Name of journal: *World Journal of Cardiology*

ESPS Manuscript NO: 14636

Columns: Editorial

**Exercise training in the management of patients with resistant hypertension**

Ribeiro F *et al.* Physical exercise and resistant hypertension

Fernando Ribeiro, Rui Costa, José Mesquita-Bastos

**Fernando Ribeiro, Rui Costa, José Mesquita-Bastos,** School of Health Sciences, University of Aveiro, 3810-193 Aveiro, Portugal

**Author contributions:** All authors contributed to this manuscript.

**Conflict-of-interest:** The authors declare that there are no conflicts of interest.

**Open-Access:** This article is an open-access article which selected by an in-house editor and fully peer-reviewed by external reviewers. It distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

**Correspondence to:** Fernando Ribeiro, PhD, School of Health Sciences, University of Aveiro, Building 30, Agras do Crasto, Campus Universitário de Santiago, 3810-193 Aveiro, Portugal. fernando.ribeiro@ua.pt

**Telephone:** +351-23-4372455 **Fax:** +351-23-4401597

**Received:** October 16, 2014

**Peer-review started:** October 20, 2014

**First decision:** November 20, 2014

**Revised:** December 4, 2014

**Accepted:** December 16, 2014

**Article in press:**

**Published online:**

**Abstract**

Hypertension is a very prevalent risk factor for cardiovascular disease. The resistant hypertension, *i.e.,* uncontrolled hypertension with 3 or more antihypertensive agents including 1 diuretic, prevalence is between 5% and 30% among the hypertensive population. The causes of resistant hypertension are multifactorial and include behavioural and biological factors, such as non-adherence to pharmacological treatment. All current treatment guidelines highlight the positive role of physical exercise as a non-pharmacological tool in the treatment of hypertension. This paper draws attention to the possible role of physical exercise as an adjunct non-pharmacological tool in the management of resistance hypertension. Few studies have investigated it, employing different methodologies, but taken together they have shown promising results. In summary, the available evidence suggests that aerobic physical exercise could be a valuable addition to the optimal pharmacological treatment of patients with resistant hypertension.

© The Author(s) 2015. Published by Baishideng Publishing Group Inc. All rights reserved.

**Key words:** Exercise training; Resistant hypertension; Blood pressure; Non-pharmacological; Cardiovascular disease

**Core tip:** Taken together the available evidence indicates that, unless presenting a contra-indication to perform physical exercise, patients with resistant hypertension should be encouraged to engage on regular aerobic physical exercise in addition to the optimal pharmacological treatment.

Ribeiro F, Costa R, Mesquita-Bastos J. Exercise training in the management of patients with resistant hypertension. *World J Cardiol* 2014; In press

**RESISTANT HYPERTENSION**

Arterial hypertension (defined as blood pressure > 140/90 mmHg) is the most important risk factor for cardiovascular events and end-stage renal disease[1]. In general population arterial hypertension has a prevalence of 30%-45%[1]. The control of blood pressure is essential to avoid cardiovascular events in primary and secondary prevention[1]. In an important percentage of subjects, arterial hypertension is not controlled (< 140 and 90 mmHg) with a strategy to correct lifestyle behaviour and three antihypertensive drugs in high doses including a diuretic[1,2] and is defined as resistant hypertension. Some authors suggest that resistant hypertension should be diagnosed in those who have criteria of blood pressure control with the use of four antihypertensive drugs[2]. Several studies found that the prevalence of resistant hypertension in the hypertensive population is between 5% and 30%[1]. So, it is essential that the diagnosis of resistant hypertension is well defined in order to exclude the false resistant hypertension[3]. Normally arterial hypertension is defined by office blood pressure obtained by an electronic oscilometric device, called casual blood pressure. Ambulatory blood pressure is another way to measure blood pressure. Ambulatory blood pressure is superior to casual blood pressure in the diagnosis[1] and in the cardiovascular events prognosis[4,5].

Blood pressure shows circadian rhythm; it is higher in the morning after the awaking (morning surge), declines during the day and in a more pronounced way during the night with the sleeping (night-time dipping)[6]. In relation to cardiovascular events prognosis, several studies have shown that night-time blood pressure is superior to daytime blood pressure[4,7]. In patients with resistant hypertension the absence of night-time dipping is more prevalent than in patients with non resistant hypertension and it is associated to higher cardiovascular events[6]. Ambulatory blood pressure also makes possible the exclusion of the alert reaction (difference between casual blood pressure and day blood pressure determined by ambulatory blood pressure), which is one of the causes of false resistant hypertension or pseudo resistant hypertension[3]. In pseudo resistant hypertension, blood pressure is not controlled in office behaviour but has normal values in ambulatory blood pressure. Non-adherence to the prescribed treatment is another cause of false resistant hypertension[5].

