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BIBLIOGRAPHIC REVIEW

Effectiveness of physical exercise in the control of arterial hypertension in adults: systematic review and meta-analysis

Efectividad del ejercicio físico en el control de la hipertensión arterial en adultos: revisión sistemática y metaanálisis

Efetividade do exercício físico no controle da hipertensão arterial em adultos: revisão sistemática e metanálise

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ABSTRACT

Introduction: high blood pressure (HBP) is the most common cardiovascular disease in adults. There are studies that suggest that physical exercise can be implemented as therapy and prophylaxis of HBP, given its hypotensive effects. **Objective:** to evaluate the effect systematically of physical exercise on blood pressure levels in patients with high blood pressure, pooling evidence from randomized clinical trials. **Method:** A systematic review was performed in accordance with the PRISMA statement. We searched electronic databases for randomized controlled trials between 2004 and 2024. Risk of Bias 2 was used to assess risk of bias. Subsequently, a meta-analysis was carried out using the inverse variance method for random models to evaluate the outcome variable through the difference in means. **Results:** 11 trials were included in which aerobic exercise predominated as the main intervention exercise. The grouped analysis showed a difference between the blood pressure (BP) figures recorded before and after exercise: systolic BP ($\chi 2=22.82$; $p<0.01$), and diastolic BP ($\chi 2=8.69$; $p<0.01$), there was statistical evidence of heterogeneity among the included studies. The standard mean difference of systolic BP (-0.34) had a significant negative value 95 % CI (-0.63, -0.04); on the other hand, the difference in diastolic BP, although negative (-0.15), was not significant, 95 % CI (-0.81, 0.09). **Conclusions:** aerobic exercise was the most used modality to explore the hypotensive effect. In general, the pooled statistical evidence from the studies analyzed suggests that performing physical exercise had positive repercussions on the control and reduction of blood pressure in hypertensive adults.

Keywords: arterial hypertension; adult; physical exercise; review; meta-analysis

RESUMEN

Introducción: la hipertensión arterial es la enfermedad cardiovascular más común en los adultos. Existen estudios que sugieren que el ejercicio físico puede ser implementado como terapia y profilaxis de la hipertensión arterial por sus efectos hipotensores. **Objetivo:** evaluar sistemáticamente el efecto del ejercicio físico en las cifras de tensión arterial en pacientes con hipertensión arterial aunando evidencia de ensayos clínicos aleatorizados. **Método:** revisión sistemática de acuerdo con la declaración PRISMA 2020, para ello fueron buscados ensayos controlados aleatorizados de entre 2004 y 2024 en bases de datos electrónicas. Se utilizó *Risk of Bias 2* para evaluar riesgo de sesgo. Una vez cumplimentada esta etapa, se realizó un metaanálisis a través del método del inverso de la varianza, mediante modelos aleatorios para evaluar la variable resultado mediante la diferencia de medias. **Resultados:** se incluyeron once ensayos en los que predominó el aeróbico como principal ejercicio de intervención. El análisis agrupado mostró diferencia entre las cifras de tensión arterial (TA) registradas antes y después del ejercicio: TA sistólica (χ^2==22,82; p<0,01), y TA diastólica (χ^2=8,69; p<0,01), hubo evidencia estadística de heterogeneidad entre los estudios incluidos. La diferencia media estándar de las TA sistólicas (-0,34) tuvo un valor negativo significativo IC95 % (-0,63; -0,04); en contraparte, la diferencia de TA diastólicas, aunque negativa (-0,15) no fue significativa IC95 % (-0,81; 0,09).**Conclusiones:** el ejercicio aeróbico fue la modalidad más utilizada para explorar el efecto hipotensor. La evidencia estadística agrupada de los estudios analizados, sugiere que realizar ejercicio físico tuvo repercusiones positivas en el control y disminución de la tensión arterial en adultos hipertensos.

Palabras clave: hipertensión arterial; adulto; ejercicio físico; revisión; metaanálisis

RESUMO

Introdução: a hipertensão arterial é a doença cardiovascular mais comum em adultos. Existem estudos que sugerem que o exercício físico pode ser implementado como terapia e profilaxia da hipertensão devido aos seus efeitos hipotensores. **Objetivo:** avaliar sistematicamente o efeito do exercício físico nos níveis pressóricos em pacientes com hipertensão arterial, reunindo evidências de ensaios clínicos randomizados. **Método:** revisão sistemática de acordo com a declaração PRISMA, para a qual foram pesquisados ensaios clínicos randomizados entre 2004 e 2024 em bases de dados eletrônicas. Risco de viés 2 foi utilizado para avaliar o risco de viés. Concluída essa etapa, foi realizada metanálise pelo método de variância inversa, utilizando modelos aleatórios para avaliar a variável desfecho por meio da diferença de médias. **Resultados:** foram incluídos onze ensaios nos quais predominou o exercício aeróbico como principal exercício de intervenção. A análise agrupada mostrou diferença entre os valores de pressão arterial (PA) registrados antes e após o exercício: PA sistólica (χ2=22,82; p<0,01) e PA diastólica (χ2=8,69; p<0,01), houve evidência estatística de heterogeneidade entre os estudos incluídos. A diferença média padrão da PA sistólica (-0,34) teve um valor negativo significativo IC 95% (-0,63, -0,04); Em contraste, a diferença na PA diastólica, embora negativa (-0,15), não foi significativa, IC 95% (-0,81, 0,09).**Conclusões:** o exercício aeróbico foi a modalidade mais utilizada para explorar o efeito hipotensor. As evidências estatísticas agrupadas dos estudos analisados sugerem que a prática de exercício físico teve repercussões positivas no controle e na redução da pressão arterial em adultos hipertensos.

Palavras-chave: hipertensão arterial; adulto; exercício físico; revisão; meta-análise

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INTRODUCTION

With the rapid development of the social economy and the improvement of living standards, the prevalence of cardiovascular diseases is on rise.(1) In recent decades, population aging has accelerated in both the total number and the proportion of people turning 60 years of age and older. It is estimated that the proportion of the adult population will triple in the first half of the 21st century. The increase in life expectancy and population aging portend a relative increase in the diseases associated with this stage of life.(2)

Hypertension (HTN) is the most common cardiovascular disease in adults.(3) The World Health Organization (WHO) estimated that 25% of adults worldwide have hypertension, accounting for 4.5% of the global burden of disease.(1) The prevalence of HTN is increasing in the United States.

