INFLUÊNCIA DAS VARIÁVEIS DO TREINAMENTO COMBINADO NA REDUÇÃO DA PRESSÃO ARTERIAL EM INDIVÍDUOS ADULTOS COM HIPERTENSÃO: UMA REVISÃO SISTEMÁTICA COM META-ANÁLISE E META-REGRESSÃO

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MENSAGEM

Não fui eu que ordenei a você? Seja forte e corajoso!

Não se apavore nem desanime, pois o Senhor, o seu Deus,

estará com você por onde você andar".

(Josué 1:9)

SUMÁRIO

LISTA DE ABREVIATURAS E SIGLAS

1RM = % de uma repetição máxima

EF = Exercício Físico

HAS = Hipertensão Arterial Sistêmica

HPE = Hipotensão Pós-Exercício

NO = Oxido nítrico

PA = Pressão Arterial

TC = Treinamento Combinado

VO_{2max} = % do consumo máximo de oxigênio

RESUMO

Objetivo: Esta revisão sistemática com meta-análise e meta-regressão avaliou a efetividade do treinamento combinado e a influência das variáveis do exercício aeróbio e de força, dentro de um programa de treinamento combinado (TC), na redução da PA em adultos com hipertensão. **Métodos:** Foram incluídos ensaios clínicos randomizados, em adultos com hipertensão, de intervenções envolvendo TC versus um grupo controle sem exercício (CG). As pesquisas nas bases de dados MEDLINE via PubMed, Cochrane Central, EMBASE, Scopus, e LILACS foram pesquisadas até dezembro de 2021 para busca dos estudos. A qualidade metodológica dos estudos foi avaliada utilizando a lista de verificação da TESTEX. Foi realizada uma meta-análise de efeitos aleatórios utilizando como base a diferença média (MD) de alteração da PA em relação à linha de base comparando o TC versus CG. Foram realizadas análises de meta-regressão para avaliar a relação entre as variáveis do TC (duração da intervenção, frequência semanal, intensidade, volume semanal, e frequência) e as mudanças sobre a PA. **Resultados:** Foram analisados trinta e sete estudos com 41 intervenções (1942 participantes). Os resultados agrupados com 95% de intervalo de confiança (95% IC) na PA sistólica (PAS) e diastólica (PAD) indicaram uma diminuição significativa do TC em comparação com o CG, mas contendo uma heterogeneidade significativa (PAS, -6,4 mmHg; 95% IC, -9,1 a -3,6; PAD, -3,7 mmHg; 95% IC, -4,9 a -2,4). A análise de meta-regressão revelou que um aumento da intensidade do exercício e do volume semanal de treinamento está associado a uma maior magnitude de redução na PAS. Já na PAD, apenas o aumento da intensidade apresentou tal associação. **Conclusão:** O TC é uma intervenção eficaz para reduzir a PAS/PAD e a manipulação de diferentes variáveis do treinamento influencia a magnitude de redução da PA em adultos com hipertensão.

Palavras-chave: Exercício Físico; Exercícios em Circuitos; Pressão Arterial; Hipertensão; Fatores de Risco de Doenças Cardíacas

1 INTRODUÇÃO

A hipertensão arterial sistêmica (HAS) é o principal fator de risco para doenças cardiovasculares, contribuindo de maneira importante para morbidade e mortalidade da população no Brasil e no mundo[1,2]. Estima-se que a prevalência global de HAS em adultos de 30 a 79 anos é 32% em mulheres e 34% em homens[3]. Dada a alta prevalência e as consequências negativas da HAS, diferentes estratégias têm sido utilizadas no manejo desta condição. Além de estratégias farmacológicas, mudanças no estilo de vida através da prática regular de exercícios físicos (EF) são altamente recomendadas[6], incluindo naqueles que já fazem uso de tratamento medicamentoso[4,5], podendo ser tão eficaz quanto a maioria dos medicamentos anti-hipertensivos para a redução da PA em indivíduos adultos com HAS[7,8].

