

## Systematic Review

# Aerobic exercises and ambulatory blood pressure monitoring in resistant hypertension population: a systematic review

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## ABSTRACT

Resistant hypertension associated with increased risk of morbidity and mortality. Here our aim was to systematically evaluate and sum up evidence on the impact of aerobic exercise on ambulatory blood pressure (ABP) in resistant hypertension population. This systematic review followed PRISMA guidelines, and we explored PubMed, Cochrane Library, SCOPUS, and Science Direct for apropos studies. This systematic review included randomized controlled trials and crossover trials focusing on resistant hypertension population undergoing aerobic exercise compared to routine management. The primary outcome was blood pressure (BP) control, which was measured using 24-hour ambulatory blood pressure monitoring (ABPM). Secondary outcome were office blood pressure and adverse effects. Three authors independently selected studies, extracted data, and assessed the risk of bias. The conflicts were resolved by consensus. This systematic review summarizes findings of six randomized controlled trials with 187 participants assessing the impact of exercise on ambulatory blood pressure in resistant hypertension population. Aerobic training was associated with significant reduction of 5-10 mmHg in 24- hour ambulatory BP. Similar pattern was observed in day time BP, while night time BP were less pronounced. Office BP showed inconsistent changes. Exercise interventions, particularly supervised programs and light-to-moderate intensity activities, also improved cardiorespiratory fitness and physical performance. In studies exercise intervention were usually safe and well tolerated without serious adverse events. Moderate evidence supports the addition of aerobic exercise to usual care in resistant hypertension population. However small number of participants and heterogeneity in methodology and outcome limiting the strength of findings.

**Keywords:** Aerobic exercise, Resistant hypertension, Ambulatory blood pressure, Monitoring

## INTRODUCTION

Hypertension is one of the most common non-communicable diseases all over the world. Although different treatment options are available, many individuals with high BP face difficulties in achieving long-term control of their blood pressure.<sup>1</sup> According to the latest European Society of Hypertension (ESH) guidelines, true

resistant hypertension (RH) is characterized by persistently elevated systolic blood pressure (SBP  $\geq 140$  mmHg) or diastolic blood pressure (DBP  $\geq 90$  mmHg), even after implementing appropriate lifestyle modifications and administering a combination of three antihypertensive agent at optimal or maximally tolerated doses. This combination should include a renin-angiotensin-aldosterone system (RAAS) inhibitors (either an ACE inhibitor or an ARB), a calcium channel blocker, and a

thiazide or thiazide-like diuretic.<sup>2</sup> Determining the exact prevalence of RH is complex, as it is influenced by several factors such as the clinical setting, the type of antihypertensive regimen, patient adherence, the method of blood pressure measurement, and the definition of target blood pressure.<sup>3</sup>

Based on the aforementioned criteria, RH is estimated to affect approximately 5% of patients diagnosed with hypertension.<sup>2</sup> ABPM is BP measurement at regular intervals over 24 hours period, while a person goes about their daily activities and sleep. It is typically measured by using portable device worn on the body of person. ABPM provide more accurate information of blood pressure pattern compared to clinic BP measurement, helping to detect conditions like nocturnal hypertension or white coat hypertension.

The regards study found that uncontrolled apparent resistant hypertension was linked to a higher risk of coronary heart disease, but not stroke and had no effect on overall mortality.<sup>4</sup> A recent consensus statement by Ebinger et al reinforced that resistant hypertensive patients had higher risk of poor clinical outcome of nearly all parameters, including death.<sup>5</sup> This indicate that requirement of more medication to treat hypertension in mid- life associated with poor clinical outcome.

Aerobic exercise is a nonpharmacological treatment approach that is recommended by both American and European hypertension guidelines for lowering blood pressure. Existing research on the impact of exercise interventions in resistant hypertension population has shown encouraging outcomes, as highlighted by several non-systematic reviews.<sup>6</sup>

However, to our knowledge, while previous attempts have been made to systematically compile and analyse the available evidence on the effect of acute or regular exercise on blood pressure measurement in the population with RH, the studies included did not consist entirely of population with RH. Therefore, this study aimed to summarize the current findings on how acute and regular exercise influences ABP in individuals with resistant hypertension. This systematic review aimed to understand the influence of aerobic exercise on ABP in resistant hypertension population.

## METHODS

This current systematic review was carried out following the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guideline.<sup>7</sup> The study was registered in PROSPERO (CRD420250652569) and registration link is <https://www.crd.york.ac.uk/PROSPERO/view/CRD420250652569>.

Electronic searches were conducted across multiple databases, including PubMed, SCOPUS, Cochrane

Central Register of Controlled Trials (CENTRAL), and ScienceDirect from inception to 22 February 2025. The focus of the review was on person diagnosed with resistant hypertension, defined as uncontrolled blood pressure despite treatment with three or more antihypertensive medication at optimal doses- including a diuretic or blood pressure controlled with four or more antihypertensive medications. The intervention examined was aerobic exercise, with comparisons made against standard care or a non-exercise control group. The primary outcome was blood pressure control, which was assessed through 24-hour ABPM.