The prevalence of HTN increases with age, affects more than 60 % of people over 60 years of age and is one of the leading causes of cardiovascular disease and premature death worldwide.(4) It carries high health care costs, approximately a global estimate of 370 billion dollars per year.(3,5)

In Spain, the prevalence of this chronic disease was 18.48% in the general population in 2022; men were less represented than women (18.10% vs. 18.84%). In the Autonomous Community of the Basque Country, the figures are 16.14 % for the general population, but it is more prevalent in men than women (16.22 % vs. 16.06 %).(6)

The 2017 American College of Cardiology/American Heart Association proposed an office blood pressure (BP) of more than 130/80 mmHg as a new threshold for the diagnosis of hypertension, while the European Society of Cardiology/European Society of Hypertension in 2018 maintained an office BP threshold of 140/90 mmHg to define hypertension, similar to previous guidelines.(4,7)

Monitoring of BP at regular intervals during normal daily life [i.e., ambulatory blood pressure (ABR)] has become the strongest predictor of cardiovascular disease and mortality, with threshold criteria for defining hypertension based on 24-hour ABR set at 125/75 and 130/80 mm/Hg in the United States and European guidelines, respectively.(8)

Increased 24-hour and overnight BP is associated with a high risk of cardiovascular disease, even if office BP is apparently well controlled (i.e., <130/80 mm/Hg), leading to a prevalent and, especially, unfavorable hypertension phenotype, so-called *"uncontrolled masked hypertension."*(9)

Antihypertensive therapies

The American Heart Association defines "alternative approaches" as non-pharmacological treatments capable of lowering blood pressure, classifying them into three main categories: behavioral therapies, non-invasive procedures and exercise-based regimens. In recent decades several studies have revealed that exercise and fitness produce beneficial effects in the general population, reducing the relative risk of death by 20%-35%, particularly death caused by cardiovascular disease.(10)

It has been suggested that personalized exercise not only reduces office BP in people with hypertension, but is also as effective as most antihypertensive medications in reducing office BP.[11] Aerobic exercise also alleviates associated lipid abnormalities, which may also contribute to the prevention of cardiovascular disease.[1]

Hypertensives are encouraged to engage in regular aerobic exercise, such as walking, jogging, or swimming for 30 to 45 minutes, three to four times per week. However, it is unknown whether patients with advanced age still experience any cardiovascular benefit from sport.[12]

Despite its obvious benefits, exercise can trigger sudden cardiac death, particularly in previously sedentary adults or those with advanced pathology, so it is of fundamental importance to perform adequate cardiovascular risk stratification to prescribe the appropriate "dose" of physical activity that maximizes the benefits and minimizes the risks.[13]

Regarding advanced atherosclerotic wall changes, comorbidities and limited physical fitness, skepticism has been expressed as to whether elderly patients can achieve relevant changes in AT and vasoregulatory function. Data from randomized studies on the cardiovascular effects of physical exercise in hypertensives aged 60 years and older are sparse and inconsistent.[14,15]

Aging is associated with increased vascular stiffening and reduced Windkessel function of large arteries (buffering of outward blood flow by making it more constant and uniform). Thus, systolic blood pressure gradually increases throughout life, while diastolic blood pressure begins to decrease again in the sixth decade of life, leading to an increase in pulse pressure and so-called "isolated systolic hypertension" (ISH).[16]

The magnitude of pulse pressure can be considered as a mark of vascular aging. ISH is the most common form of hypertension in the elderly. The Framingham study revealed that 57.4% of men and 65.1% of women aged 65 years have ISH. Hypertension in the elderly, once considered an irrelevant part of the aging process, is now considered an important predictor of adverse cardiovascular outcomes.[17]

Lowering systolic BP in the elderly has been shown to markedly reduce mortality and cardiovascular morbidity. Although it is now generally recognized that systolic BP is a very valuable measure of cardiovascular outcome, systolic BP is notoriously difficult to normalize in older patients.[18] Exercise reduces BP during exertion. Several not fully described mechanisms are responsible for the AT-lowering effect of exercise.[19]

Aerobic exercises are able to create a physiological adaptation in the efficiency of the aerobic energy system. They also enhance the functional capacity of the person even in conditions of disease progression. Other advantages of regular exercise in this group of patients include increased power, improved body posture, decreased fatigue, improved mood, increased self-confidence and sense of well-being.[3]

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Effects of physical exercise on blood pressure regulation

Improvement of endothelial function

An important mechanism by which physical exercise may affect BP is the regulation of endothelial function. Vascular homeostasis depends on the activity of the endothelium, fundamental regulator of vasomotor responses that modulates vessel resistance.(10). Nitric oxide (NO) is a key mediator of endothelial function, a vasoactive molecule that normally dilates blood vessels and prevents platelet activation, thereby lowering blood pressure and protecting the cardiovascular system.(1).Both clinical and preclinical studies have confirmed the ability of exercise to enhance NO-dependent endothelial vasodilatation.(10)

At the same time, oxidative stress is associated with the pathogenesis of hypertension. In hypertensive subjects, reactive oxygen species (ROS), which counteract NO, increase, reducing its bioavailability. Consequently, poor NO bioavailability is often present in hypertension and is the main feature of endothelial dysfunction.(1)

A study of the response of endothelial function to physical training in 81 hypertensive individuals by Pedralli et al.(20) reveals two crucial phenomena: physical activity improves endothelium-dependent vasodilatation in the hypertensive population; and the magnitude of the improvement in endothelial function depends on the type of training (aerobic, resistance or concurrent).(10)

Effects on the renin-angiotensin system (RAS)

Physical exercise induces a negative regulation of the systemic and tissue ACE/Ang II/AT1 receptor axis, a positive regulation of the ACE2/Ang 1-7/Mas axis, and a shift in the RAS toward the ACE2/Ang (1-7)/Mas axis. In this context, the effects of exercise on the RAS are in line with that sought by pharmacological strategies of RAS manipulation for the treatment of AHT.(21)

Stimulation of angiogenesis

Hypertension is characterized by microvascular rarefaction caused by impaired angiogenesis. Constant physical exercise has been shown to induce vessel adaptation to increase blood flow reserves. Morphological changes in the vascular tree result from exercise-induced angiogenesis (increase in the size and number of blood vessels) regulated by vascular endothelial growth factor (VEGF) and other mediators. In response to physical training, VEGF is released and induces endothelial cell proliferation and migration. Other factors, including angiopoietins and metalloproteinases, initiate the degradation of the extracellular matrix, essential for the formation of vascular networks.(10)

