.03 mmHg. The exercise intensity was 18.1 ± 10.3 watts in the BFRE and 18.4 ± 8.8 watts in the AE group. There were no interruptions due to low or high blood pressure safety threshold.

Mean systolic and diastolic pressures were not different between groups before, at 60 and 120 minutes of hemodialysis. There was a significant decrease in systolic and diastolic pressures from baseline to 60 and 120 minutes in all groups, but the decrease was greater in the exercised groups compared with the control group (Table 1, Fig. 1). The overall effect size of exercise on BP change compared with control sessions was small to medium (overall d = 0.49; BFRG vs. CG d = 0.45; AE vs. CG d = 0.41) and very small to small between the two exercise modalities (BFRG vs. AE f = 0.03)

Table 1: Systolic and diastolic blood pressure at baseline, 60 min. and 120 min. during hemodialysis according to allocation groups; repeated measures mixed-models analysis with time and group vs. time effects.

	BFRE (mean/sd)	AE (mean/sd)	CG* (mean/sd)	Time	
SBP (mmHg)				Estimate (95% CI)	p-value
Baseline**	148.2 (23.7)	148.7 (22.2)	148.1 (23.0)		
60 min.	137.8 (23.5)	138.4 (20.3)	140.8 (22.3)	-7.2 (-8.6 -5.8)	< 0.001
120 min.	134.2 (23.6)	134.6 (19.0)	139.3 (21.9)	-8.7 (-10 -7.3)	< 0.001
Group vs. time 60 min.					
Estimate (95% CI)	-3.2 (-5.2 -1.3)	-3.1 (-5.0 -1.1)			
p-value	0.001	0.002			
Group vs. time 120 min.					
Estimate (95% CI)	-5.4 (-7.4 -3.4)	-5.4 (-7.3 -3.4)			
p-value	< 0.001	< 0.001			
DBP (mmHg)					
Baseline**	88.9 (16.1)	84.7 (13.0)	86.5 (17.1)		
60 min.	83.5 (13.9)	80.4 (11.2)	83.3 (15.1)	-3.2 (-4.1 -2.3)	< 0.001
120 min.	81.9 (13.4)	78.8 (10.8)	81.9 (14.4)	-4.6 (-5.5 -3.6)	< 0.001
Group vs. time 60 min.					
Estimate (95% CI)	-2.2 (-3.5 -.9)	-1.2 (-2.4 .1)			
p-value	0.001	0.075			
Group vs. time 120 min.					

Estimate (95% CI)	-2.5 (-3.8 -1.2)	-1.3 (-2.6 -.1)
p-value	< 0.001	0.038

BFRE blood flow restriction exercise group; AE conventional aerobic exercise group; CG control group; SBP systolic blood pressure; DBP diastolic blood pressure; *reference group; **reference time.

There was no difference in the frequency of diastolic blood pressure below 60 mmHg among groups. There was a higher percentage of low systolic blood pressure in the BFRE at 60 minutes (3%) and 120 minutes (5%) on hemodialysis. The lowest systolic pressure recorded in BFRE was 60 mmHg, whereas most systolic hypotensive episodes in all groups was 80 mmHg (Fig. 2).

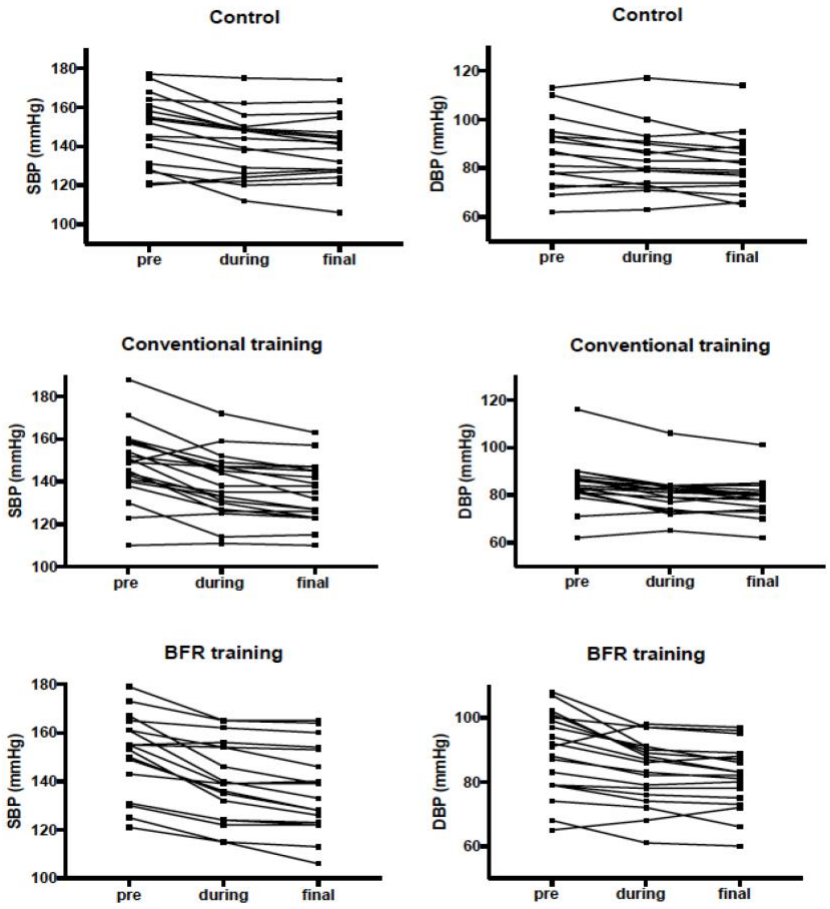

Figure 1: Systolic and diastolic mean blood pressure by patient at baseline, 60 min. and 120 min. during hemodialysis, according to allocation groups