Resistant hypertension is associated with higher organ damage and cardiovascular events, and worse renal prognosis[1]. Resistant hypertension can be caused by obesity, excessive alcohol ingestion, high salt intake, and obstructive sleep apnoea[5]. Secondary hypertension can be the cause of resistant hypertension[8], secondary causes of hypertension include hyperaldosteronism, obstructive sleep apnea, renal artery stenosis, and pheochromocytoma[9]. Hyperaldosteronism is the most common secondary cause of hypertension; nonetheless many newly diagnosed hypertensive patients[10] and resistant hypertension patients[11] can have undetected primary aldosteronism. So, it is recommendable, in studies looking for the impact of life style changes on blood pressure of patients with resistant hypertension, to assess at least plasma aldosterone-renin ratio even if the serum potassium level is normal[9]. The treatment of arterial hypertension implies changes in life style attitudes namely regarding exercise habits[8]. Recently, a prospective, blinded, randomized, sham-controlled trial assessing the effect of renal denervation or a sham procedure on ambulatory blood pressure monitoring measurements 6 mo post-randomization failed to demonstrate a benefit of renal artery denervation on reduction in ambulatory blood pressure[12].However, recently several preditors of blood pressure response in the SYMPLICITY HTN-3 trial were identified, which could at least partially explain the results of the trial[13]; among the predictors are the total number of ablation attempts, baseline office SBP ≥ 180 mmHg, prescription of an aldosterone antagonist at baseline, and age < 65 years in age[13]. This information is significant to design future studies in this field.

**EXERCISE TRAINING AND RESISTANT HYPERTENSION**

The cardioprotective benefits of exercise training among those with cardiovascular diseases include the modification of traditional cardiovascular risk factors, the improvement of exercise tolerance, myocardial and peripheral perfusion, cardiac function, arterial stiffness, autonomic function, endothelial repair, as well as the mitigation of endothelial dysfunction and low-grade vascular wall inflammation, and, most importantly, the reduction of the morbidity and mortality[14-25]. Indeed, it is widely accepted that exercise training is a polypill with several beneficial effects, including antihypertensive effects. Indeed, exercise is able to induce a decrease of 5-7 mmHg in systolic blood pressure in patients with hypertension[26]. Nonetheless, the antihypertensive effects of exercise in patients with cardiovascular disease are often underestimated, because the analysis is frequently made without assessing the influence of the baseline blood pressure on the effects of exercise training. We showed[17,27] in previous studies that if cardiovascular disease patients with high and low blood pressure at baseline are considered together, an exercise training intervention has no effect on blood pressure. But, if the analysis is conducted dividing patients into two subgroups on the basis of baseline blood pressure (pre-hypertension/hypertension versus normotension), exercise training decreases significantly systolic blood pressure[17,27]. An interesting aspect of exercise for patients with hypertension is that they could benefit from the antihypertensive effect of aerobic exercise after just three exercise sessions, additionally the duration of the exercise sessions can be as short as 10 min and the intensity of exercise can be relatively low (40% to < 60% VO2peak)[26]. The exercise prescription recommendation of the American College of Sports Medicine for those with high blood pressure is to perform 30 min of continuous or accumulated aerobic exercise of moderate-intensity (40%-60% of VO2Reserve) per day, on most, preferably all, days of the week[28]. The aerobic exercise could be supplemented by resistance exercise[28].

The management of resistant hypertension includes lifestyle interventions aiming to reduce sodium intake and increase the levels of daily physical activity[29]. Nonetheless, there are few studies evaluating the effects of lifestyle interventions including physical exercise in patients with resistant hypertension. The potential of aerobic physical exercise as an adjunct non-pharmacological therapeutic tool to manage resistant hypertension was recently address in three studies[30-32].