Increased insulin sensitivity

Murine models of hypertension and metabolic syndrome have demonstrated attenuation of insulin resistance and AT due to moderate-intensity physical activity, suggesting a strong pathophysiological link between essential hypertension and hyperinsulinemia, as well as the role of exercise in the regulation of AT and insulin sensitivity. These elements reaffirm the hypothesis that physical activity may prevent the development and progression of hypertension via its influence on insulin responsiveness.(10)

Various research studies have reported different results on the impact of exercise on blood pressure by considering the type of exercise, its conditions, duration and frequency within a specific period, and its relationship to blood pressure reduction.(3,12,22,23)

Regarding the impact of exercise on blood pressure in older adults with hypertension, some preliminary studies have been conducted in Asia, Europe, and America, which have found conflicting results. One of the uses of meta-analysis study is to address these assumptions and provide a global idea about the issue to be addressed.(3) In this case, a systematic review and meta-analysis would be of great importance.

The COVID-19 pandemic has brought with it an interruption in research and a notable lack of studies on this subject, and during this period there was a lack of knowledge in this area. This systematic review aims to compile, analyze and synthesize the existing evidence to provide an updated and comprehensive view of the impact of physical exercise on hypertension. This will not only fill an important gap in the scientific literature, but will also provide health professionals and patients with valuable, evidence-based information for the management of hypertension, as well as promote interventions that are more effective and contribute new knowledge to public health.

Along with the increase in the numbers and prevalence of hypertension in ambulatory older adults, there is a low level of studies on the relationship of this disease with other conditions or activities that can control it, such as physical exercise.(24)

The aim of the present study was to determine the effect of physical exercise on BP in patients with arterial hypertension by combining evidence from randomized clinical trials. In addition, it allowed us to define the contribution of the duration of the intervention and combined therapy with medication to the effect of physical exercise on BP.

METHOD

A systematic review was conducted according to the preferred reporting elements for systematic review guidelines (PRISMA). The methodology used is in line with the methods developed by the Cochrane Collaboration to search, retrieve, quality assess, and synthesize the findings of randomized controlled trials. The electronic databases consulted were Medline/PubMed, Scopus, ScienceDirect, Web of Science, ClinicalTrials.gov, EU Clinical Trials Register, Cochrane Central Register of Controlled Trials and bibliographic databases of the Spanish National Research Council (CSIC).

Search methods

Eligible studies published between 2004 and 2024 were identified. The search terms selected were descriptors for each component of the PICO question (patient, intervention, comparison, and outcome). Studies were searched using the combined search terms: (((high blood pressure) OR (hypertension)) AND (adults)) AND (exercise)) AND (randomized trial)) AND (controlled). To substantiate the search process, a manual search of relevant journals and references of retrieved articles was performed, important for those journals less likely to be indexed. Studies that matched the keywords were included in the review.

Inclusion and exclusion criteria

Studies with the following criteria were included:

- Type of study: randomized controlled clinical trials
- Language: papers written in English and Spanish
- Chronological coverage: all papers published between 2004 and 2024
- Population: adults with hypertension aged 40 years or older, with or without drug treatment
- Intervention: physical exercise (aerobic, endurance or strength training, lasting at least 8 weeks)
- Comparison: hypertensive controls, with or without treatment, who have maintained their regular or light physical activity during the intervention.
- Outcome: control of arterial hypertension (decrease in BP in hypertensive patients)
- Data report: mean systolic and diastolic blood pressures of each group, intervention and control, before and after the intervention.

Studies that did not meet the inclusion criteria were excluded, and protocols, congresses, abstracts, academic theses, editorials, commentaries, and opinion articles were excluded. Review articles were excluded, although they were used to crosscheck relevant primary articles.

Data management

Zotero 6.0.35 bibliographic software was used to store and organize all the results from the bibliographic databases. Microsoft Excel 2021 was used for the article selection and data extraction process, and Microsoft Word 2021 was used for the quality assessment process.

Study selection

All identified articles were screened for relevance by title and abstract, followed by a full-text reading of all relevant articles. The review was not blinded as to the authors of an article.

Data extraction

The following data were extracted: year of publication, place (city and country) where the study was conducted, number of participating subjects, exercise performed in the intervention, duration of the intervention, activity assigned to the controls, mean systolic and diastolic BP before and after the intervention, of the intervened subjects and controls, and the main conclusions of each study.

Risk of bias in individual studies

The risk of bias of randomized controlled trials was assessed using the updated Cochrane Risk of Bias 2 (RoB 2) tool. Sources of bias included in the Cochrane RoB2 library were random sequence generation and allocation masking (selection bias), blinding of participants and personnel (performance bias), blinding of data assessors (detection bias), incomplete outcome data (attrition bias), selective outcome reporting (reporting bias), and other biases. Each study was rated as high, low, or uncertain risk of bias.

Quantitative analysis

A meta-analysis was performed to estimate the overall effects of physical exercise interventions on BP. Mean systolic and diastolic BP (with their respective standard deviation) were used as the outcome variable; the mean difference was used as the effect measure in the analysis, with the methodological approach of the inverse of the variance. Because the true effects were expected to be related but not equal for the included studies, a random-effects model was used for all analyses. Statistical heterogeneity between studies was assessed using the I2 test. The Meta-mar Meta-analysis Calculator v3.5.1[(24)] web application was used for statistical analyses; interface based on R statistical software.

RESULTS

The electronic database search with the descriptors and Boolean operators yielded a total of 1519 entries. Of these, 878 were discarded for evaluating the behavior of other chronic diseases (chronic kidney disease, diabetes) and another 230 were determined to be duplicate records.

There remained 411 records of publications that were evaluated individually by title and abstract, leaving 106 articles to be retrieved. The difference, 305 records were excluded because they met some exclusion criterion (mainly not being randomized controlled studies). It was possible to retrieve 59 articles, which were then evaluated to decide their eligibility. Forty-eight publications were excluded for various reasons: they included non-hypertensive subjects in their analysis [(10)], did not report the required data[(17)], did not include subjects in the desired age range for this study [(14)], the subjects in the control group of the study performed some type of exercise [(2)], or did not have a control group. [(5)]

Some of the preselected trials involved several groups of individuals or applied different training regimens. Finally, eleven studies were available for the qualitative and quantitative synthesis of the present review.