The frequency of diastolic pressure above 90 mmHg was higher in the BFRE at baseline, but similar between the BFRE and CG and lower in the AE at 60 and 120 min of hemodialysis. The occurrence of systolic pressure above 140 mmHg was similar among the groups at baseline and at 60 min, but lower in the AE at 120 min. In a post-hoc analysis, the AE also had a lower occurrence of systolic pressure above 160 mmHg and 180 mmHg at 60 and 120 min (Fig 2).

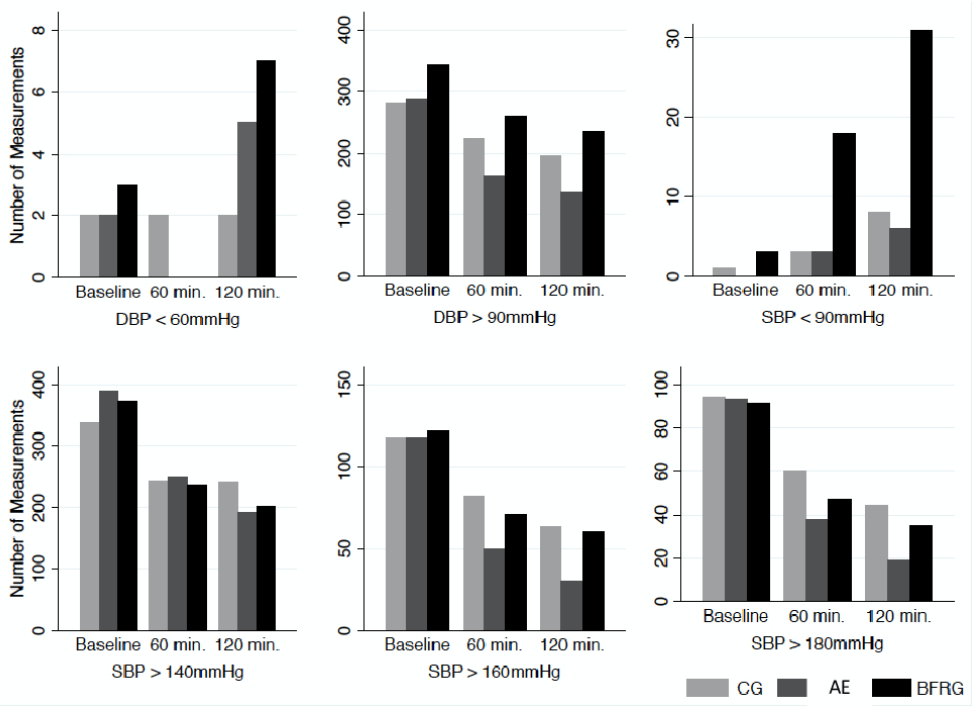

Figure 2: Frequency of systolic and diastolic blood pressure below and above specified limits according to allocation groups

DISCUSSION

The present analysis found a greater decrease in blood pressure among patients submitted to intradialytic aerobic conventional and blood flow restriction exercise during the first two hours of hemodialysis. Despite the similar decrease in blood pressure in both exercise groups, a higher percentage of measures met the criteria for low systolic pressure in the blood flow restriction group at 60 and 120 minutes of dialysis.

Long-lasting decreases in blood pressure are often seen after a bout of exercise. This hemodynamic response has been attributed to an imbalance between the fast decrease in cardiac output and the slower recovery of peripheral vascular resistance. The post-exercise hypotension lasts about two hours in healthy individuals, but it can last longer than 12 hours in hypertensive patients (8). Exercise with blood flow restriction usually induce rebound vasodilation, which can exacerbate the post-exercise hypotension. As hypotension is one of the most frequent hemodialysis complications (2) due to the continuous decrease in circulatory volume during volume ultrafiltration, the degree of this hemodynamic response could preclude blood flow restriction during dialysis.

The present analysis extended the blood pressure monitoring to the first two hours of dialysis and found that the decrease in blood pressure in BFRE was not greater than conventional exercise group. Although there was a greater number of measurements below the normal range

in the BFRE, the difference in the percentage below systolic threshold between the groups was small and the degree of hypotension very similar, with no symptomatic or requiring medical intervention episode.