Another outcome was daytime and night-time blood pressure control. The objective of this review is to evaluate the effectiveness of aerobic exercise in enhancing blood pressure control in resistant hypertension population compared to those managed without structured exercise programs. The search phrases are outlined in Table 1.

Three writers (Mahadev Meena, Yasmee Khan, Amit Agrawal) individually screened the studies as per inclusion criteria. Eligible studies included those involving resistant hypertension population who were adherent to treatment and physically capable of performing exercise. Only Randomized Controlled Trials (RCT) and crossover trials that assessed aerobic exercise and used ABPM were included. According to American College of Sport Medicine, aerobic exercise defined as continuous, rhythmic physical activity of large muscle group and using aerobic metabolism for energy production. Cycling, walking, jogging, swimming, dancing are some examples of aerobic exercise. The effectiveness of aerobic exercise measured by peak oxygen consumption.

Titles, abstracts, and full texts of identified studies were reviewed, with disagreements were resolved by consensus. Corresponding authors were contacted when additional data were required. Studies that were quasi-randomized, observational (both prospective and retrospective) case series, case reports, letters, editorials, comments, animal studies and non-English publications were excluded.

Data extraction was conducted using a pre-formatted data collection sheet, capturing details included study authors, study years, country, inclusion/exclusion criteria, sample size, age, gender, type of aerobic intervention, reported outcomes, and any adverse events. The risk of bias was assessed using the Cochrane Risk of Bias (RoB) tool within Review Manager (RevMan) version 5.4.

## RESULTS

During the search, we found a total of 251 articles; 183 articles were screened after the removal of duplication, and based on title, abstract, and keywords, 150 records were excluded (Figure 1). Thirty-three full texts were further reviewed, and 27 articles (Supplementary material Table S1) were excluded with reasons. We included six articles in qualitative synthesis, and Table 2 shows study characteristics.<sup>8-13</sup>

### Results of individual studies

In a randomized controlled trial conducted by Dimeo et al, a total of 50 persons with resistant hypertension were enrolled and randomly assigned to either an exercise group (n=24) or a control group (n=26).<sup>8</sup> Baseline characteristics between the groups were largely similar, with the exception of age ( $p=0.02$ ) as mentioned in Table 2. Inclusion, exclusion criteria are mentioned in Table 2. Participants underwent assessments before and after the intervention period, which included 24-hour ABPM, vascular compliance, cardiac index, and physical performance. Physical capacity was evaluated using a treadmill stress test based on a modified Bruce protocol under continuous ECG surveillance. The exercise regimen involved treadmill-based interval training, performed three times a week over 8 to 12 weeks, with a target blood lactate concentration of  $2.0 \pm 0.5$  mmol/l. The mean follow-up duration was  $9.8 \pm 2.0$  weeks in the exercise group and  $10.2 \pm 2.0$  weeks in the control group.

One patient from the control group and two from the exercise group dropped out during the study. Four patients did not complete the follow-up treadmill test; for these cases, their baseline treadmill test data were excluded from analysis. The study found significant reduction in daytime systolic ABP ( $-5.9 \pm 11.6$  mmHg,  $p=0.03$ ) and diastolic ABP ( $3.3 \pm 6.5$  mmHg,  $p=0.03$ ). Although reductions were also observed in night-time systolic, diastolic ABP, and office SBP and DBP, but these were not statistical significance. However, 24-hour ABP demonstrated significant reductions: systolic by  $5.4 \pm 12.2$  mmHg ( $p=0.03$ ) and diastolic by  $2.8 \pm 5.9$  mmHg ( $p=0.01$ ). Importantly, the exercise protocol was well-tolerated across participants.

In a separate randomized controlled trial by Lopes et al 365 persons were initially screened, out of which 305 were excluded.<sup>9</sup> The remaining 60 participants with confirmed resistant hypertension were randomly divided into an exercise group (n=30) and a control group receiving usual care (n=30). Baseline characteristics and inclusion, exclusion criteria mentioned in table 2. Patients in exercise group participated in supervised aerobic training program of 12 weeks with three sessions per week. Each session consists of 10 minutes warm-up, 40 minutes of aerobic exercise like cycling or walking followed by 10 minutes cooldown.

They started with 20 minutes of exercise at lower intensity (50% of VO<sub>2</sub> maximum) and gradually increase either intensity or duration each week, aiming for 40 minutes at 70% of their maximum if tolerated. The control group was on standard medical care and life style advice without structured exercise intervention. Baseline demographic and clinical variables were well-matched between groups.