The flow chart followed for the selection of review papers, suggested by the PRISMA (*Preferred Reporting Items for Systematic Reviews and Meta-Analyses*) 2020 statement, is shown in Figure 1.

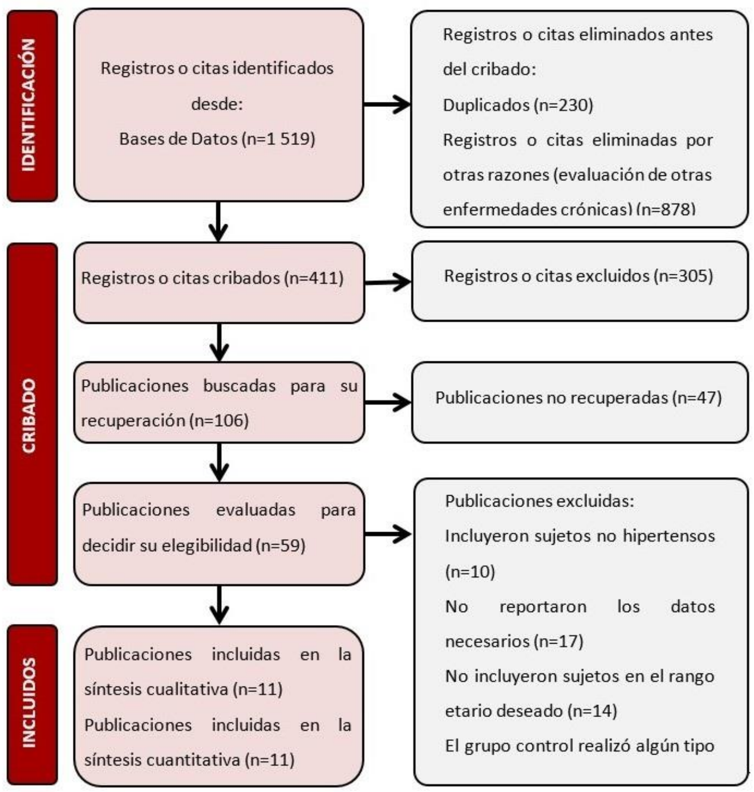

Fig. 1: Flow chart suggested by the PRISMA 2020 statement. Adapted from Page MJ, et al.[(25)]

Characteristics of the studies

The eleven articles included in the review provided information from 457 subjects. The exercise interventions ranged from eight weeks to six months in duration. They consisted of sessions lasting between 20 and 60 minutes, depending on the participants' tolerance, with a frequency of three to five times per week. Exercise sessions (aerobic and resistance) were supervised in all selected studies.

Nine studies included participants who were taking antihypertensive drugs and maintained their treatments during the intervention.[26,27,28,29,30,31,32,33,34]) In ten studies, some variant of aerobic exercise (walking, swimming, pedaling) was applied. [26-33,35,36] One study included an intervention group with resistance exercises in addition to aerobic exercise (multicomponent training)[29] and another applied strength exercises for the respiratory musculature.[34] No study reported any type of adverse event related to the exercise sessions (musculoskeletal injury or excessive hypertensive/hypotensive response). The particularities of the included studies are summarized in Table 1.

Table 1: Main characteristics of the included studies

1st author	Year	Sample	Subjects on medication	Place	Duration	Intervention exercise
Westhoff *et al.*[26]	2007	27 intervened, 27 controls, Over 60 years old	Yes, antihypertensives: not specified.	Berlin, Germany	12 weeks	Aerobic, 30-minute sessions, three times a week.
Pagonas *et al.*[27]	2014	36 intervened, 36 controls, Between 42 and 79 years old	Yes, antihypertensives: Beta-blockers, ACE inhibitors, Ang receptor blockers, calcium channel blockers, aliskiren, diuretics, others.	Berlin, Germany	8 - 12 weeks	Aerobic, 30-minute sessions, three times a week.
Dimeo *et al.*[28]	2012	24 intervened. 26 controls Between 42 and 78 years old	Yes, antihypertensives: diuretics, calcium channel blockers, alpha- and beta-blockers, ACE inhibitors, Ang blockers, aliskiren, moxonidine, clonidine, minoxidil.	Berlin, Germany	8 - 12 weeks	Aerobic, 30-minute sessions with rest intervals of 3 to 15 minutes, three times a week.
Lima *et al.*[29]	2017	15 intervened with aerobics. 15 with aerobics and resistance, 14 controls, Between 60 and 75 years old	Yes, antihypertensives: hydrochlorothiazide, ACE inhibitors or Ang II receptor blockers.	Sao Pablo, Brazil	10 weeks	Aerobic, 20 to 30 minute sessions, three times per week Aerobic with resistance, nine resistance exercises were added 15 to 20 repetitions.
Tjønna *et al.*[30]	2008	12 intervened with interval aerobics. 10 intervened with continuous moderate exercise. 10 controls Between 40 and 65 years old	Yes, antihypertensives: calcium channel blockers, alpha- and beta-blockers.	Trondheim, Norway	16 weeks	Aerobic: walking on the treadmill uphill, three times a week, Those treated with aerobics warmed up for 10 minutes and performed exercises in intervals of 4 minutes with 3 minutes of rest. Up to 40 minutes, The

						moderate exercise group trained at lower intensity for 47 minutes.
He *et al*.[31]	2018	23 intervened 23 controls 23 negative controls (non-hypertensive). From 55 to 60 years old	Yes, antihypertensives: not specified.	Shanghai, China	12 weeks	Aerobic (brisk walking) three times a week, 60-minute sessions
Mora *et al*.[32]	2017	23 intervened 23 controls Age: 53.5 ±8.9 years old	Yes, antihypertensives: not specified.	Toledo, Spain	6 weeks	Aerobic: supervised training, 45-minute pedaling sessions, three times a week
Guimaraes *et al*.[33]	2014	16 intervened 16 controls Between 40 and 65 years old..	Yes, antihypertensives: not specified.	Sao Pablo, Brazil	12 weeks	60 min sessions in warm water (warm-up, calisthenics against water resistance, walking and stretching), three times a week
Craighead *et al*.[34]	2021	18 intervened 18 controls Age: 67±2 years	Yes, antihypertensives and any other prescribed not specified.	Boulder Colorado EEUU	6 weeks	Inspiratory muscle strength training with POWER breathe K3 Subjects performed 30 inspiratory maneuvers (5 sets of 6, with 1 minute rest between sets), six days per week
Nualnim *et al*.[35]	2012	24 intervened 19 controls Between 50 and 80 years old	No, having antihypertensive treatment was exclusion criterion.	Austin Texas, EE.UU.	12 weeks	Swimming, initially 15-20 minutes per session, progressively increasing to 40-45 minutes per session Three to four sessions per week
Glodzik *et al*.[36]	2018	31 operated 14 controls Between 40 and 60 years old	No, having antihypertensive treatment was exclusion criterion.	Cracow, Poland	12 weeks	Aerobics, supervised on a cycloergometer three times a week, 40-60 minute sessions.

