Acute and Chronic Effects of Exercise in Health

Sedentary postmenopausal women not undergoing hormone replacement therapy can have their blood pressure lowered by performing resistance training: a systematic review and meta-analysis of randomized controlled trials

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Abstract - Aim: This systematic review and meta-analysis aimed at examining the literature regarding the effects of resistance training (RT) on blood pressure (BP) in postmenopausal women. **Methods:** The Pubmed, Scopus, Embase, and BVS databases were accessed by two independent reviewers between July 2020, and June 2021 to search for studies that investigated the effects of RT on BP. The eligibility criteria were determined by the PICOT strategy. P: postmenopausal women, I: RT, in which training variables are presented, C: presence of a control group that does not receive any type of intervention, O: BP measured in both groups, at least before and after the intervention, T: randomized controlled trial. For the studies included in the meta-analysis, we calculated the effects sizes based on the net changes in the systolic (SBP) and diastolic (DBP) BP for a random effect model with a confidence interval of 95% and a statistical significance of p < 0.05. **Results:** The RT group presented a significantly lower SBP (-7.25 mmHg [95% CI: -14.04, -0.45], p = 0.04), while DBP was not statistically significantly different compared to controlled conditions (-2.54 mmHg [95% CI: -5.52, 0.44], p = 0.09). **Conclusions:** Physically-inactive postmenopausal women who did not take hormone replacement but performed RT exercise had a lower BP value when compared to the control group.

Keywords: exercise, systolic pressure, aging, cardiovascular system.

Introduction

Postmenopausal period is characterized by a higher association with cardiovascular risks¹. Women tend to go through menopause in their early 50s. Although it can usually occur between the ages of 35 to 59^2 . And yet, with increasing life expectancy, women spend ~ 40% of their lives in the postmenopausal phase³. Changes in the levels of circulating estrogens and androgens⁴, associated with a decrease in the level of physical activity due to age⁵, may indicate a possible mechanism through which the woman's blood pressure (BP) is higher after menopause. In fact, the aging process is linked to higher BP in women⁶.

One of the main steps in the treatment of hypertension is based on lifestyle interventions⁷. In this context,

exercise training is a non-pharmacological intervention widely recommended for BP control and reduction in hypertensive individuals⁸. The mechanisms responsible for BP regulation due to exercise are several, including hormonal, neural and hemodynamic responses. Some explanations described in the literature mention an attenuation in sympathetic activity, secretion of vasoactive substances, improvement in insulin sensitivity, increase in vascular diameter, neoangiogenesis⁹ and a decrease in inflammation and adiposity¹⁰.

Slightly reductions in BP (i.g., 10 mmHg) have already demonstrated a 20% decrease in the major cardiovascular disease events¹¹. Endurance exercise is already recommended and established for BP control¹². On the other hand, some authors present controversial data about impacts of resistance training (RT) alone on cardiovascular health^{13,14}. At the beginning of the 21st century, two meta-analyses with the general population showed a beneficial effect on BP with resistance training^{15,16}. These data cannot be extrapolated to postmenopausal women. However, they raise questions about its impact on postmenopausal population once resistance exercise can contribute to an increase in bone mineral density and improve muscle strength¹⁷.

Thus, since the guidelines of hypertension treatment recommend exercise training for BP control¹⁸ and postmenopausal women tend to have BP problems. Knowing that, the effects of RT on postmenopausal women is still not well established. It is important to investigate the potential benefits of RT to postmenopausal-period hemodynamics, thus protecting from future cardiovascular related problems. So, the aim of this study was to systematically review and conduct a meta-analysis of the literature regarding the effect of RT on BP of postmenopausal women in randomized controlled trials.

Methods

This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyzes (PRISMA) protocol.

Eligibility criteria

The eligibility criteria were determined by the PICOT strategy. P: clinically-healthy postmenopausal women (except for hypertension), who were not undergoing hormone replacement therapy or dietetic interventions, I: RT on the ground, whose training variables were presented in the article (frequency, volume, intensity and total training period), with at least a four-week training, C: presence of a control group that had not received any type of intervention, O: BP measured in both groups at least before and after the intervention, T: randomized controlled trial. We considered that participants were under no hormone replacement therapy or dietetic interventions when the authors did not mention so. No language and date filters were used in the literature search.