Of the 60 patients, seven did not complete the study (four from the exercise group and three from the control group), leaving 53 participants in the final analysis. Among them,

24 (45%) were female. The mean age was  $60.1 \pm 8.7$  years. In exercise group 14 (54%) were males and 12 (46%) were females. In control group 15 (56%) were males and 12 (44%) were females. The reduction in 24-hour systolic ABP was significantly greater in the exercise group compared to the control group, with a between-group difference of  $-7.1$  mmHg (95% CI:  $-12.8$  to  $-1.4$ ;  $p=0.02$ ). The study found significant reductions in 24-hour systolic ABP ( $-6.2 \pm 12.2$  mmHg,  $p=0.02$ ) and diastolic ABP ( $-5.1 \pm 7.9$  mmHg,  $p=0.001$ ). Daytime systolic ABP decreased by  $-8.4$  mmHg ( $p=0.006$ ) and diastolic ABP by  $-5.7$  mmHg ( $p=0.001$ ). Office systolic BP was significantly lowered by  $-10.0$  mmHg ( $p=0.01$ ). The study concluded that the observed results were specific to aerobic exercise. Participants in the exercise group showed a 14% improvement in cardiorespiratory fitness and significant reductions in heart rates compared to the control group, highlighting the cardiovascular benefits of aerobic training. However, there were no significant differences in night-time ABP or in office diastolic BP between the two groups.

In a randomized clinical rehearsal trial conducted by Pinheiro et al 30 participants with resistant hypertension were initially enrolled but only 15 participants, 8 in experimental group and 7 in control group were included in final analysis.<sup>10</sup> The study was conducted over an 8-week intervention period. Baseline characteristics and inclusion exclusion criteria mentioned in table 2. The intervention in the experimental arm was delivered in four structured blocks: a preparatory block (Block 1), two neuromuscular blocks (Blocks 2 and 3), and a cardiometabolic training block (Block 4).

Among the 15 participants, 13 (86.7%) were elderly females, with a mean age of  $70.1 \pm 6.3$  years. There were statistically significant differences in height and weight between the groups, although these differences did not affect the interpretation of the outcomes. The intervention led to significant reduction in 24-hour ambulatory BP, with systolic BP decreasing by 8.2 mmHg and diastolic BP by 6.4 mmHg. Daytime and night-time BP also improved significantly in the intervention group compared to control. Additionally, participants in the experimental group showed marked improvements in physical fitness parameters including strength, mobility, and aerobic endurance. However, the small sample size and baseline differences between groups limit the generalizability of results.

In a randomized crossover trial conducted by Pires et al a total of 20 participants 10 with resistant hypertension and 10 with non-resistant hypertension were enrolled to evaluate the acute effects of different exercise modalities on 24-hour ABP.<sup>11</sup> Age was 40-80 years. The gender distribution was 6 females and 4 males in the RH group, and 5 females and 5 males in the non-RH group. The baseline clinical characteristics were similar across all groups. Inclusion and exclusion criteria mentioned in Table 2. Participants were randomized in a 1:1:1:1 ratio to

undergo four distinct exercise sessions: aerobic exercise, resistance training, combined exercise, and a control session, with a minimum washout period of 96 hours between sessions. The treadmill was used for aerobic exercise for 45 minutes at 50-60 % of the maximum heart rate. Resistance training included four sets of 6 exercises with 12 repetitions. It consists of squatting, bench press, seated knee raise, seated row, dorsiflexion and plantar flexion, shoulder abduction. It was performed as twelve repetitions with moderate intensity. Combined exercise was performed as a combination of aerobic and resistance exercise.

In the resistant hypertension group, all exercise modalities significantly reduced systolic and diastolic ambulatory BP compared to baseline. Aerobic exercise lowered SBP by up to 18.0 mmHg and DBP by 14.1 mmHg. Resistance training showed SBP reduction up to 19.5 mmHg and DBP up to 11.3 mmHg. The combined exercise produced most prolonged post-exercise hypotension with SBP reduction up to 19.5 mmHg and DBP up to 14. mmHg. These changes were statistically significant with 24- hours systolic BP reduction in the combined group ( $p=0.001$ ).

No significant changes in either systolic or diastolic BP were observed in the control group, underscoring the potential of structured exercise especially combined modalities in managing resistant hypertension through prolonged blood pressure-lowering effects.

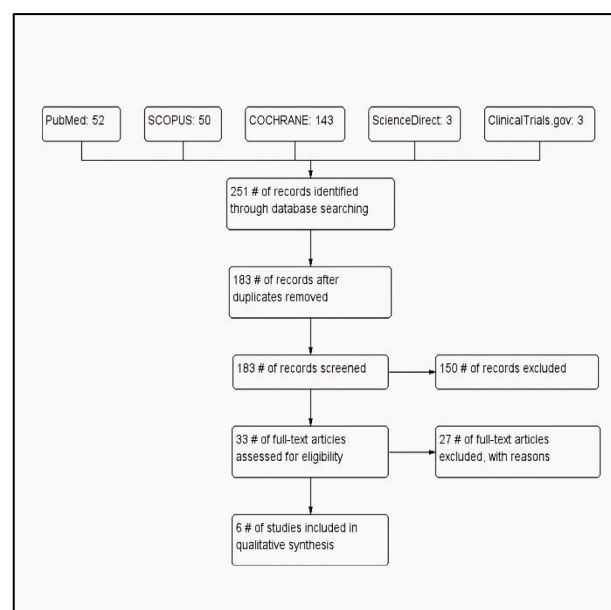
In a single-blind, randomized, controlled crossover trial conducted by Saco-Ledo et al, ten participants with resistant hypertension were evaluated across three different visits, each separated by a week.<sup>12</sup> Participants were randomized to one of three sessions: moderate-intensity continuous exercise (MICE), high-intensity interval exercise (HIIE), or a control session. Moderate-intensity continuous exercise consists of 3-minute warm-up at 2-3 metabolic equivalent of task (METs) followed by 40-50 minutes of walking at 3-4 METs and a calm-down phase at 2-3 METs. High-intensity interval exercise included a 3-minute warm-up followed by six to eight intervals of three minutes duration at METs 6-7 interspersed with 1.5 minutes recovery at 3 METs, followed by a calm-down of 3 minutes at 2-3 METs.