Effects of the interventions

In ten of the studies analyzed there were agreements that the use of physical exercise training sessions had hypotensive effects, which significantly ($p<0.05$) decreased 24-hour systolic and diastolic BP figures measured ambulatory.[26-35]. No significant benefits were observed for multicomponent training interventions on any measure of BP.[29]. Table 2 summarizes the results described by the authors, with regard to BP and the main conclusions reached.

Table 2: Summary of results reported in the included studies

1st author	Results	Conclusions	Possible biases
Westhoff *et al.*[26]	The ASR remained almost unchanged in the control group, but decreased significantly in the exercise group. In the exercise group, systolic blood pressure decreased significantly from 140.5 ±12.4 to 131.2 ±9.6 mmHg and DBT from 79.3 ±7.2 to 74.2 ±7.6 mmHg during the day and from 130.0 ±15.2 to 123.5 ±12.1 mmHg (systolic) and 71.1 ±8.5 to 66.2 ±7.2 mmHg (diastolic) during the night (p<0.01 each). In the control group, baseline TAS and TAD were 138.0 ±11.1 and 75.3 ±7.1 mmHg during the day and 129.2 ±13.9 and 67.8 ±9.2 mmHg during the night.	Aerobic exercise reduced systolic and diastolic BP. The reduction in AT was highly dependent on baseline AT.	Selection: suggests randomization, but does not indicate the method. Does not make allocation blinding clear Performance: no blinding of participants and staff Detection: there was no blinding of data evaluators.
Pagonas *et al.*[27]	Exercise significantly reduced systolic and diastolic BP during the day (p<0.001 and p=0.04 respectively). Exercise did not significantly affect systolic (p=0.21) and diastolic (p=0.69) BP during the night. The coefficient of variation (CV) of daytime ASR did not change in response to the exercise program (10.2 ±2.7 vs. 9.8 ±2.6 %, p=0.30). The CV of nocturnal TAS also did not differ significantly from baseline to follow-up (8.9 ±3.2 vs. 10.5 ±4.1 %, p=0.10). Furthermore, exercise had no significant effect on daytime and nighttime CV of DBT (p<0.05 each). However, there was a statistical trend in daytime TAD CV (p=0.06). This trend resulted from an increase in CV in the control group (12.9 ±3.3 vs. 13.6 ±3.8 %), while CV in the exercise group remained exactly unchanged (11.5 ±3.3 vs. 11.5 ±3.1 %). The CV of TAS and TAD was not affected by the exercise program (p<0.05 each).	Aerobic exercise reduced diurnal systolic and diastolic BP. No effect was found on AT measured at night.	Selection: does not make clear the assignment masking. Performance: no blinding of participants and staff Detection: no blinding of data evaluators
Dimeo *et al.*[28]	The exercise program significantly reduced daytime systolic and diastolic BP by 5.9±11.6 and 3.3±6.5 mmHg, respectively (p=0.03 each). Nocturnal systolic and diastolic BP values were numerically lower after the exercise program, but the changes did not reach significance (3.8±17.1 and 1.9±8.2 mmHg; p=0.05 each). The 24-hour systolic and diastolic BP decreased significantly by 5.4±12.2 (p=0.03) and 2.8±5.9 mm Hg (p=0.01). Systolic and diastolic BP were numerically, but not significantly, reduced with physical training (6.6±15.7 and 2.7±8.0 mmHg; p=0.32 and p=0.82 respectively) in the control group.	Aerobic exercise reduced systolic and diastolic blood pressures measured during the day.	Selection: does not make clear the assignment masking. Performance: no blinding of participants and staff Detection: no blinding of data evaluators
Lima *et al.*[29]	Regarding the AAR values, the groups with aerobics (p=0.02) and aerobics with resistance (p<0.001) showed a decrease in 24-hour AAR in the training period and the control group showed a slight increase in AT (p>0.001). The decrease was similar for both interventional groups. The 24-hour DBT decreased significantly for both intervened groups (p<0.01); no difference for the	The group that performed combined exercise did not show a greater decrease in AT than those who only did aerobics. (Both interventions had a similar hypotensive effect).	Selection: does not make clear the assignment masking. Performance: no blinding of participants and staff, Detection: no blinding of data evaluators