Dimeo *et al*[30] first showed that patients with a reduced responsiveness to medication do not necessarily have reduced responsiveness to non-pharmacological therapies, *i.e.,* aerobic physical exercise, to lower blood pressure. The authors conducted a randomized trial encompassing fifty patients with resistant hypertension submitted to an exercise-training program, consisting of walking on a treadmill 3 times per week, for 8 to 12 wk. Initially the duration of the sessions was 30 min (interval training until the fifth week) and then was gradually increased to 30, 32 and 36 min of continuous training. Dimeo *et al*[30] observed a 6 ± 12 and 3 ± 7 mmHg reduction in ambulatory systolic and diastolic daytime ambulatory blood pressure, respectively. More recently, Guimaraes *et al*[31] confirmed these positive results using a different exercise approach. They enrolled 32 patients to a heated-water exercise program or to a control group. The heated-water exercise program was performed three times per week, for 12 wk, and consisted of callisthenic exercises (*i.e.*, exercises performed in a rhythmic, systematic way using the body weight for resistance) against water resistance and walking inside a pool with controlled temperature (30–32 °C). After 12 wk, the exercise program group showed a decrease in 24-h systolic (from 137 ± 23 to 120 ± 12 mmHg) and diastolic blood pressure (from 81 ± 13 to 72 ± 10 mmHg), daytime systolic (from 141 ± 24 to 120 ± 13 mmHg) and diastolic blood pressure (from 84 ± 14 to 73 ± 11 mmHg), and night-time systolic (from 129 ± 22 to 114 ± 12 mmHg) and diastolic blood pressure (from 74 ± 11 to 66 ± 10 mmHg). This reduction in blood pressure is of great importance, as higher ambulatory blood pressure predicts cardiovascular morbidity and mortality in resistant hypertensive patients[33].

Concern for safety must come first in all that prescribe or supervise exercise. Thus, patients with resistance hypertension should consult a physician prior to engagement in exercise training, particularly vigorous-intensity exercise[34]. The progression of intensity of aerobic exercise should be gradual to enhance compliance; slow progression of frequency and intensity of resistance exercise is also encouraged to avoid injuries. Isometric exercise is not recommend. In patients with poorly controlled blood pressure, vigorous-intensity exercise should be discouraged or postponed until appropriate drug treatment has been instituted and blood pressure lowered[34]. It seems prudent to keep systolic blood pressures at ≤ 220 mmHg and/or diastolic blood pressures ≤ 105 mmHg during exercise[35]. It is also important to know that in some patients, β-blockers and diuretics have an adverse impact on thermoregulatory function and could cause hypoglycaemia[35,36]. Additionally, patients treated with calcium channel blockers, β-blockers and vasodilators should stop exercise gradually, as they have increased likelihood of hypotension post-exercise[35,36]. Hence, it is important to monitor the room temperature during exercise, use the Borg scale as adjunct to heart rate to monitor exercise intensity, and extend the cool-down period.

**FUTURE PERSPECTIVES**

The above-mentioned results are promising and provide good perspectives for the future. Nonetheless, more studies enrolling a large number of patients are clearly needed to reinforce the role of physical exercise associated with antihypertensive medication in the control of blood pressure in patients with resistant hypertension. Future studies are also warranted to disclose the mechanisms responsible for the positive effects of exercise. Several mechanisms, none of them definitive, have been proposed to explain the benefits of exercise training in these patients, including the decrease of sympathetic and the increase of vagal nerve activity, the improvement of the sensitivity of the baroreceptor reflex, the improvement of endothelial function and arterial stiffness, the decrease in the concentration of rennin, angiotensin II, and aldosterone, and the reduction of renal sympathetic outflow. These aspects seem to merit close attention in future studies.

**REFERENCES**

1 **Goldstein LB**, Bushnell CD, Adams RJ, Appel LJ, Braun LT, Chaturvedi S, Creager MA, Culebras A, Eckel RH, Hart RG, Hinchey JA, Howard VJ, Jauch EC, Levine SR, Meschia JF, Moore WS, Nixon JV, Pearson TA. Guidelines for the primary prevention of stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2011; **42**: 517-584 [PMID: 21127304 DOI: 10.1161/STR.0b013e3181fcb238]

2 **Persell SD**. Prevalence of resistant hypertension in the United States, 2003-2008. *Hypertension* 2011; **57**: 1076-1080 [PMID: 21502568 DOI: 10.1161/HYPERTENSIONAHA.111.170308]

3 **Myers MG**. Pseudoresistant hypertension attributed to white-coat effect. *Hypertension* 2012; **59**: 532-533 [PMID: 22252395 DOI: 10.1161/HYPERTENSIONAHA.111.189472]