The total duration was 30-40 minutes. The average participant age was  $57\pm7$  years, and 20% were female. The study found no significant changes in 24-hour SBP ( $p=0.996$ ) or DBP ( $p=0.978$ ), including daytime and night-time BP. However, both HIIE and MICE significantly reduced clinic SBP immediately post-exercise ( $p<0.001$ ) and 90 minutes post-exercise (HIIE:  $p=0.001$ , MICE:  $p=0.041$ ). Clinic DBP also decreased significantly (HIIE:  $p=0.003$ , MICE:  $p=0.025$ ). The study concluded that both exercise interventions effectively reduced blood pressure in resistant hypertension population. The study was conducted over a 24-hour period. Limitations included a small sample size.

Similarly, in a randomized, controlled, three-intervention crossover trial by Santos et al 20 participants with resistant hypertension were enrolled and randomized to three different sessions: control, light-intensity exercise (light), and moderate-intensity exercise (moderate).<sup>13</sup> In the light and moderate groups, patients performed 45 minutes of cycling at 50% and 75% of their maximum heart rate (HRmax), respectively, while in the control group, they remained seated for 45 minutes. The mean age was  $53.8\pm5.5$  years, and 60% of participants were female. Baseline BP was similar across all sessions. Compared to control, the SBP reductions during the first 5 hours post-exercise were significant in both light ( $-7.7$  mmHg) and moderate ( $-9.4$  mmHg) groups ( $p<0.005$  for both).

Daytime SBP was significantly reduced only in the light group compared to control ( $-3.8$  mmHg,  $p=0.011$ ), but not in the moderate group. A similar trend was observed for night-time SBP. Over a 19-hour period, light showed a borderline significant reduction in SBP compared to control ( $-4.7$  mmHg,  $p=0.053$ ), while moderate did not differ from control. For DBP, the light group showed significantly lower values during the first 5 hours post-intervention ( $-5.7$  mmHg,  $p=0.03$ ) and also during awake time when compared to both control ( $-4.0$  mmHg,  $p=0.006$ ) and moderate ( $-3.1$  mmHg,  $p=0.02$ ).

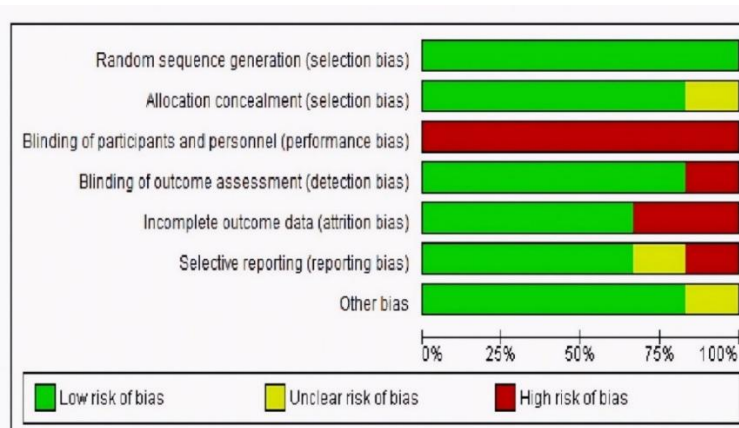
Night-time DBP was also significantly reduced in the light group compared to control ( $-6.1$  mmHg,  $p=0.001$ ), and over the 19-hour period, DBP remained significantly lower compared to control ( $-4.8$  mmHg,  $p<0.001$ ). No such differences were observed in the moderate group compared to control for DBP across any time period. The study concluded that both light and moderate exercise sessions effectively reduced blood pressure in patients with resistant hypertension.