	control group.		
Tjønna *et al.*[30]	Both aerobic and moderate exercise interventions reduced systolic and diastolic SBT by approximately 10 mmHg (both p<0.05) and 6 mmHg (aerobic, p<0.05; and moderate exercise, p=0.24); respectively.	Both exercise regimens reduced systolic and diastolic blood pressures. High-intensity exercise is superior to moderate-intensity exercise in terms of reversing metabolic syndrome risk factors.	Selection: it does not clarify the method of randomization or the performance of allocation blinding. Performance: there was no blinding of participants and personnel. Detection: there was no blinding of data evaluators.
He *et al.*[31]	Significant differences in BP were observed between groups before and after exercise. The SBT and DBT in patients with essential hypertension were significantly higher compared to subjects with normal BP. The SBT in the treatment group was significantly reduced by 8.3 mmHg, 15.6 mmHg and 22.6 mmHg, respectively. After the intervention, the ASR in the treated group was significantly reduced after the increase in exercise intensity compared to non-hypertensives and controls.	Brisk walking reduced BP in hypertensive patients.	Selection: does not clarify the assignment masking. Performance: no blinding of participants and personnel Detection: no blinding of data evaluators
Mora *et al.*[32]	In participants in the training group, brachial arterial systolic and diastolic BP was reduced, which reduced the prevalence of hypertension from 79% to 41%. After 6 months, BPs decreased by 6 to 9 % with physical training compared to controls, resulting in lower systolic (-12±3 mmHg, p= 0.001) and diastolic (-6±2 mmHg, p=0.007) pressures after treatment.	The intervention reduced the systolic and diastolic BP of those who underwent the intervention.	Selection: does not indicate the randomization method. It does not clarify whether there is allocation blinding. Performance: does not clarify the blinding of participants. Detection: does not clarify the blinding of data evaluators.
Guimaraes *et al.*[33]	Systolic and diastolic AT decreased after hot water immersion exercise by 36.5 ±7.8 mmHg (p<0.0001) and 11.9 ±1.9 mmHg (p=0.004), respectively, but did not change in the control group after follow-up. Exercise significantly decreased systolic and diastolic AHT, respectively, in the 24-hour period (19.5±11.0 and 11.1±3.1 mmHg), during the day (22.3±12.6 and 13.0±3.6 mmHg) and during the night (17.4±9.1 and 8.5±2.1 mmHg). In the control group, there was a significant increase in systolic and diastolic BP, respectively (24 hours: 3.0±0.1 and 2.1±1.2 mmHg; daytime: 4.4±2.2 and 3.5±2.1 mmHg and nighttime diastolic 3.1±1.9 mmHg).	Exercises in warm water were an effective antihypertensive therapy.	Selection: does not make clear the assignment masking. Performance: no blinding of participants and staff Detection: no blinding of data evaluators
Craighead *et al.*[34]	TAS decreased from 135 ±2 mmHg to 126 ±3 mmHg after 6 weeks of exercise (p<0.01), but did not change with sham training (baseline: 134 ±2 mmHg; at the end of the intervention: 131 ±3 mmHg; p=0.07). There was a significant interaction effect for casual TAS (p=0.02). When stratified by sex, exercise reduced casual TAS in both men (baseline: 136 ±3mmHg, end: 125 ±3 mmHg; p<0.01) and women (baseline: 134 ±3 mmHg, end: 127 ±4 mmHg; p=0.02). Casual DBP decreased from 79 ±2 mmHg at baseline to 77 ±2 mmHg after 6 weeks of training (p=0.03), but did not change with sham training (p=0.75). The decrease in AAR from baseline to the end of the	Inspiratory muscle strength training decreased systolic and diastolic BP in middle-aged and older male subjects and postmenopausal women. The reduction in BP numbers was maintained for at least 6 weeks after the end of training.	Selection: allocation masking was not possible for all subjects.

	intervention (135 ±2 mm Hg vs 126 ±3 mmHg, p<0.01) was identical to that of the whole group. Six weeks after discontinuation of exercise, the AAR in the subgroup remained significantly lower (128 ±4 mmHg, p<0.01) than baseline and was not different from that at the end of the intervention (p=0.71). The AAR did not change at any time in the subgroup of sham subjects (all p>0.05).		
Nualnim *et al.*[35]	Changes in systolic BP differed in the exercise and control groups. The ASR remained almost unchanged in the control group, but decreased significantly in the exercise group from 140.5 ±12.4 to 131.2 ±9.6 mmHg and the DBT from 79.3 ±7.2 to 74.2 ±7.6 mmHg during the day and from 130.0 ±15.2 to 123.5 ±12.1 mmHg (systolic) and 71.1 ±8.5 to 66.2 ±7.2 mmHg (diastolic) during the night (p<0.01 each). In the control group, baseline systolic and diastolic BP were 138.0 ±11.1 and 75.3 ±7.1 mmHg during the day and 129.2 ±13.9 and 67.8 ±9.2 mmHg during the night.	Swimming-based exercises have hypotensive effects and improve vascular function.	Selection: does not clarify the assignment masking. Performance: no blinding of participants and personnel Detection: no blinding of data evaluators
Glodzik *et al.*[36]	It was not found that the BP of the intervention group, before and after, were significantly different. The SBT (initial value: 131.65 ± 3.57 mmHg, final value: 130.74 ± 4.00; p=0.066187) and DBT (initial value: 80.65 ±5.21; final value: 79.71 ±5.03 p=0.051512). For the control group, there was no significant difference between systolic (initial value: 131.66 ±5.74 mmHg; final value: 133.00 ±6.5 mmHg; p=0.610120) and diastolic (initial value: 83.00 ±12.50 mmHg; final value: 81.50 ±3.88 mmHg; p=0.556299) BP figures before and after 12 weeks.	No significant changes in AT were recorded.	Selection: it does not clarify the method of randomization or the implementation of allocation blinding. Performance: blinding of participants is not evident. Detection: blinding of data evaluators is not evident.

DBT, diastolic blood pressure; SBP, systolic blood pressure
Note: only results related to blood pressure were collected in each study.

Table 3 shows the mean systolic and diastolic BP recorded for the intervention and control groups in each study.

Table 3: Mean pre- and post-intervention arterial blood pressures

Study		Intervention groups			Control groups		
		Initial value	Final value	Δ	Initial value	Final value	Δ
Westhoff *et al.*[26]	TAS	136,6	128,1	-8,5	134,8	136,1	1,3
	TAD	76,3	71,2	-5,1	72,8	72,6	-1,3
Pagonas *et al.*[27]	TAS	137,9	131,7	-6,2	133,1	135,1	2
	TAD	78,1	75,1	-3	73,8	74,6	-2
Dimeo *et al.*[28]	TAS	138,4	132,5	-5,9	131,2	133,8	2,6
	TAD	78,3	75,0	-3,3	72,3	73,5	-2,6
Lima *et al.*[29]	TAS	132,2	127,4	-4,8	130,3	135,3	5
	TAD	79,0	79,0	-	75,5	75,5	-5
Tjønna *et al.*[30]	TAS	144,0	135,0	-9	146,0	141,0	-5
	TAD	95,0	89,0	-6	95,0	96,0	5
He *et al.*[31]	TAS	147,7	139,4	-8,3	146,1	148,3	2,2
	TAD	85,2	84,1	-1,1	86,1	86,9	-2,2
Mora *et al.*[32]	TAS	136,0	127,0	-9	138,0	140,0	2
	TAD	84,0	77,0	-7	84,0	83,0	-2
Guimaraes *et al.*[33]	TAS	160,2	136,4	-23,8	157,6	157,8	0,2
	TAD	82,8	76,7	-6,1	86,3	87,1	-0,2
Craighead *et al.*[34]	TAS	136,0	133,0	-3	146,0	140,0	-6
	TAD	79,0	78,0	-1	79,0	83,0	6
Nualnim *et al.*[35]	TAS	131,0	122,0	-9	129,0	129,0	-
	TAD	76,0	72,0	-4	76,0	75,0	-
Glodzik *et al.*[36]	TAS	131,57	130,74	-0,83	131,7	133,0	1,3
	TAD	80,65	79,71	-0,94	83,0	81,5	-1,3

