

Can exercise training reduce central systolic blood pressure among patients with resistant hypertension?

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Introduction:

Resistant hypertension is a problematic phenotype marked by the limited efficacy of available blood pressure-lowering treatments [1], such as antihypertensive medicines and kidney denervation [2-4]. Given its health-related and economic impact, it is an important medical and societal issue. Patients with resistant hypertension have a higher risk of myocardial infarction, stroke, heart failure, chronic renal disease, and death, in addition to the cost of multiple drugs [5,6]. Cardiovascular disease risk is associated to central blood pressure. Central blood pressure seems to better relate with target organ damage and long-term cardiovascular outcomes, compared to traditional brachial blood pressure [7,8]. Increased aortic stiffness, assessed by carotid-femoral pulse wave velocity, is also an independent predictor of cardiovascular risk [9]. However, there are few studies on exercise interventions to improve these markers in people with resistant hypertension.

The EnRicH (The Exercise Training in the Treatment of Resistant Hypertension) was a prospective, single-blinded randomized clinical trial. The current analysis details the effect of aerobic exercise training intervention or usual care on central blood pressure and carotid–femoral pulse wave velocity.

Methods:

Patients with resistant hypertension were randomized 1:1 to a 12-week moderate-intensity aerobic exercise program (added to usual care) or usual care. Exercise training sessions were supervised and took place three times per week. Each session included a 10-min warm-up and cool-down period, and 40 minutes of aerobic exercise. Walking and cycling were the main chosen exercises and intensity was 50-70% of maximum oxygen uptake (VO₂ max). Secondary outcome measures included central blood pressure and carotid–femoral pulse wave velocity. The Complior Analyse (Alam Medical, Saint Quentin Fallavier, France) and the SphygmoCor (AtCor Medical, Sydney, NSW, Australia) were used to measure central blood pressure and carotid–femoral pulse wave velocity. The two devices offer highly correlated measurements and similar outcomes. The carotid–femoral pulse wave velocity measurements were taken in accordance with Van Bortel et al. [10] expert's consensus document. SPSS version 28.0 was used for all statistical analyses (SPSS Inc., Chicago, Illinois, USA). Student's independent t-test was used to compare between-group differences at baseline, following the exercise program, and between changes in continuous variables from baseline to the end of the study. Student's paired t-tests were performed for within-group comparisons from baseline to the end of the study. The level of significance was set as $P \leq 0.05$.

Results:

Fifty-three patients (exercise $n = 26$, mean age 59.3 ± 8.2 ; control $n = 27$, mean age 60.8 ± 9.2) completed the study. No differences were found between groups at baseline. The change in central systolic blood pressure was significantly different between groups by -12.2 (95% CI, -22.6 to -1.9 , $P = 0.022$), with a mean change of -11.3 ± 19.2 mm Hg in the exercise arm vs 0.9 ± 11.8 mm Hg in the control arm. There were no differences in carotid–femoral pulse wave velocity between groups ($P = 0.197$).

Discussion:

Keywords:

Central systolic pressure, Cardiac rehabilitation, hypertension, arterial stiffness

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Conflict of interest:

The authors declare no conflict of interests

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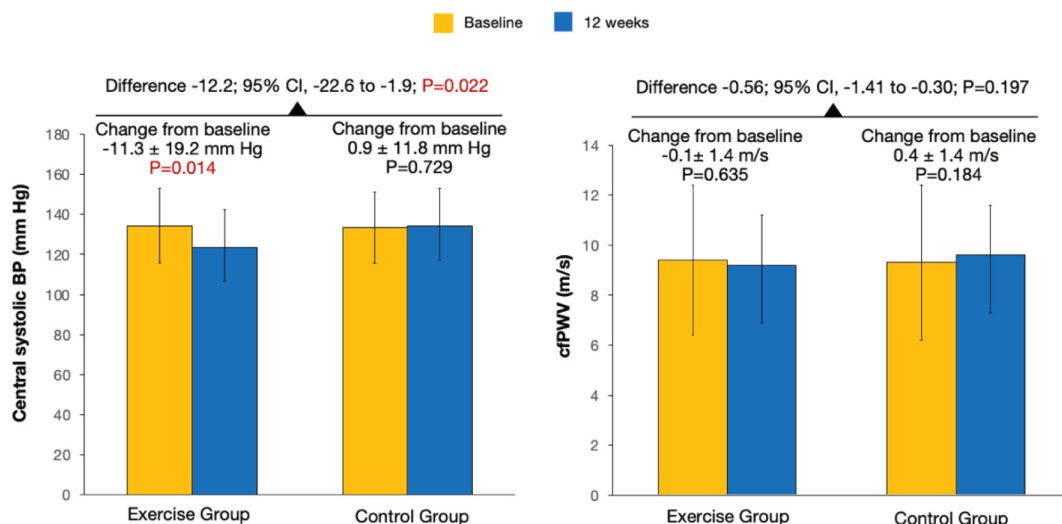


Figure 1 - Change from baseline to the end of treatment in central blood pressure and carotid-femoral pulse wave velocity in both study groups.