4 **Mesquita-Bastos J**, Bertoquini S, Polónia J. Cardiovascular prognostic value of ambulatory blood pressure monitoring in a Portuguese hypertensive population followed up for 8.2 years. *Blood Press Monit* 2010; **15**: 240-246 [PMID: 20616705 DOI: 10.1097/MBP.0b013e32833c8b08]

5 **Mancia G**, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Böhm M, Christiaens T, Cifkova R, De Backer G, Dominiczak A, Galderisi M, Grobbee DE, Jaarsma T, Kirchhof P, Kjeldsen SE, Laurent S, Manolis AJ, Nilsson PM, Ruilope LM, Schmieder RE, Sirnes PA, Sleight P, Viigimaa M, Waeber B, Zannad F, Redon J, Dominiczak A, Narkiewicz K, Nilsson PM, Burnier M, Viigimaa M, Ambrosioni E, Caufield M, Coca A, Olsen MH, Schmieder RE, Tsioufis C, van de Borne P, Zamorano JL, Achenbach S, Baumgartner H, Bax JJ, Bueno H, Dean V, Deaton C, Erol C, Fagard R, Ferrari R, Hasdai D, Hoes AW, Kirchhof P, Knuuti J, Kolh P, Lancellotti P, Linhart A, Nihoyannopoulos P, Piepoli MF, Ponikowski P, Sirnes PA, Tamargo JL, Tendera M, Torbicki A, Wijns W, Windecker S, Clement DL, Coca A, Gillebert TC, Tendera M, Rosei EA, Ambrosioni E, Anker SD, Bauersachs J, Hitij JB, Caulfield M, De Buyzere M, De Geest S, Derumeaux GA, Erdine S, Farsang C, Funck-Brentano C, Gerc V, Germano G, Gielen S, Haller H, Hoes AW, Jordan J, Kahan T, Komajda M, Lovic D, Mahrholdt H, Olsen MH, Ostergren J, Parati G, Perk J, Polonia J, Popescu BA, Reiner Z, Rydén L, Sirenko Y, Stanton A, Struijker-Boudier H, Tsioufis C, van de Borne P, Vlachopoulos C, Volpe M, Wood DA. 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Eur Heart J* 2013; **34**: 2159-2219 [PMID: 23771844 DOI: 10.1093/eurheartj/eht151]

6 **Syrseloudis D**, Andrikou I, Andrikou E, Dimitriadis K, Stefanadis C. Ambulatory blood pressure monitoring in resistant hypertension. *Int J Hypertens* 2011; **2011**: 285612 [PMID: 21629865 DOI: 10.4061/2011/285612]

7 **Bastos JM**, Bertoquini S, Polónia J. Prognostic value of subdivisions of nighttime blood pressure fall in hypertensives followed up for 8.2 years. Does nondipping classification need to be redefined? *J Clin Hypertens (Greenwich)* 2010; **12**: 508-515 [PMID: 20629813 DOI: 10.1111/j.1751-7176.2010.00291.x]

8 **Acelajado MC**, Calhoun DA. Resistant hypertension, secondary hypertension, and hypertensive crises: diagnostic evaluation and treatment. *Cardiol Clin* 2010; **28**: 639-654 [PMID: 20937447 DOI: 10.1016/j.ccl.2010.07.002]

9 **Pimenta E**, Calhoun DA. Resistant hypertension and aldosteronism. *Curr Hypertens Rep* 2007; **9**: 353-359 [PMID: 18177580 DOI: 10.1007/s11906-007-0066-7]

10 **Rossi GP**, Bernini G, Caliumi C, Desideri G, Fabris B, Ferri C, Ganzaroli C, Giacchetti G, Letizia C, Maccario M, Mallamaci F, Mannelli M, Mattarello MJ, Moretti A, Palumbo G, Parenti G, Porteri E, Semplicini A, Rizzoni D, Rossi E, Boscaro M, Pessina AC, Mantero F. A prospective study of the prevalence of primary aldosteronism in 1,125 hypertensive patients. *J Am Coll Cardiol* 2006; **48**: 2293-2300 [PMID: 17161262 DOI: 10.1016/j.jacc.2006.07.059]

11 **Douma S**, Petidis K, Doumas M, Papaefthimiou P, Triantafyllou A, Kartali N, Papadopoulos N, Vogiatzis K, Zamboulis C. Prevalence of primary hyperaldosteronism in resistant hypertension: a retrospective observational study. *Lancet* 2008; **371**: 1921-1926 [PMID: 18539224 DOI: 10.1016/S0140-6736(08)60834-X]