Indivíduos adultos com HAS são aconselhados a praticar pelo menos 30 minutos de exercícios aeróbios de intensidade moderada, em 5-7 dias/semana por pelo menos 150 minutos por semana. Além disso, exercícios resistidos são recomendados em 2-3 dias por semana[5,9]. O treinamento físico composto por exercícios aeróbios é considerado o principal tipo de EF para a prevenção, tratamento e controle da HAS, existindo um amplo consenso de evidências de que o treinamento aeróbio é altamente eficaz na redução PA, com magnitudes interessantes de redução (-6/10 mmHg),[10,11]. Já os programas de treinamento compostos apenas por exercícios resistidos, embora eficazes, parecem promover reduções mais modestas na PA em indivíduos adultos com HAS (-2/4 mmHg)[12,13].

Estratégias que associem a realização de exercícios resistidos e aeróbios em um mesmo treinamento (i.e., treinamento combinado - TC) tem sido amplamente indicadas para promoção da saúde, justamente por permitir que diferentes benefícios, oriundos de cada tipo de treinamento, sejam obtidos simultaneamente[14]. O treinamento aeróbio é considerado a melhor estratégia para melhorar a aptidão cardiorrespiratória e outros fatores de risco cardiometabólicos (i.e., obesidade, dislipidemia e perfil glicêmico)[15,16], enquanto o treinamento resistido é a intervenção fundamental para ganhos de força, potência e massa muscular[17].

Devido aos potenciais benefícios da combinação de exercícios aeróbios e resistidos na saúde da população, diferentes estudos têm sido conduzidos para avaliar os efeitos do TC na PA de adultos normotensos e hipertensos. Reduções importantes na PA sistólica e diastólica (-5/4 mmHg) podem ser obtidas através desse modelo de treinamento, com maiores magnitudes em indivíduos com valores de PA repouso mais elevadas[11]. Entretanto, ainda não é claro a influência das diferentes variáveis de cada tipo de exercício relacionados a frequência, intensidade do exercício, volume e ordem de execução dos exercícios aeróbios e resistidos[19], nas mudanças da pressão arterial ao final de programas de TC em indivíduos adultos com HAS.

2 REVISÃO DE LITERATURA

2.1 Hipertensão Arterial Sistêmica

A HAS é caracterizada pela elevação crônica da pressão arterial (PA) acima de 140 mmHg ou 90 mmHg para PA sistólica e diastólica, respectivamente, sendo a PA o produto do débito cardíaco e da resistência vascular periférica[5]. Pacientes com HAS podem apresentar aumento de um fator ou ambos, no qual, em adultos mais novos o débito cardíaco é frequentemente elevado, enquanto em idosos o aumento da resistência vascular periférica desempenha um papel dominante[20]. O controle da PA é de enorme importância clínica e de saúde pública devido à alta prevalência de HAS, com um aumento consistente nas tendências de prevalência. Estima-se que a prevalência global de HAS em adultos de 30 a 79 anos é 32% em mulheres e 34% em homens em todo mundo, e no Brasil o percentual de mulheres e homens com PA maior ou igual que 140 por 90 mmHg é de 42% e 47%, respectivamente[3,21].

A elevada sustentação da PA é responsável a longo prazo por danos aos órgãos-alvo que resultam em aumento da morbidade e mortalidade, sendo responsável por 8,5 milhões de mortes por acidente vascular cerebral, doença isquêmica do coração e outras doenças vasculares e renais em todo o mundo[3,4]. Em média, uma redução de 5 mmHg da PA sistólica é capaz de reduzir o risco de um evento cardiovascular maior em cerca de 10%, e para acidente vascular cerebral, insuficiência cardíaca e doença cardíaca isquêmica em 13%, 12% e 8%, respectivamente[22]. A causa da HAS é de natureza multifatorial, com fatores ambientais, genéticos e determinantes sociais possuindo o potencial para contribuir para o seu desenvolvimento[23]. Embora a causa da PA elevada é complexa e multifacetada entre adultos, evidências consistentes destacam a inatividade física, tabagismo, consumo excessivo de álcool e maus hábitos alimentares (i.e., alto teor de sódio, baixo teor de potássio, frutas limitadas e pouca ingestão de vegetais) como os principais contribuintes[24,25].