The databases used were: Embase, Scopus, Pubmed and Biblioteca Virtual de Saúde (BVS), the grey literature was not included. The first search in the databases was performed in July 2020 and updated in June 2021.

Search strategy

In the Scopus and BVS databases, the "title / abstract / keywords" filter was used, while in the Embase and Pubmed platforms, no filters were used.

The search strategy used in the databases was: (("Resistance Training" OR "Strength Training" OR "Weight Lifting Exercise Program") AND (Postmenopause OR "Postmenopausal Period" OR post-menopause OR "Post Menopause")) AND ("Randomized Controlled Trial").

Selection process and data collection process

According to the established criteria, the studies selection was conducted by two independent authors (GFAB and RFO). The search results were downloaded and then uploaded to the Mendeley software, which was used for the studies selection.

First, the duplicates were excluded. Afterwards, the studies were examined by title and abstract. The selected articles were read in full, and those meeting the inclusion criteria were included in the review. References from previous meta-analyses and systematic reviews in the topic were also analyzed.

Data items

The data extracted from the included articles were: authors, sample, withdrawal, age, quality assessment, frequency, volume, repetition range and intensity, time under tension (concentric and eccentric movement), rest between sets, exercises, total time of training intervention, body mass index (BMI), systolic (SBP) and diastolic (DBP) BP, moment and method of measurement of BP. BMI, SBP and DBP data were extracted in two moments: before and after the intervention. Since some articles presented measurements after the training intervention and after some functional tests, the only two BP measurements used in the analysis were the resting BP of the pre- and post-intervention training.

Quality assessment

The instrument Physiotherapy Evidence Database (PEDro) was used to assess the quality of each article included in the review. The tool assesses the quality based on 11 criteria. Each fully-satisfied criterion received 1 point (with exception of the 1st criterion), totalizing 10 points at maximum. Scores between 6 and 10 were considered a high-quality study; between 4 and 5, moderate quality; and between 0 and 3, low quality. The quality assessment was conducted by the same authors who led the article selection. The inter-agreement value of both evaluators was used as the final quality assessment value. A third author (IAS) was used to resolve disagreements between the two authors.

Effect magnitude and synthesis methods

All analyses were conducted in the software Review Manager 5.3. The mean age and BMI (pre- and post-intervention training) were calculated by the sum of all mean values divided by the total number of studies. If the study did not report the BMI indexes, but reported the height and weight of the participants, the BMI was calculated by dividing the participants' mean weight by the mean height squared. The effect sizes for the studies included in the meta-analysis were net changes in the SBP and DBP, as described in previous meta-analysis¹⁵. The change in the standard deviation was calculated from the pooled standard deviation of change scores in both groups by using a

correlation value of 0.5 and the formula described in the Cochrane Handbook for Systematic Reviews of Interventions,

$$SD_{\rm E,change} = \sqrt{SD_{\rm E,baseline}^2 + SD_{\rm E,final}^2 - (2XCorrXSD_{\rm E,baseline}XSD_{\rm E,final})}$$
(1)

For the overall effect size of training on SBP or DBP, each trial was weighted by the inverse of the total variance for SBP or DBP changes. The confidence interval used was 95%, for a random effect model.

For the heterogeneity analyses, the I² test was used. The $p \le 0.05$ was considered for statistical significance, I² > 50% was considered indicative of high heterogeneity, and publication bias was accessed visually from funnel plots; more asymmetry from the vertical axis indicates publication bias.

Results

Study selection

A total of 713 articles was identified in the searched databases: 173 in Pubmed, 204 in Scopus, 131 in BVS and 205 in Embase. Another 4 articles were added based on the reference lists in other articles selected for reference analysis. The selection process is depicted in the PRISMA flow diagram (Figure 1). After excluding duplicates, 332

articles remained for the exclusion of title and abstract, of which 319 were excluded for not meeting the eligibility criteria. The remaining 17 articles were read in full and their eligibility was assessed.