**Figure 1: PRISMA.**



**Figure 2: Risk of bias summary.**



**Figure 3: Risk of bias graph.**

### ***Risk of bias and quality assessment***

All included studies had a high risk of performance bias as no blinding of participants was done (Figures 2 and 3). This lack of blinding can influence the results and is a significant limitation of the studies reviewed. Study of Dimeo et al had a moderate risk of selection bias because allocation concealment was unclear. Another study by Lopes et al had a high risk of attrition bias due to dropout and reporting bias. Specifically, serum markers were not reported in this study, which limits the completeness of the data and the ability to draw robust conclusions. Pires et al detection biases were also high. Detection bias can occur when the methods used to assess outcomes differ between groups, leading to inaccurate results. Ledo et al study

reporting biases were unclear as they reported primary outcomes but did not report biochemistry-related secondary outcomes. This selective reporting can skew the interpretation of the study's effectiveness. Publication bias was not assessed because the number of studies included in the review was less than 10. Publication bias can occur when studies with statistically significant results are more likely to be published than those with non-significant results, potentially skewing the overall findings of the review. Given the high risk of various biases in the included studies, the overall quality of evidence is limited. This highlights the need for future studies with better methodological rigor, including blinding, clear allocation concealment, and comprehensive reporting of all relevant outcomes.



**Table 1: Details of search strategy.**

Database	Search details
COCHRANE	143 Trials matching hypertension resistant ambulatory blood pressure exercise in Title Abstract Keyword
PubMed	((("hypertense"(All Fields) OR "hypertension"(MeSH Terms) OR "hypertension"(All Fields) OR "hypertension s"(All Fields) OR "hypertensions"(All Fields) OR "hypertensive"(All Fields) OR "hypertensive s"(All Fields) OR "hypertensives"(All Fields)) AND ("resist"(All Fields) OR "resistance"(All Fields) OR "resistances"(All Fields) OR "resistant"(All Fields) OR "resistants"(All Fields) OR "resisted"(All Fields) OR "resistence"(All Fields) OR "resistences"(All Fields) OR "resistent"(All Fields) OR "resistibility"(All Fields) OR "resisting"(All Fields) OR "resistive"(All Fields) OR "resistively"(All Fields) OR "resistivities"(All Fields) OR "resistivity"(All Fields) OR "resists"(All Fields)) AND ("ambulatories"(All Fields) OR "ambulatory"(All Fields)) AND ("blood pressure"(MeSH Terms) OR ("blood"(All Fields) AND "pressure"(All Fields)) OR "blood pressure"(All Fields) OR "blood pressure determination"(MeSH Terms) OR ("blood"(All Fields) AND "pressure"(All Fields) AND "determination"(All Fields)) OR "blood pressure determination"(All Fields) OR "arterial pressure"(MeSH Terms) OR ("arterial"(All Fields) AND "pressure"(All Fields)) OR "arterial pressure"(All Fields)) AND ("exercise"(MeSH Terms) OR "exercise"(All Fields) OR "exercises"(All Fields) OR "exercise therapy"(MeSH Terms) OR ("exercise"(All Fields) AND "therapy"(All Fields)) OR "exercise therapy"(All Fields) OR "exercising"(All Fields) OR "exercise s"(All Fields) OR "exercised"(All Fields) OR "exerciser"(All Fields) OR "exercisers"(All Fields))) AND ((randomized controlled trial (Filter)) AND (1000/1/1:2025/1/21(pdat)))
ScienceDirect	Titles, abstracts, keywords: hypertension resistant ambulatory blood pressure exercise
SCOPUS	TITLE-ABS-KEY (hypertension AND resistant AND ambulatory AND blood AND pressure AND exercise)
ClinicalTrials.gov	hypertension resistant ambulatory blood pressure exercise

**Table 2: Characteristics of included studies.**

Study Auth ors (Year )	Coun try	Study Type	Partici pants	Sample size	Age (years)	Sex	Race/Et hnicity	Inclusion criteria	Exclusion criteria	Co- morbidities	Interven tion Groups	Outcome s	Follow up	Remar ks
Dime o, 2012 <sup>8</sup>	Germ any	Rando mized control trial	50	46	Exercise group- 62.8+- 8.1 (42-78) years Control group 67.9+- 6.2 (43-76) years	Both sex Female 54.2 % in exercise group 61.5% in control group.	White exercise group 10 (38.5), control 26 (100)	Patients with resistant hypertension.	Regular physical exercise within four weeks of inclusion. Symptomatic peripheral arterial disease, More than stage I aortic regurgitation or stenosis, Hypertrophic obstructive cardiomyopathy, NYHA-II or more CHF, Symptomatic and uncontrolled arrhythmia, Ischemic changes in exercise ECG and hypertensive changes,	Diabetes mellitus, Hyperlipida emia, coronary artery disease	Treadmil l interval training of 8-12 weeks	1) 24- hours SBP - 5.4 mmHg and DBP - 2.8 mmHg. Similar trend in daytime SBP and DBP.	Follow -ups were conduc ted within 5 days of the last training session.	Young er particip ant in exercis e group. No signific ant change in night BP and Office BP.