O manejo adequado da HAS é vital para amenizar as possíveis incapacidades e perda de qualidade de vida, além do aumento de custos dos sistemas de saúde, com importante impacto socioeconômico[26]. Para tanto, a abordagem terapêutica inclui medidas não-farmacológicas e o uso de fármacos anti-hipertensivos, a fim de reduzir a PA, proteger órgãos-alvo e prevenir desfechos cardiovasculares e renais[27]. Diretrizes mais recentes para o manejo da HAS[4,5] recomendam a instituição de medidas com estilo de vida, sempre que apropriado, em todos os indivíduos adultos com HAS, incluindo aqueles que necessitam de tratamento medicamentoso. A redução da ingestão de álcool e sal, cessação do tabagismo, realização de EF regular, perda de peso e dieta, são as principais mudanças no estilo de vida que determinam os melhores resultados para prevenção e tratamento da HAS[28].

2.2 Exercício Físico e Pressão Arterial

Mudanças no estilo de vida são essenciais para o tratamento da HAS, fato corroborado por diretrizes nacionais[5] e internacionais[4] sobre o tema, que recomendam abordagens baseadas apenas no estilo de vida como a primeira linha de terapia para redução da PA. O EF é considerado uma estratégia não-farmacológica eficaz na prevenção e tratamento da HAS, podendo fazer parte do tratamento através de mudanças no estilo de vida para adultos de baixo risco ou pode ser usado em combinação com fármacos para indivíduos adultos com HAS com perfil de risco aumentado[8,29].

Em meta-análise de rede recente[7], no qual 391 ensaios clínicos randomizados foram incluídos (n=39.742), foi realizado uma comparação sobre os efeitos na redução da PA sistólica do uso de medicamentos anti-hipertensivos e intervenções de EF, onde foram observados que diferentes tipos de intervenções de EF parecem ser tão eficazes quanto a maioria dos medicamentos anti-hipertensivos em adultos com PA elevada (>140/90 mmHg) com redução semelhante de -8 mmHg na PA sistólica. Descobertas que possibilitam formar a base de discussões baseadas em evidências sobre os benefícios do EF na redução da PA.

Ainda não é claro os mecanismos responsáveis exatos dos efeitos benéficos que o EF produz sobre a PA, provavelmente porque a regulação da PA é complexa e multifatorial, entretanto o possível principal mecanismo pelo qual o EF pode afetar a PA é a regulação da função endotelial. O óxido nítrico (NO) é um mediador chave da função endotelial, e estudos clínicos e pré-clínicos confirmaram a capacidade do EF de melhorar a vasodilatação endotelial dependente de NO[30]. A alta produção de NO ocorre em resposta ao aumento do fluxo sanguíneo para compensar o estresse de cisalhamento por vasodilatação[31], de forma que, o EF resulta em exposição repetida ao estresse de cisalhamento, melhorando assim a biodisponibilidade do NO[32]. Além disso, mecanismos subjacentes como: aumento na complacência vascular (capacidade do vaso de se contrair e relaxar); aumento na capacidade de bombeamento do coração, reduzindo a frequência cardíaca e a pressão do fluxo coronário; atenuação da atividade nervosa simpática, pelo aumento da atividade vagal; neovascularização e melhora da sensibilidade a insulina, são possíveis mecanismos responsáveis pela redução da PA através do EF[33,34].