The occurrence of hypertensive episodes at 60 and 120 minutes of dialysis was similar between BFRE and CG and lower in AE. Although increases in blood pressure during intradialytic blood flow restriction exercise have already been described (5), our findings showed that these increases are likely to be short-lived, with no effect on the mean arterial pressure to which the patient was submitted during the hemodialysis session. The smaller occurrence of hypertension in the AE is also an interesting finding. If confirmed by other studies, this may be another reason for exercising during hemodialysis.

The present analysis did not include blood pressure measurements during exercise. However, throughout the training blood pressure was also monitored for safety reasons, guiding training interruptions in case of exceeding safety thresholds. No case of training interruption for hemodynamic reasons was recorded. Another weakness of the analysis is that there was no exact time synchronization between exercise and blood pressure measurements due to the retrospective collection of the blood pressure data. However, to the best of the authors' knowledge, this is the larger investigation on blood pressure in intradialytic exercise with blood flow restriction, including more than six thousand blood pressure measurements during the first two hours of dialysis. The mild blood pressure response to intradialytic aerobic exercise, even using blood flow restriction, is an auspicious finding, potentially increasing the agreement of patients and dialysis staff to apply the technique.

The golden rule of health care remains, despite the centuries passed since this statement, *Primum non nocere*, first do not harm. Therefore, safety is a sine qua non condition for a new intervention to be implemented, or old interventions be extrapolated to different populations. We hope to be contributing to ensure the hemodynamic safety of intradialytic aerobic exercise with blood flow restriction in hemodialysis patients.

Clinical Messages:

1. Intradialytic exercise is associated with a greater decrease in blood pressure during the first two hours of hemodialysis;
2. Aerobic exercise with or without blood flow restriction causes similar reductions in blood pressure during the first two hours of hemodialysis;
3. Patients practicing blood flow restriction exercise presented a greater number of systolic blood pressure measurements below 90mmHg.

REFERENCES

1. Araújo JP, Silva JC, Souza TS, Lima OE, Guerra I, Sousa MS. The acute effect of resistance exercise with blood flow restriction with hemodynamic variables on hypertensive subjects. J Hum Kinet 43: 79-85, 2014.

2. Caplin B, Kumar S, Davenport A. Patients' perspective of haemodialysis-associated symptoms. Nephrol Dial Transplant 26(8): 2656-2663, 2011.

3. Cardoso RK, Araujo AM, Del Vechio FB, Bohlke M, Barcellos FC, Oses JP, de Freitas MP, Rombaldi AJ. Intradialytic exercise with blood flow restriction is more effective than conventional exercise in improving walking endurance in hemodialysis patients: a randomized controlled trial. Clin Rehabil 34(1): 91-8, 2020.

4. Cardoso RK, Araujo AM, Orcy RB, Bohlke M, Oses JP, Del Vecchio FB, Barcellos FC, Gonzalez MC, Rombaldi AJ. Effects of continuous moderate exercise with partial blood flow restriction during hemodialysis: A protocol for a randomized clinical trial. MethodsX 6: 190-198, 2019.

5. Clarkson MJ, C, Fraser SF, McMahon LP, Bennett PN, Warmington SA. Haemodynamic and perceptual responses to blood flow restricted exercise among dialysis patients. Am J Physiol Renal Physiol 318(3): F843-F850, 2020.

6. Cuyul-Vásquez I, Leiva-Sepúlveda A, Catalán-Medallaa O. Berríos-Contreras L. Blood flow restriction training for people with cardiovascular disease: An exploratory review. Rehabilitacion (Madr) 54(2): 116-27, 2020.

7. Jiang Pu, Zheng Jiang, Weihua Wu, Li Li, Liling Zhang, Ying Li, Qi Liu, Santao Ou. Efficacy and safety of intradialytic exercise in haemodialysis patients: A systematic review and meta-analysis. BMJ Open 9(1): e020633, 2019.

8. Kenny MJ, Seals DR. Postexercise hypotension: Key features, mechanisms, and clinical significance. Hypertension 22(5): 653–664, 1993.

9. Kittiskulnam P, Chertow GM, Carrero JJ, Delgado C, Kaysen GA, Johansen KL. Sarcopenia and its individual criteria are associated, in part, with mortality among patients on hemodialysis. Kidney Int 92(1): 238-247, 2017.

10. Navalta JW, Stone WJ, Lyons TS. Ethical issues relating to scientific discovery in exercise science. Int J Exerc Sci 12(1): 1-8, 2020.

11. Pinto RR, Karabulut M, Poton R, Polito MD. Acute resistance exercise with blood flow restriction in elderly hypertensive women: Haemodynamic, rating of perceived exertion, and blood lactate. Clin Physiol Funct Imaging 38(1): 17-24, 2018.

12. Sato Y. The history and future of KAATSU training. Int J Kaatsu Training Res 1(1): 1-5, 2005.

13. Slysz J, Stultz J, Burr JF. The efficacy of blood flow restricted exercise: A systematic review & meta-analysis. J Sci Med Sport 19(8): 669-75, 2016.

14. Webster AC, Nagler EV, Morton RL, Masson P. Chronic Kidney Disease. Lancet 389(10075): 1238-1252, 2017.