Study Authors (Year)	Country	Study Type	Participants	Sample size	Age (years)	Sex	Race/Ethnicity	Inclusion criteria	Exclusion criteria	Co-morbidities	Intervention Groups	Outcomes	Follow up	Remarks
									Office SBP 180 mmHg, change in medication in last 4 weeks before inclusion and during study and follow-up					
Lopes, 2021 <sup>9</sup>	Portugal	A 2-center, prospective, single-blinded randomized clinical trial with parallel two arms.	60	53	40-75 years	Both sex.	White	Resistant Hypertensive Patients. (SBP <sup>3</sup> 130 mmHg on three antihypertensive including diuretic or BP controlled with four antihypertensive).  Patients' adherence to medication	Patients with target organ damage (LVH, Renal disease). Secondary hypertension. Heart failure. An acute cardiovascular event within the last year. Peripheral arterial disease. COPD Limitation to exercise. Involvement in regular exercise. Change in antihypertensive medication within 3 months before inclusion.	Hyperlipidaemia, Diabetes, Obesity, Myocardial infarction, Stroke, Transient ischemic attack.	Aerobic cycling or walking for 12 weeks.	24 hours SBP and DBP $\sim$ 6.2 mmHg and 5.1 mmHg in the exercise group. Similar trend was observed in Daytime ambulatory SBP and DBP. Office SBP $\sim$ 10 mmHg. Cardiorespiratory fitness was significantly improved.	12 weeks during exercise.	Results are specific to aerobic exercise. There was no significant change in night-time ambulatory BP and office diastolic BP.
Pinheiro, 2024 <sup>10</sup>	Brazil	Randomized and controlled clinical rehearsal.	15 Resistant hypertensive older adults	Total-15, the control group-7 the experimental	60 years or more	Both, 2 Males and 13 females.	White and black	Patients with resistant hypertension. Age <sup>3</sup> 60 years. The patient has had a sedentary lifestyle for the last six months and is using three or more	Advanced heart failure. Dementia. Alzheimer disease. Parkinsonian disease. Physically disabled. Morbid obesity (BMI <sup>3</sup> 40 kg/m <sup>2</sup> ) Malignancy,	Not mentioned	Multi block neuromuscular and cardiometabolic exercise	24 hours SAP $\sim$ 9 mmHg and DAP $\sim$ 6 mmHg. Similar pattern found in	8 week during intervention.	Small sample size limit subgroup analysis. High

Continued.

Study Authors (Year)	Country	Study Type	Participants	Sample size	Age (years)	Sex	Race/Ethnicity	Inclusion criteria	Exclusion criteria	Co-morbidities	Intervention Groups	Outcomes	Follow up	Remarks
				group-8				antihypertensive medications. Patient adherent to treatment.	Acute CAD. A disease that limits exercise. Those did not complete 90 sessions of exercise. The patient did not undergo ABPM.		over 8 weeks.	daytime SAP and DAP, Night-time SAP and DAP. In all p <0.01. The physical fitness was also improved.		and weight significantly different between groups. Elderly female-dominated.
Pires, 2020 <sup>1</sup>	Brazil	Randomized controlled crossover trial.	20	20	40-80 years	In RH 6 female and 4 male. In non RH 5 female and 5 male.	White and black	Patients with non-resistant and resistant hypertension. Age 40 to 80 years and able to perform exercise.	Patients with significant ECG changes. Dropped out patients. Patients who changed antihypertensive drugs in the last 6 months before being included in the study. Patients with cerebrovascular and cardiac disease. Heart failure and renal failure. Patients with secondary hypertension and pseudo-resistant hypertension. Patients who were involved in regular physical training over 6 months before inclusion. Smokers and patients with hormone replacement therapy.	Diabetes mellitus	The treadmill was used for AER exercise for 45 minutes at 50-60 % of the maximum heart rate. RES included four sets of 6 exercises. It was performed as twelve repetitions with moderate intensity. COM exercise was performed as a	In AER group with RHT 24 hours SBP and DBP – 15.4-18 mmHg and 11.6 - 14.1 mmHg respectively. In all exercise groups change in SBP and DBP was observed in RHT patients.	24 hours	Acute effect and short term multiple arms. Small sample size and uncontrolled obesity as eligibility criteria were limitation.



Study Authors (Year)	Country	Study Type	Participants	Sample size	Age (years)	Sex	Race/Ethnicity	Inclusion criteria	Exclusion criteria	Co-morbidities	Intervention Groups	Outcomes	Follow up	Remarks
											combination of AER and RES exercise.			
Gonzalo Saco-Ledo, 2024 <sup>1 2</sup>	Spain	Single-blind Crossover Randomized control design	10 patients with RH	10	57 ± 7 years	Both sex	White	Individuals with resistant hypertension. Individuals who were taking similar treatment for at least one year.	Myocardial infarction within the last year. Psychiatric illness and other diseases that interfere with the study.	Diabetes, history of CKD, History of stroke, History of MI,	Moderate-intensity continuous exercise and High-intensity interval exercise treadmill walking	No significant change was observed in 24-hour SBP(p-0.996), DBP (-0.978), and daytime and nighttime BP.	24 hours	This study assessed the short-duration effect of acute HIIE in patients with RH. The small sample size was a limitation of this study.
Santos, 2016 <sup>1 3</sup>	Brazil	Randomized, control, three intervention crossover study.	20	20	53.8 (5.5) years	Both sex	Black 6 (30.0) White 14 (70.0)	Patients with resistant hypertension (25). Patients were adherent to medication. only	If BP < 130/80 mmHg with three antihypertensive drugs without exercise during ABPM.	Type II diabetes 4 (20.0) Dyslipidemia 7 (35.0)	LIGHT and MODERATE session of cycling.	24- hours SBP -7.7 mmHg in LIGHT session and 9.4 mmHg in MODERATE session. 24 hours DBP -5.7 mmHg.	3-31 days	Sample size limits further analysis. BP benefit in LIGHT only, short term.