Indivíduos adultos com HAS são aconselhados a praticar pelo menos 30 minutos de exercícios aeróbios de intensidade moderada, em 5-7 dias/semana por pelo menos 150 minutos por semana. Além disso, exercícios resistidos são recomendados 2-3 dias por semana[5,9]. Mais de 20 meta-análises foram realizadas desde o ano 2000 para verificar os efeitos da redução PA através de programas de treinamento com exercícios aeróbios, existindo um amplo consenso de evidências de que o exercício aeróbio deve ser prescrito como o principal tipo de EF para a prevenção, tratamento e controle da HAS, em particular, devido ao treinamento aeróbio ser capaz em reduzir a PA em maiores magnitudes (-6/10 mmHg), possuir mais estudos de qualidade sobre o tema, e por reunir inúmeros estudos que utilizaram a medida ambulatorial de pressão arterial como método de avaliação[10,11]. Já nos programas de exercícios resistidos, mais de 7 meta-análises foram realizadas acerca do tema[12,35]. Esses estudos também sugerem que esse tipo de treinamento pode ser eficaz na redução de PA, especialmente naqueles com PA de repouso mais elevada. Entretanto, os programas de treinamento compostos apenas por exercícios resistidos, embora eficazes, parecem promover reduções mais modestas na PA em indivíduos adultos com HAS (-2/4 mmHg)[12,13].

2.3 Treinamento Combinado e Pressão Arterial

O treinamento combinado (TC), que envolve a combinação de exercícios aeróbios e resistidos em um mesmo programa de treinamento, tem sido a modalidade de EF mais indicada para promoção da saúde, devido ao seu potencial de induzir simultaneamente ganhos oriundos dessas duas formas de treinamento[14]. De certa forma, o treinamento aeróbio é considerado a melhor estratégia de EF para melhorar a aptidão cardiorrespiratória e outros fatores de risco cardiometabólicos (i.e., obesidade, dislipidemia e perfil glicêmico)[15,16], enquanto o treinamento resistido é a intervenção fundamental para ganhos de força muscular, ganho de massa muscular e densidade óssea, embora também é capaz de produzir melhorias na saúde cardiometabólica[17].

Até a presente revisão, poucos estudos originais foram conduzidos para avaliar os efeitos do TC na PA, quando essa é o desfecho primário do estudo. Em um estudo recente, publicado na *European Association of Preventive Cardiology*[11], os autores realizaram uma análise agrupada de 6 meta-análises acerca do tema, onde observaram reduções da PA sistólica e diastólica com TC (-5/4 mmHg) com maiores reduções em adultos com PA mais elevadas. Em outra meta-análise de rede recente, ao comparar 5 modalidades diferentes de EF, o TC foi o melhor tratamento de EF para diminuir a PA em adultos com sobrepeso e obesidade[36]. Entretanto, uma alta heterogeneidade estatística foi encontrada nas meta-análises com TC na redução da PA, fato que sugere cautela ao interpretar os resultados. Em particular, a heterogeneidade estatística se deve a grande heterogeneidade metodológica envolvida na manipulação e prescrição do TC, que envolve a manipulação das variáveis do treinamento, tanto do aeróbio quanto do resistido.

Diferentes variáveis podem ser capazes de influenciar as respostas cardiovasculares e hemodinâmicas do treinamento realizado. Destaca-se, entre as mais comuns, a frequência (duração da intervenção [semanas], frequência semanal [dias] e comparecimento às sessões de treino [%]) intensidade (%VO_{2max} e %1RM para treinamento aeróbio e resistido, respectivamente), volume (treinamento aeróbio [min/semana] e resistido [séries*repetições*exercícios/semana) e ordem de execução dos exercícios aeróbios e resistidos[19].

Em relação as variáveis de frequência semanal e duração da intervenção, é recomendado que o EF seja realizado em uma maior frequência por semana (≥3 dias) por um período de no mínimo 12 semanas para redução da PA[37]. O motivo pelo qual o EF deve ser recomendado na maioria dos dias, é devido a PA ser mais baixa nos dias em que as pessoas se exercitam em comparação com os dias em que não realizam EF. Esta resposta fisiológica é denominada hipotensão pós-exercício (HPE)[38], onde a HPE é a redução imediata na PA que ocorre após uma única sessão isolada de EF[39], sendo a magnitude da HPE fortemente relacionado as mudanças no longo prazo na PA com o treinamento físico[40].