This study demonstrated that a 12-week exercise training program reduces central systolic blood pressure among patients with resistant hypertension. However, no significant changes were found for carotid-femoral pulse wave velocity. Our study agrees with previous evidence of aerobic exercise with similar programs in patients with prehypertension and hypertension [11,12]. Possibly, higher exercise intensities or longer duration programs may be necessary to induce changes to arterial stiffness.

A limitation of this study is that exercise training program consisted of moderate-intensity aerobic exercises. Therefore, other types of exercise and intensities need future investigation.

This trial demonstrated a benefit of 12-week of moderate-intensity aerobic exercise training on reducing central blood pressure in patients with resistant hypertension. The central blood pressure reduction is clinically promising as this indicator is associated with target organ damage, cardiovascular risk, and mortality.

Ethics committee and informed consent:

All patients provided written informed consent. The study was approved by the Ethics Committee of the Centro Hospitalar do Baixo Vouga

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References:

- Carey RM, Calhoun DA, Bakris GL, Brook RD, Daugherty SL, Dennison-Himmelfarb CR, et al. Resistant Hypertension: Detection, Evaluation, and Management: A Scientific Statement From the American Heart Association. *Hypertension*. 2018;72(5):e53-e90. Epub 2018/10/26. <https://doi.org/10.1161/HYP.0000000000000084>
- Bakris GL, Townsend RR, Liu M, Cohen SA, D'Agostino R, Flack JM, et al. Impact of renal denervation on 24-hour ambulatory blood pressure: results from SYMPPLICITY HTN-3. *Journal of the American College of Cardiology*. 2014;64(11):1071-8. Epub 2014/05/27. <https://doi.org/10.1016/j.jacc.2014.05.012>
- Agasthi P, Shipman J, Arsanjani R, Ashukem M, Girardo ME, Yerasi C, et al. Renal Denervation for Resistant Hypertension in the contemporary era: A Systematic Review and Meta-analysis. *Sci Rep*. 2019;9(1):6200. Epub 2019/04/19. <https://doi.org/10.1038/s41598-019-42695-9>
- Bhatt DL, Kandzari DE, O'Neill WW, D'Agostino R, Flack JM, Katzen BT, et al. A controlled trial of renal denervation for resistant hypertension. *The New England journal of medicine*. 2014;370(15):1393-401. Epub 2014/04/01. <https://doi.org/10.1056/NEJMoa1402670>
- Daugherty SL, Powers JD, Magid DJ, Tavel HM, Masoudi FA, Margolis KL, et al. Incidence and prognosis of resistant hypertension in hypertensive patients. *Circulation*. 2012;125(13):1635-42. <https://doi.org/10.1161/CIRCULATIONAHA.111.068064>
- Sapoval M, Hale BC, Armstrong S, Da Deppo L, Hertz D, Briggs A. The Burden of Resistant Hypertension in 5 European Countries. *Value in Health*. 2013;16:A520-A1. <https://doi.org/10.1016/j.jval.2013.08.1252>
- Kollias A, Lagou S, Zeniodi ME, Boubouchairopoulou N, Stergiou GS. Association of Central Versus Brachial Blood Pressure With Target-Organ Damage: Systematic Review and Meta-Analysis. *Hypertension*. 2016;67(1):183-90. Epub 2015/11/26. <https://doi.org/10.1161/HYPERTENSIONAHA.115.06066>

8. Vlachopoulos C, Aznaouridis K, O'Rourke MF, Safar ME, Baou K, Stefanadis C. Prediction of cardiovascular events and all-cause mortality with central haemodynamics: a systematic review and meta-analysis. *European heart journal*. 2010;31(15):1865-71. Epub 2010/03/04. <https://doi.org/10.1093/eurheartj/ehq024>
9. Cardoso CRL, Salles GF. Prognostic Value of Changes in Aortic Stiffness for Cardiovascular Outcomes and Mortality in Resistant Hypertension: a Cohort Study. *Hypertension*. 2022;79(2):447-56. Epub 2022/01/13. <https://doi.org/10.1161/HYPERTENSIONAHA.121.18498>
- 10.10. Van Bortel LM, Laurent S, Boutouyrie P, Chowienczyk P, Cruickshank JK, De Backer T, Filipovsky J, Huybrechts S, Mattace-Raso FU, Protogerou AD, Schillaci G, Segers P, Vermeersch S, Weber T; Artery Society; European Society of Hypertension Working Group on Vascular Structure and Function; European Network for Noninvasive Investigation of Large Arteries. Expert consensus document on the measurement of aortic stiffness in daily practice using carotid-femoral pulse wave velocity. *J Hypertens*. 2012 Mar;30(3):445-8. <https://doi.org/10.1097/HJH.0b013e32834fa8b0>
11. Beck DT, Martin JS, Casey DP, Braith RW. Exercise Training Reduces Peripheral Arterial Stiffness and Myocardial Oxygen Demand in Young Prehypertensive Subjects. *American Journal of Hypertension*. 2013;26:1093-102. <https://doi.org/10.1093/ajh/hpt080>
12. Nualnim N, Parkhurst K, Dhindsa M, Tarumi T, Vavrek J, Tanaka H. Effects of Swimming Training on Blood Pressure and Vascular Function in Adults > 50 Years of Age. *American Journal of Cardiology*. 2012;109:1005-10. <https://doi.org/10.1016/j.amjcard.2011.11.029>