Three studies were excluded due to the use of hormone replacement therapy in the sample; five studies were excluded because the control group received any kind of intervention; one study was excluded due to the lack of access; one study was excluded because there was no BP measurement; one study was excluded because did not report any type of randomization; and one study was excluded because the training intervention lasted less than 4 weeks. The remaining five articles^{13,19-22} were included in this meta-analysis.

Study characteristics

A total of 175 physically inactive women participated in the studies. Four studies^{13,20-22} had losses in their samples, both by exclusion and/or by "dropout", which totalized 27 women. Therefore, 148 women completed the



Figure 1 - PRISMA flow diagram.

studies. The average age of the women in the training group was 56.06 and in the control group 55.33. The mean pre- and post- intervention BMI were 26.93 and 26.38 kg/m² for the training groups and 26.52 and 25.78 kg/m² for the control groups, respectively. One study did not provide data of post-intervention BMI²². The intervention period ranged from 8 to 16 weeks. Based on the PEDro method, two studies were classified as high quality^{20,22} and three studies as moderate quality^{13,19,21}. The information on the author, sample, withdrawal, age, total time of intervention, pre- and post-intervention BMI, and the quality assessment of each article, are presented in Table 1.

The RT frequency varied from 2 to 3 times a week; the number of sets ranged from 2 to 4; the number of repetitions ranged from 6 to 15. The rest time between sets ranged from 30 to 120 s. Only one study did not report the rest time performed²². The time under tension ranged from 2 to 5 s of concentric movement and 2 to 3 s of eccentric movement, three studies did not report the time under tension^{13,19,22}. Four studies performed exercises for body's main muscle groups^{13,19-21} and one study performed exercises only for the lower limbs and abdomen²². The RT variables for each article are presented in Table 2.

Table 1 - Study characteristics.

Author	Sample	Withdrawal	Age (y/o)	Total time of train- ing intervention	BMI pre (kg/m ²)	BMI post (kg/m ²)	Quality Assessment
Conceição ¹⁹	20 Physically inactive	No With- drawals	$TG = 53.40 \pm 3.95;$ $CG = 53.0 \pm 5.7$	16 Weeks	$TG = 26.22 \pm 3.26;$ CG = 25.26 \pm 1.81	$TG = 26.00 \pm 3.11;$ CG = 25.53 \pm 2.11	5 (Moderate)
Elliott ¹³	25 Physically inactive	10 With- drawals	$TG = 58 \pm 4;$ $CG = 53 \pm 3$	8 Weeks	$TG = 26.89 \pm 5.94;$ $CG = 23.97 \pm 2.58$	$TG = 26.63 \pm 5.92;$ CG = 24.13 \pm 2.53	5 (Moderate)
Gelecek ²⁰	51 Physically inactive	6 With- drawals	$TG = 54.33 \pm 5.3;$ CG = 51.80 ± 3.65	12 Weeks	$TG = 28.00 \pm 3.7;$ CG = 27.17 ± 3.50	$TG = 27.70 \pm$ 3.62*; CG = 27.28 \pm 3.53	9 (High)
Gurjão ²¹	21 Physically inactive	4 With- drawals	$TG = 61.7 \pm 4.8;$ $CG = 65.0 \pm 5.1$	8 Weeks	$TG = 25.0 \pm 4.2;$ $CG = 26.1 \pm 5.4$	$TG = 25.2 \pm 4.4;$ $CG = 26.2 \pm 5.5$	5 (Moderate)
Reis ²²	58 Physically inactive	7 With- drawals	$TG = 52.91 \pm 4.02;$ $CG = 53.86 \pm 5.11$	12 Weeks	TG = 28,57; CG = 30,12	No Data	6 (High)

BMI: Body mass index; CG: Control group; kg: kilograms; m: meters TG: Training group; y/o: years old * Statistical significance reported by the author between pre- and post-intervention.

Table 2 - Intervention characteristics.