**Table 3: Characteristics of excluded studies.**

Study author (in year)	Reason of exclusion
Alves et al, 2018	Conference paper
Bertani et al, 2018	Patient populations did not have resistant hypertension
Blumenthal et al, 2000	Patient populations did not have resistant hypertension
Boeno et al, 2020	Patient populations did not have resistant hypertension and were a convenience sample.
Brito et al, 2019	Patient populations did not have resistant hypertension
Caminiti et al, 2021	Patient populations did not have resistant hypertension
Cordeiro et al, 2018	The patient population did not have resistant hypertension, and the outcome was the presence of post-exercise hypotension
Cornelissen et al, 2009	Patient populations did not have resistant hypertension
Dassanayake et al, 2022	Systematic review
de Oliveira Campos et al, 2021	Patient populations did not have resistant hypertension
dos Santos et al, 2013	Not in English
Ferrari et al, 2017	Patient populations did not have resistant hypertension
Ferrari et al, 2021	Study protocol
Halbert et al, 1997	Systematic review
Imazu et al, 2017	Patient populations did not have resistant hypertension
Junior et al, 2020	Patient populations did not have resistant hypertension
Lee et al, 2021	Study protocol
Maggio et al, 2011	The patient population was children who did not have resistant hypertension.
Molmen-Hansen et al, 2012	Patient populations did not have resistant hypertension
Nascimento et al, 2017	Study protocol
Pedralli et al, 2016	Study protocol
Pedralli et al, 2020	The patient population did not have resistant hypertension
Ramis et al, 2022	The patient population did not have resistant hypertension
Rinder et al, 2004	The patient population did not have resistant hypertension
Saco-Ledo et al, 2022	Systematic review
Thompson et al, 2019	Study protocol
Waib et al, 2011	Study protocol
Ash et al, 2017	Patient populations did not have resistant hypertension

## DISCUSSION

Resistant hypertension affects approximately 12–15% of individuals with hypertension and is associated with a significantly increased risk of serious cardiovascular events, including stroke and acute coronary syndrome.<sup>14</sup> Regular aerobic exercise is well established as an effective strategy for lowering blood pressure in general hypertensive population. However, its specific effects in people with RH remain unclear.<sup>14</sup> ABPM offers a comprehensive evaluation of blood pressure over a 24-hour period, capturing fluctuations that may be missed during clinic visits. This makes ABPM particularly valuable for assessing the true impact of interventions such as aerobic exercise in resistant hypertension population.<sup>15</sup> Research has shown that engaging in moderate-intensity aerobic exercise can effectively lower both systolic blood pressure and diastolic blood pressure in patients with essential hypertension, particularly at the pre-hypertension or stage 1 level.<sup>16</sup> However, the utility of ABPM in patients with RH remains a topic of ongoing debate.<sup>17,18</sup>

Several studies have demonstrated that both acute and regular aerobic exercise can beneficially influence office blood pressure and ambulatory blood pressure in resistant hypertension population. However, the findings of individual studies remain inconsistent. In this context, a systematic review and meta-analysis is warranted to synthesize the existing evidence and provide more definitive insights into the efficacy of aerobic exercise in managing blood pressure among resistant hypertension population.<sup>15</sup>

Interestingly, a large-scale study involving over 40,000 people with resistant hypertension demonstrated that achieving blood pressure control was associated with a reduced incidence of stroke and coronary artery disease, although the reduction was less pronounced compared to people without RH.<sup>19</sup> Findings from the Chronic Renal Insufficiency Cohort (CRIC) study further highlighted that, while overall mortality rates did not significantly differ, patients with refractory hypertension experienced a substantially higher risk of cardiovascular and renal complications than those with RH.<sup>20</sup> ABPM, which records blood pressure over a 24-hour period, provides valuable insights into pressure variability. It enables the identification of circadian patterns such as nocturnal dipping and morning surges, along with fluctuations related to environmental and emotional factors.<sup>21</sup> In this systematic review, we aimed to explore and analyze the positive impact of exercise interventions on blood pressure control in resistant hypertension population. Across the randomized controlled trials included, a consistent pattern of BP reduction was observed following various forms of exercise, reinforcing the potential role of physical activity as an adjunctive therapeutic strategy for RH management. Patients with elevated resting and/or exercise BP typically exhibit lower cardiorespiratory fitness, which is associated with an increased risk of cardiovascular mortality compared to those with normal BP levels.