Legend: Δ (delta): difference between post intervention and pre intervention value; SST: systolic blood pressure; DBT: diastolic blood pressure

Risk of bias of the selected studies

The risk of bias with respect to randomization was considered low in five of the eleven studies.[26-36] Although all stated that they performed randomized allocation of the included subjects, six did not indicate the method used for this effect.[30,32-36]. The risk of bias arising from "allocation concealment" was considered imprecise for all the trials; in none was concealment of the groups to which the participating subjects were assigned found, two of the studies reported blinding[32,34] and only one[34] reported double blinding. The risk of incomplete results was considered low in all included articles, all indicated dropouts/exclusions and their reasons if any. Reporting bias was rated as low; studies reported positive and negative results, significant or not, and discussed them, according to the main objectives of each study (i.e., not all the trials analyzed had AT as their main object).

Publication bias is a common problem in scientific research and may affect the validity of the conclusions of the present type of study by distorting the true picture of the available evidence on the effect of physical exercise on arterial hypertension:[37,38]

First, studies that find a significant effect of physical exercise on HTM may be more likely to be published (publication bias for significant results). Editors and reviewers may have a preference for positive results, which may lead to an overrepresentation of the positive effects of physical exercise in the literature reviewed.(37)

Consequently, published studies are more likely to be indexed in bibliographic databases and are therefore more likely to be retrieved (retrieval bias) in literature searches. On the other hand, studies that are unpublished or published in unconventional sources may be more difficult to find and thus may be underrepresented in the review.(37)

To mitigate the impact of publication bias, assessment of potential bias can be implemented through tools such as the publication funnel.(37,38) The funnel plot of exercise on systolic BP was asymmetric. Egger's regression test ($t=-2.26$; $p=0.0352$) was significant for publication bias. Similarly, the funnel plot of exercise on diastolic BP was asymmetric; however, Egger's regression test ($t=-1.80$; $p=0.0873$) did not show sufficient evidence of publication bias for this parameter.

Quantitative synthesis

The overall pooled analysis of the standardized mean differences showed statistically significant difference between the AT figures recorded before and after the exercise sessions; for systolic AT: $\chi^2=22.82$; $p<0.01$; and diastolic AT: $\chi^2=8.69$; $p<0.01$. There was significant heterogeneity when assessing systolic BP ($\chi^2=83.98$; $p<0.01$; I2=75 %) and diastolic BP ($\chi^2=57.18$; $p<0.01$; I2=63 %).

The mean standard difference of systolic blood pressures (-0.34) had a negative value with 95 % confidence interval of -0.63 to -0.04. In contrast, the difference in diastolic blood pressures (-0.15) was not significant 95% CI -0.81, 0.09.

The meta-analysis result for systolic BP showed statistically significant reductions for systolic BP after training in ten of the eleven papers reviewed.(26-33,33-35) Subgroup analysis by time (before and after intervention) showed only significant results for post-intervention data in the studies (-0.80 for systolic BP and -0.44 for diastolic BP). Likewise, heterogeneity was only significant at post-intervention time points for both BP figures (systolic: $\chi^2=29.37$; $p<0.01$; diastolic: $\chi^2=28.27$; $p<0.01$).

Subgroup analysis was performed by comparing studies that had interventions lasting less than 12 weeks and those whose interventions lasted twelve weeks or more. The standardized mean differences of the subgroups with longer interventions (twelve weeks or more) indicated statistically significant reductions for systolic (-1.06) and diastolic (-0.71) blood pressures with respect to controls after the physical exercise interventions. Tables 4 and 5 show the results of the quantitative analysis for systolic and diastolic blood pressures.

Studies with interventions shorter than twelve weeks had no statistically significant differences in systolic BP or diastolic BP figures with respect to controls; however, there was a statistically significant difference between subgroups: χ^2=8.17; p<0.01 for systolic BP and χ^2=8.51; p<0.01 for diastolic BP. This could suggest that the hypotensive effects of physical exercise could depend on the duration of the treatment performed. There was significant heterogeneity between studies, both for systolic BP (χ^2=29.37; p<0.01; I2=66 %) and diastolic BP (χ^2=28.27; p<0.01; I2=65 %). Tables 6 and 7 show the subgroup analyses according to the duration of the interventions for systolic BP and diastolic BP, respectively.

Subgroup analysis was also performed to compare those studies that included subjects with antihypertensive drug treatment and those that did not (Tables 8 and 9). Both subgroups showed standardized mean differences with negative values for both systolic and diastolic BP; however, only the subgroup with drug treatment had significant differences (-0.74 [95%CI -1.17, -0.32]) in the systolic BP figures with respect to the controls. It was observed that there were no statistically significant differences between subgroups when assessing systolic (χ^2=0.25; p=0.61) and diastolic (χ^2=1.07; p=0.3) blood pressure figures. Therefore, it could be inferred that the hypotensive effects of physical exercise were independent of the effects that treatments with hypotensive drugs may have had on the individuals in the studies included in this meta-analysis.

DISCUSSION

The individual studies analyzed showed 75% heterogeneity when comparing systolic blood pressures before and after the intervention. This indicates that the observed variability in the effects of physical exercise on AT may be due to actual differences between the studies compared; factors such as duration, type and intensity of exercise, characteristics of the participants. An analysis of the cumulative standardized mean differences of pre- and post-intervention stresses (0.17 and -0.34, respectively) shows the positive effect of physical exercise in a general way, by decreasing the mean figures of the intervened group with respect to those of the control.

Something similar was observed for diastolic BP values. There was a decrease in the absolute value of the standard mean difference, indicating that the intervention succeeded in reducing the variability of diastolic BP D. However, for this parameter, it is not possible to be sure of this effect since the statistical evidence is insufficient (note that the range of the post-intervention confidence interval includes negative and positive values). Nevertheless, the test for differences between subgroups showed a significant disparity between diastolic BP before and after exercise.