Author	Frequency (Training)	Volume (Series)	Repetitions range and intensity	Time under ten- sion (Concentric: Eccentric)	Rest between sets (s)	Exercises
Conceição ¹⁹	3 Training ses- sions per week	3 Sets	10 RM (8 first weeks); 8 RM (8 final weeks)	No data	60 (8 first weeks); 90 (8 first weeks)	Leg press, leg extension, leg curl, bench press, lat pulldown, lateral raise, triceps pushdown, arm curl, and basic abdominal crunch
Elliott ¹³	3 Training ses- sions per week (8 first weeks)	3 Sets	8 Repetitions (80% 10 RM)	No data	120	Leg press, bench press, knee extension, knee flexion, and lat pull-down
Gelecek ²⁰	3 Training ses- sions per week	2 Sets	8-12 Repetitions (60% 1 RM)	3-5:2	30 - 60	10 muscle-including upper extremities (biceps and triceps), lower extremities (thigh and calf), and trunk (chest, back, abdominal)
Gurjão ²¹	3 Training ses- sions per week	3 Sets	10-12 RM	2:3	90	Fly (pectoralis); leg press (quadriceps femoris and gluteus); front pulldown (latis- simus dorsi); triceps pulley (triceps bra- chii); leg press calf raise (gastrocnemius); dumbbell screw curl (biceps brachii) and abdominal bench (rectus abdominis)
Reis ²²	2 Training ses- sions per week	2;3;4 sets	10-15 (60% 1 RM); 8- 10 (70-80% 1 RM); 6 Repetitions (85% 1 RM)	No data	No data	Exercises for quadriceps, hamstring, calf, tibialis anterior, gluteus maximus, and abdominal muscles

RM: Repetition maximum.

The mean pre and post intervention of SBP were 126.68 and 118.77 mmHg for the training group, and 120.45 and 121.45 mmHg for the control group. The mean pre- and post- intervention of DBP were 79.77 and 75.74 mmHg for the training group, and 76.36 and 76.24 mmHg for the control group. Two studies^{20,21} observed a significant decrease in SBP at the end of the training intervention. One study²¹ found significant differences in participants' DBP. All studies measured the BP of their samples at the beginning and the end of the training intervention; however, in some studies^{13,20,22} these were not the only moments of measurement. Three studies used the standard method to measure pressure (sphygmomanometer and stethoscope)¹⁹⁻²¹, one study¹³ used the automatic sphygmomanometer, model 8111; Critikon Dynamap 8100T, and one study²² did not report the measurement method. The BP values, the moment and method of measurement, are presented in Table 3.

Table 3 - Blood pressure of studies included.

Synthesis of the results

The meta-analysis indicated a significant decrease in SBP for the training group (-7.25 mmHg [95% CI: -14.04, -0.45], p = 0.04), and the heterogeneity observed was high ($I^2 = 52\%$; p = 0.08). For DBP, there was no significant reduction for the training group (-2.54 mmHg [95% CI: -5.52, 0.44], p = 0.09) and the heterogeneity observed was low ($I^2 = 9\%$; p = 0.35). Figure 2 shows the forest plot of the meta-analysis for the SBP and DBP. The funnel plots indicate a slight publication bias for SBP and no bias for DBP. They are presented in Figure 3.

Discussion

The main aim of this study was to systematically review the literature and conduct a meta-analysis regarding the effect of RT on postmenopausal women's BP in randomized controlled trials. We observed a statistically significant reduction in SBP for postmenopausal women