Moreover, even modest reductions in BP have been linked to a lower risk of cardiovascular events, particularly among hypertensive patients.<sup>22,23</sup> To date, only six studies have evaluated the short-term effects of aerobic exercise on ABPM in people with RH.<sup>8–13</sup> Authors reviewed data from a total of 495 patients across these six RCTs to assess the impact of aerobic exercise on RH in adults. The studies by Dimeo et al and Lopes et al underscore the significant impact of structured aerobic exercise on blood pressure control in resistant hypertension population. Dimeo et al reported significant reductions in daytime systolic and diastolic ambulatory BP following 8–12 weeks of treadmill exercise. Similarly, Lopes et al reinforced these findings by demonstrating decreases in 24-hour systolic BP, daytime systolic and diastolic BP, as well as office systolic BP. Additionally, participants showed a significant improvement in cardiorespiratory fitness (14%). Collectively, these studies highlight the dual benefit of aerobic exercise in reducing BP and enhancing cardiovascular health in people with RH.

The trials by Pires et al and Saco-ledo et al suggest that combined and light -intensity exercise modalities are effective in reducing blood pressure in participants with resistant hypertension, with combined producing prolonged post-exercise hypotension and light demonstrating BP reductions over both short- and longer-term periods. In contrast, the study by Santos et al did not observe significant reductions in ABP following moderate-intensity exercise.<sup>13</sup> Pinheiro et al however reported significant reductions in 24-hour systolic and diastolic ambulatory BP after a structured multi-block exercise intervention.<sup>10</sup> These reductions were sustained from the 5th to the 22nd hour post-exercise. Additionally, daytime and night time BP also decreased significantly in intervention group. On the other hand, Saco-Ledo et al, further demonstrated that both high-intensity interval exercise and moderate-intensity continuous exercise significantly reduced clinic systolic and diastolic BP immediately and 90 minutes post-exercise; however, no significant changes were observed in 24-hour ambulatory BP.<sup>12</sup>

The trials by Pinheiro et al and Santos et al highlighted the acute effects of different exercise modalities on BP in participants with resistant RH. Pires et al demonstrated significant reductions in both systolic and diastolic ambulatory BP following aerobic, resistance, and combined exercise sessions, with combined eliciting the most prolonged post-exercise hypotension. Similarly, Santos et al found that light-intensity exercise significantly lowered ambulatory systolic and diastolic BP compared to control, both within the initial 5 hours and over a 19-hour period, whereas moderate-intensity exercise had a more limited effect. Collectively, these findings suggest that structured and varied exercise protocols particularly combine and light can effectively reduce BP in people with RH. Consistent with findings, a recent meta-analysis reported that a single session of aerobic exercise can

induce temporary reductions in ABP among people with hypertension.<sup>24</sup>

This systematic review of six randomized controlled trials on aerobic exercise's effects on ABP in resistant hypertension population has limitations. The studies showed significant heterogeneity in design, intervention protocols, outcome reporting formats, and measurement time points. Variations in resistant hypertension definition, exercise interventions, follow-up duration, and reporting of ABP outcomes were also present. The small number of eligible studies limited the statistical power and appropriateness of quantitative synthesis. These limitations precluded the performance of a comprehensive meta-analysis.

In this review studies had high risk of bias at least in one methodological domain resulting limitation in internal validity of some findings. In review inconsistency was observed between ABP and office BP responses to exercise. This may be due potential white coat hypertension, measurement variability, and methodological differences. Despite this, the review provides a valuable qualitative synthesis of current evidence and highlights consistent trends in aerobic exercises efficacy in improving ABP control in resistant hypertensive patients.

Furthermore, additional research is warranted to determine whether the benefits of aerobic exercise demonstrated in the general hypertensive population are similarly applicable to resistant hypertension population. Importantly, future studies should also explore whether structured exercise interventions could reduce the number and/or dosage of antihypertensive medications required in this population. This question holds clinical significance, as reduced medication burden has been associated with lower mortality in people with RH.

## CONCLUSION

This systematic review demonstrates the positive impact of exercise interventions on BP control resistant hypertension population. Across the randomized controlled trials analyzed, aerobic, resistance, combined, and light-intensity exercises consistently demonstrated reductions in systolic and diastolic ambulatory BP, reinforcing the role of aerobic activity as an effective adjunctive strategy for RH management. While both aerobic and combined exercises showed sustained post-exercise hypotension, light-intensity exercise provided notable short- and long-term overall BP benefits. Although meta-analysis was not possible due to data limitations, the collective evidence suggests the importance of structured, varied exercise regimens in improving BP control and cardiovascular risks in person with RH. Although findings of this review offer preliminary perception, but they are based on limited number of patients. This limited the robustness of the conclusions. These results should be

interpreted cautiously, and further large studies are required to validate the findings.

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