Clinically, this could be interpreted to mean that exercise had a stabilizing effect on diastolic blood pressure. For this marker the studies showed no heterogeneity, revealing that the variation in intervention effects between individual studies was not due to actual differences between them.

Previous evidence has indicated an overall beneficial effect of physical training on AAR. A meta-analysis by Fagard et al.(39) (72 trials and 105 study groups) involving hyper- and normotensive individuals found that physical exercise reduces daytime BP by approximately 3.3 mmHg. Another meta-analysis, by Cornelissen and Smart(40), of 93 angiotensin-converting enzyme (ACE) inhibitors (5223 subjects) reported a significant reduction in daytime BP (≈-3,2 mmHg) when analyzing individuals with normotension and hypertension, and this effect remained significant in separate analyses for individuals with hypertension only (≈-3,8 mmHg). Similarly, Carpio et al.(41) conducted a meta-analysis of 65 studies and concluded that regardless of participant and exercise characteristics, there is a reduction in BP following an exercise session. This indicates that the cardiovascular benefit of physical exercise is mediated and immediate.(43)

At the same time, and in agreement with other studies(40,43), the present results suggest that physical training reduces BP. The data show that aerobic exercise leads to a significant reduction in BP in hypertension. The degree of exercise-induced blood pressure reduction seems to vary considerably from study to study, ranging from 5 mmHg to 15 mmHg. The meta-analysis by Cornelissen et al.(44) found a mean reduction of 7/5 mmHg.

Gao et al.(45) performed a network meta-analysis with 19 studies including 2385 subjects. Their results coincided with those of the present study in terms of the significant hypotensive effect of aerobic physical exercise in middle-aged and older adults. However, they only obtained significant results for systolic BP, not for diastolic BP.

For their part, Marça et al.(46) analyzed 14 RCTs that included 276 subjects and obtained results similar to the present study; they agreed on the hypotensive effect of low- and moderate-intensity physical exercise. Their statistics showed significant results for both systolic and diastolic BP.

The meta-analysis by Zhou et al.(47) of twelve randomized controlled trials showed similarities to the present study, obtaining significant differences in the mean systolic and diastolic blood pressures between the exercise groups and the controls. In their summary, 10 studies applied aerobic exercise interventions and achieved joint decreases in systolic BP up to 3.51 mmHg and diastolic BP up to 2.77 mmHg.

For their part, Edwards et al.(48) analyzed data from 270 relevant RCTs involving 15827 participants to establish optimal exercise prescription practices in the treatment of resting BP. The analyses demonstrated a significant reduction in systolic BP and diastolic BP after all modes of exercise. While all exercise modes demonstrated statistically significant reductions in systolic BP in the normal BP cohorts, all reductions were substantially greater in those with hypertension.(48)

These findings are clinically important, particularly given the role of BP as a predictor of cardiovascular disease and mortality. Reductions in AT have been shown to reduce the risk of stroke and coronary heart disease.(43)

Cornelissen and Smart[40], in their meta-analysis, found that exercise programs of less than six months induced greater reductions in AT compared to programs of longer duration, which differs with the results of this research. This could be explained by the fact that their research had a high representation of studies with groups subjected to resistance exercise, generally unsupervised; [441] which differs from the present one in which supervised interventions with aerobic exercise were more frequent to ensure adherence.[26-32,35,37]

Dai et al.[49] performed a network meta-analysis (30 RCTs) comparing the hypotensive effect of three traditional Chinese fitness exercises (Tai Chi, Baduanjin and Wuqinxi) with that of antihypertensive drug therapy. Their results showed that the associated exercise and antihypertensive drug therapies had greater antihypertensive effects on both systolic and diastolic BP than antihypertensive drug therapy alone. This is partially consistent with the results of this investigation in which a reduction in systolic BP was found in the subgroup of studies with associated therapies (exercise + medication); however, there was no statistical evidence of a significant difference between the hypotensive effects in studies with and without medication for either systolic or diastolic BPs. The present analysis did not compare with studies using only drug therapy; and Gao et al.[45] did not compare studies with exercise-only interventions. Also, this meta-analysis did not include any studies with traditional Chinese exercise.

To estimate the comparative efficacy of antihypertensive medications and exercise interventions in reducing BP in people with hypertension, Noone et al.[50] conducted a systematic review with network meta-analysis. Of 93 RCTs (32404 participants) in their synthesis, only 12 trials were related to exercise (1057 participants). These authors' estimates suggest that antihypertensive medications were more effective than exercise, but they did not obtain sufficient evidence to suggest that medications significantly reduced BP largely than exercise interventions. These findings reflect a bias toward gathering evidence on pharmacologic interventions to control one of the most common health problems of adulthood.[50]

An important question that remains to be resolved is the sustainability of the benefits of exercise on AT, as the longest exercise intervention lasted 6 months and only one of the included studies conducted follow-up.[32,34]

Lifestyle modifications could offset the genetic risk of hypertension and reduce blood pressure in high-risk participants. In addition to aerobic exercise, many lifestyle factors are associated with hypertension, including body mass index, diet, smoking, alcohol consumption, sedentary behaviors, and stress. The findings of this meta-analysis on the benefits of physical exercise as an alternative antihypertensive therapy are in line with the results of previous reviews on nonpharmacological treatment to reduce BP in hypertensive patients.[42,48,50,51,52,53,54]

Some limitations should be acknowledged, in particular, the relatively low number of included studies and particularly for some exercise modalities such as resistance or multicomponent training. The small sample size of the included studies may introduce publication bias, generate imprecise estimates and contribute to variability, which would affect the reliability of the conclusions of the meta-analysis.

Undoubtedly, the lifestyle of individuals is the axis that drives the health-disease process throughout life. Achieving behavioral changes and modifications in people is complicated if we take as a reference that the population does not have an adequate perception of risk in relation to the factors that favor the appearance of diseases such as HT, although these characteristics are considered by the literature as risk factors for this disease. The authors of this study consider it vitally important to know the benefits of adequate physical activity.[55,56]

CONCLUSIONS

The results of this review suggest that physical exercise has a positive impact on blood pressure control and lowering in adults with hypertension. The hypotensive effects of physical exercise seem to vary according to the duration of training, being more robust after interventions of more than 12 weeks. Physical exercise was shown to lower blood pressure independently of the use of antihypertensive drugs.

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