Author	BP (mmHg)	Groups		Values	Moment of measurement of BP	Method of measurement of BP	
			Baseline	After training intervention			
Conceição ¹⁹	SBP	TG	138.40 ± 15.37	130.80 ± 16.06	At baseline and after 16	Mercury sphygmomanometer and	
		CG	111.80 ± 7.30	113.30 ± 8.40	weeks	stethoscope	
	DBP	TG	89.80 ± 7.27	88.20 ± 5.45			
		CG	78.40 ± 6.50	78.00 ± 7.70			
			Baseline	After training intervention	At baseline, after 8 weeks of	Automatic sphygmomanometer (model 8111; Dynamap 8100T; Cri- tikon, Orange Park, Florida, USA)	
Elliott ¹³	SBP	TG	133 (20)	118 (15)	training and after 8 weeks of detraining		
		CG	133 (20)	132 (15)	0		
	DBP	TG	72 (11)	66 (10)			
		CG	75 (10)	78 (11)			
			Baseline	After training intervention			
Gelecek ²⁰	SBP	TG	111.87 ± 11.11	$108.12 \pm 8.68^{*}$	At baseline, before and after the 6MWT; after 12 weeks	Standard mercury sphygmoman-	
		CG	112.61 ± 14.88	113.09 ± 13.27		ometer	
	DBP	TG	70.00 ± 9.44	70.20 ± 8.64			
		CG	72.38 ± 9.03	73.80 ± 7.56			
			Baseline	After training intervention	At baseline and after 8	Mercury column sphygmoman-	
Gurjão ²¹	SBP	TG	130.6 ± 5.0	$117.4 \pm 9.2^{*}$	weeks of training	ometer by Sankey and a stethoscope by Rappaport - Premium	
		CG	120.6 ± 16.7	126.0 ± 13.3			
	DBP	TG	86.2 ± 8.5	$75.2 \pm 8.5^{*}$			
		CG	74.6 ± 7.5	71.4 ± 6.6			
			Baseline	After training intervention			
Reis ²²	Rest SBP	TG	119.56±12.96	119.56 ± 14.60	At baseline, before and after	No data	
		CG	124.28 ± 10.98	122.86 ± 18.16	the 6MWT; After 12 weeks		
	Rest DBP	TG	80.87±7.92	79.13±7.92			
		CG	81.42 <u>+</u> 9.49	80±12.4			

BP: Blood pressure; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; TG: Training group; CG: Control Group; RM: Repetition maximum *Statistical significance reported by the authors; 6MWT: 6 min walking test.



Figure 2 - Forest plot of the comparison of the effects of RT or CG on SBP and DBP.



Figure 3 - Funnel plot of the comparison of the effects of RT or CG on SBP and DBP.

who performed RT compared with the control group (-7.25 mmHg [95% CI: -14.04, -0.45], p = 0.04), and a positive non-significant effect of the RT in DBP in the training group (-2.54 mmHg [95% CI: -5.52, 0.44], p = 0.09).

Those data are in accordance with previous metaanalyses evaluating the effect of RT on BP in adults (-6.0 [-10.4, -1.6] SBP; -4.7 [-8.1, -1.4] DBP)¹⁶, (-1.8 mm Hg [-3.7, -0.011] SBP; (-3.2 mm Hg [-4.5, -2.0] DBP)¹⁵. Additionally, a recent meta-analysis²³ found a significant reduction in SBP of postmenopausal and menopausal women with RT (-3.13 [-5.14, -1.11]), but the authors did not set the use of hormonal replacement and diet intervention as an inclusion criterion. These factors may have masked the real effect on BP, since these two practices had already showed a BP reduction in postmenopausal women^{24,14}, our meta-analysis found a larger effect on SBP.

Training volume

Some RT variables, in part, can explain the benefits presented in this review. Brito et al.²⁵ demonstrated that RT performed with higher volume (three sets) induced greater post-exercise hypotension than RT with lower volume (one set). The authors attributed these results to major vasodilator responses to high volume RT. In four^{13,18,20,21} of the five articles included in this meta-analysis participants performed three sets in their training programs, which indicates a good response to this training volume amount as far as BP is concerned.

Training intensity

The intensity does not appear to impact the BP response. Two meta-analyses evaluated the effect of RT on BP with no difference between training intensity on BP response^{15,16}. Additionally, Ribeiro et al.²⁶ showed no difference between low or moderate RT intensity in older women. This seems to occur with other types of training, such as aerobic training, particularly at moderate and high intensity ^{15,27}. A brief revision highlights very well the non-agreement regarding the best intensity exercise to control the BP, ranging from 30 to 70% of the maximal exercise performance. However, the author emphasizes that BP is more affected by age, gender or body mass index²⁷.