12 **Bakris GL**, Townsend RR, Liu M, Cohen SA, D'Agostino R, Flack JM, Kandzari DE, Katzen BT, Leon MB, Mauri L, Negoita M, O'Neill WW, Oparil S, Rocha-Singh K, Bhatt DL. Impact of renal denervation on 24-hour ambulatory blood pressure: results from SYMPLICITY HTN-3. *J Am Coll Cardiol* 2014; **64**: 1071-1078 [PMID: 24858423 DOI: 10.1016/j.jacc.2014.05.012]

13 **Kandzari DE,** Bhatt DL, Brar S, Devireddy CM, Esler M, Fahy M, Flack JM, Katzen BT, Lea J, Lee DP, Leon MB, Ma A, Massaro J, Mauri L, Oparil S, O'Neill WW, Patel MR, Rocha-Singh K, Sobotka PA, Svetkey L, Townsend RR, Bakris GL. Predictors of blood pressure response in the SYMPLICITY HTN-3 trial. *Eur Heart J* 2014 [PMID: 25400162 DOI: 10.1093/eurheartj/ehu441]

14 **Oliveira NL**, Ribeiro F, Alves AJ, Campos L, Oliveira J. The effects of exercise training on arterial stiffness in coronary artery disease patients: a state-of-the-art review. *Clin Physiol Funct Imaging* 2014; **34**: 254-262 [PMID: 24138480 DOI: 10.1111/cpf.12093]

15 **Oliveira NL**, Ribeiro F, Alves AJ, Teixeira M, Miranda F, Oliveira J. Heart rate variability in myocardial infarction patients: effects of exercise training. *Rev Port Cardiol* 2013; **32**: 687-700 [PMID: 23993292 DOI: 10.1016/j.repc.2013.02.010]

16 **Ribeiro F**, Alves AJ, Duarte JA, Oliveira J. Is exercise training an effective therapy targeting endothelial dysfunction and vascular wall inflammation? *Int J Cardiol* 2010; **141**: 214-221 [PMID: 19896741 DOI: 10.1016/j.ijcard.2009.09.548]

17 **Ribeiro F**, Alves AJ, Teixeira M, Miranda F, Azevedo C, Duarte JA, Oliveira J. Exercise training enhances autonomic function after acute myocardial infarction: a randomized controlled study. *Rev Port Cardiol* 2012; **31**: 135-141 [PMID: 22226329]

18 **Ribeiro F**, Alves AJ, Teixeira M, Miranda F, Azevedo C, Duarte JA, Oliveira J. Exercise training increases interleukin-10 after an acute myocardial infarction: a randomised clinical trial. *Int J Sports Med* 2012; **33**: 192-198 [PMID: 22187388 DOI: 10.1055/s-0031-1297959]

19 **Alves AJ**, Ribeiro F, Goldhammer E, Rivlin Y, Rosenschein U, Viana JL, Duarte JA, Sagiv M, Oliveira J. Exercise training improves diastolic function in heart failure patients. *Med Sci Sports Exerc* 2012; **44**: 776-785 [PMID: 22005747 DOI: 10.1249/MSS.0b013e31823cd16a]

20 **Heran BS**, Chen JM, Ebrahim S, Moxham T, Oldridge N, Rees K, Thompson DR, Taylor RS. Exercise-based cardiac rehabilitation for coronary heart disease. *Cochrane Database Syst Rev* 2011; **(7)**: CD001800 [PMID: 21735386 DOI: 10.1002/14651858.CD001800.pub2]

21 **Gielen S**, Schuler G, Hambrecht R. Exercise training in coronary artery disease and coronary vasomotion. *Circulation* 2001; **103**: E1-E6 [PMID: 11136704 DOI: 10.1161/01.CIR.103.1.e1]

22 **Linke A**, Erbs S, Hambrecht R. Exercise and the coronary circulation-alterations and adaptations in coronary artery disease. *Prog Cardiovasc Dis* 2006; **48**: 270-284 [PMID: 16517248 DOI: 10.1016/j.pcad.2005.10.001]

23 **Oldridge N**. Exercise-based cardiac rehabilitation in patients with coronary heart disease: meta-analysis outcomes revisited. *Future Cardiol* 2012; **8**: 729-751 [PMID: 23013125 DOI: 10.2217/fca.12.34]

24 **Lavie CJ**, Milani RV. Cardiac rehabilitation and exercise training in secondary coronary heart disease prevention. *Prog Cardiovasc Dis* 2011; **53**: 397-403 [PMID: 21545925 DOI: 10.1016/j.pcad.2011.02.008]

25 **Ribeiro F**, Ribeiro IP, Alves AJ, do Céu Monteiro M, Oliveira NL, Oliveira J, Amado F, Remião F, Duarte JA. Effects of exercise training on endothelial progenitor cells in cardiovascular disease: a systematic review. *Am J Phys Med Rehabil* 2013; **92**: 1020-1030 [PMID: 23811616 DOI: 10.1097/PHM.0b013e31829b4c4f]

26 **Ash GI**, Eicher JD, Pescatello LS. The promises and challenges of the use of genomics in the prescription of exercise for hypertension: the 2013 update. *Curr Hypertens Rev* 2013; **9**: 130-147 [PMID: 23971695 DOI: 10.2174/15734021113099990010]

27 **Neves A**, Alves AJ, Ribeiro F, Gomes JL, Oliveira J. The effect of cardiac rehabilitation with relaxation therapy on psychological, hemodynamic, and hospital admission outcome variables. *J Cardiopulm Rehabil Prev* 2009; **29**: 304-309 [PMID: 19935143 DOI: 10.1097/HCR.0b013e3181b4ca27]

28 **Pescatello LS**, Franklin BA, Fagard R, Farquhar WB, Kelley GA, Ray CA. American College of Sports Medicine position stand. Exercise and hypertension. *Med Sci Sports Exerc* 2004; **36**: 533-553 [PMID: 15076798]

29 **Vongpatanasin W**. Resistant hypertension: a review of diagnosis and management. *JAMA* 2014; **311**: 2216-2224 [PMID: 24893089 DOI: 10.1001/jama.2014.5180]

30 **Dimeo F**, Pagonas N, Seibert F, Arndt R, Zidek W, Westhoff TH. Aerobic exercise reduces blood pressure in resistant hypertension. *Hypertension* 2012; **60**: 653-658 [PMID: 22802220 DOI: 10.1161/HYPERTENSIONAHA.112.197780]

31 **Guimaraes GV**, de Barros Cruz LG, Fernandes-Silva MM, Dorea EL, Bocchi EA. Heated water-based exercise training reduces 24-hour ambulatory blood pressure levels in resistant hypertensive patients: a randomized controlled trial (HEx trial). *Int J Cardiol* 2014; **172**: 434-441 [PMID: 24491874 DOI: 10.1016/j.ijcard.2014.01.100]

32 **Guimarães GV**, Cruz LG, Tavares AC, Dorea EL, Fernandes-Silva MM, Bocchi EA. Effects of short-term heated water-based exercise training on systemic blood pressure in patients with resistant hypertension: a pilot study. *Blood Press Monit* 2013; **18**: 342-345 [PMID: 24192849 DOI: 10.1097/MBP.0000000000000000]

33 **Salles GF**, Cardoso CR, Muxfeldt ES. Prognostic influence of office and ambulatory blood pressures in resistant hypertension. *Arch Intern Med* 2008; **168**: 2340-2346 [PMID: 19029499 DOI: 10.1001/archinte.168.21.2340]

34 **Thompson PD**, Buchner D, Pina IL, Balady GJ, Williams MA, Marcus BH, Berra K, Blair SN, Costa F, Franklin B, Fletcher GF, Gordon NF, Pate RR, Rodriguez BL, Yancey AK, Wenger NK. Exercise and physical activity in the prevention and treatment of atherosclerotic cardiovascular disease: a statement from the Council on Clinical Cardiology (Subcommittee on Exercise, Rehabilitation, and Prevention) and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity). *Circulation* 2003; **107**: 3109-3116 [PMID: 12821592 DOI: 10.1161/01.CIR.0000075572.40158.77]

35 **Walter R**, Gordon NF, Pescatello LS. ACSM’s guidelines for exercise testing and prescription. 8th ed. Baltimore: American College of Sports Medicine, 2010

36 **Pescatello LS**. Exercise and hypertension: recent advances in exercise prescription. *Curr Hypertens Rep* 2005; **7**: 281-286 [PMID: 16061047 DOI: 10.1007/s11906-005-0026-z]

**P-Reviewer:** Chawla M, He JY, Rossi GP **S-Editor:** Ji FF **L-Editor: E-Editor:**