This is especially important once the present article deals specifically with older women. Older individuals appear to have higher BP levels than younger ones²⁸; as a result, they show more pronounced changes in BP levels when training, since people with high BP can induce greater reductions in it performing exercise²⁷. In addition, even if training intensity have no differential effect for BP, high-intensity training can decrease their weight²⁹ and therefore, reduce BP levels³⁰.

The majority of the articles included in this review applied moderate-intensity training, in normotensive or pre-hypertensive postmenopausal women. However, even in studies with non-hypertensive women performing moderate-intensity exercises, RT appears to have a good impact on decreasing the SBP as shown in some studies included in this review^{19,20}. Perhaps, if the studies included in this review have been with high-intensity RT in hypertensive women, there could have been a decrease in DBP³¹.

Training frequency

The RT frequency performed in the studies included in this review were between 2 and 3 times per week. A meta-analysis of Halbert et al.³² argued that increase the frequency to more than 3 times per week did not show any further significant benefits to BP levels with aerobic exercise. Additionally, the *American College of Sports Medicine* (ASCM) encourages older adults to participate in 2-3 RT sessions peer week³³, however, performing more RT sessions peer week can possibly maintain the BP at optimal levels, as the hypotension after the exercise can last for some hours³⁴. Furthermore, shorter or longer RT programs appear to have no effect on BP levels¹⁶.

Blood pressure measurement and mechanism

Most of the articles used the standard mercury sphygmomanometer and stethoscope method to measure the BP. However, one study¹³ used an automatic device to measure the BP. Some mercury sphygmomanometers can present the observer bias. This can be eliminated by the use of automatic monitors. However, not all automatic monitors have a valid measure. Studies must use well-trained subjects to measure the BP when using mercury sphygmomanometer and stethoscope or comment the validity of the automatic monitors used³⁵.

The mechanisms responsible for the BP reduction remain unclear in the literature¹⁵. Furthermore, it may be that isolated and/or combined physiological pathways may interfere with this reduction. There are some indications of improved availability of nitric oxide, increased prostaglandins decreased endothelin 1 and changes in vessel resistance^{36,37}, in addition to a reduction in cardiac output due to a decrease in systolic volume and microvascular changes^{38,39} that may explain this BP decrease.

Therefore, this meta-analysis demonstrates a potential benefit of RT in postmenopausal women's BP control, especially considering that this group tends to have higher

Study strengths, limitations and future directions

compared to younger women.

BP values (due to hormonal changes³ and aging process⁴⁰)

The research limitations were: 1) The authors found only few studies that met the inclusion criteria, which prevented the authors from conducting subgroups analyses, 2) the authors did not include the grey literature in the review process, 3) the high heterogeneity in the training variables and, 4) the lack of BP measurements by the 24-hour ambulatory BP monitoring (ABPM) method, which would have led to more reliable results. Since a major indication for BP control is endurance exercises, this article provides another possible intervention that can be encouraged for prevention and treatment of hypertension in postmenopausal women. Future studies associating RT to BP may contribute to the lack of knowledge in the area. Also, authors should focus on more homogeneous training variables and count on more reliable methods to measure BP for long periods, such as ABPM.

Conclusions

This systematic review and meta-analysis showed that physically-inactive postmenopausal women who had not taken hormone replacement and performed RT had a lower BP value when compared to the control group. These results are particularly observed in SBP, but DBP also presented a positive change (i.g., lower values). Additionally, volume plays an important role in the BP control in RT. The use of higher intensities in training, and frequencies higher than 3 times a week does not necessarily lead to a more pronounced BP reduction. More research in this area controlling for confounding variables, such as diet and hormone replacement, should be conducted to reinforce these results.

Registration and Protocol

This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyzes (PRISMA) protocol, and recorded on the PROSPERO platform (https://www.crd.york.ac.uk/pros pero/) under the registration number #CRD42019110356.

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