No que diz respeito na manipulação do volume e da intensidade, parece que o exercício realizado com intensidades mais altas e em maiores volumes é capaz de promover reduções em maiores magnitudes na PA em indivíduos adultos com HAS[41,42]. Em meta-análise recente, pesquisadores decidiram investigar os efeitos na progressão da intensidade e do volume na redução da PA em indivíduos adultos com HAS. Mesmo os autores não encontrando diferença na redução da PA entre o treinamento aeróbio com e sem progressão, reduções de maiores magnitudes (-13/7 mmHg) ocorreram em estudos que progrediram nas variáveis de intensidade e volume separadamente[43]. Da mesma forma para o treinamento resistido, maiores reduções foram observadas quando realizado em maiores intensidades e volumes[12,13].

Parece existir uma relação dose-resposta dessas variáveis do treinamento sobre a PA, no qual maiores doses de EF seriam mais efetivas[42,44]. Em uma meta-análise de estudos de corte[45], foi quantificado a relação dose-resposta entre EF e incidência de hipertensão em adultos com PA normal. Entre 330.222 adultos com PA normal, ocorreram 67.698 casos incidentes de hipertensão (20,5% da amostra) após 2 a 20 anos de seguimento. O risco de hipertensão foi reduzido em 6% quando realizado 150 min/semana de EF moderado-vigoroso em adultos com PA normal. O efeito protetor aumentou em cerca de 6% para cada aumento adicional de 150 min/semana; já para adultos com 300 min/semana de EF leve, moderada e/ou vigorosa, o risco de hipertensão foi reduzido em 12%; e para aqueles com doses elevadas de EF (900 min/semana), o risco de hipertensão foi reduzido em 33%. Até o presente momento, nenhuma meta-análise incluindo ensaios clínicos randomizados investigou de que forma a manipulação das diferentes variáveis do TC influenciam nas mudanças sobre a PA em indivíduos adultos com HAS[11,16].

3 JUSTIFICATIVA

O presente estudo justifica-se pela necessidade de entender os potenciais efeitos do treinamento combinado sobre a pressão arterial em indivíduos adultos com HAS, visto que ainda existem lacunas sobre a possível relação dose-resposta entre as diferentes variáveis do treinamento combinado (frequência, intensidade, volume e ordem de execução) sobre as mudanças da PA. Tais achados serão importantes para entendermos qual é a dose ideal de exercícios aeróbios e de força, em um programa de treinamento combinado, para indivíduos adultos com HAS.

4 OBJETIVOS

4.1 Objetivo Geral

Avaliar a efetividade do treinamento combinado e verificar a influência das variáveis do exercício aeróbio e de força, em um programa de treinamento combinado, sobre a redução da pressão arterial em indivíduos adultos com hipertensão arterial.

4.2 Objetivos Específicos

Sumarizar, através de abordagem meta-analítica, a variação na pressão arterial após programa de treinamento combinado versus um grupo controle sem exercício em indivíduos adultos com hipertensão arterial.

Verificar uma possível relação dose-resposta das seguintes variáveis do treinamento combinado: frequência (duração da intervenção [semanas], frequência semanal [dias] e comparecimento às sessões de treino [%]) intensidade (%VO_{2max} e %1RM para treinamento aeróbio e resistido, respectivamente), volume (treinamento aeróbio [min/semana] e resistido [séries*repetições*exercícios/semana) e ordem de execução dos exercícios aeróbios e resistidos, através de meta-regressões sobre as mudanças da pressão arterial em indivíduos adultos com hipertensão arterial.

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6 ARTIGO CIENTÍFICO

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Influence of variables in combined training on blood pressure reduction in adults with hypertension: a systematic review with meta-analysis and meta-regression

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ABSTRACT

Aim: The purpose of this systematic review with meta-analysis and meta-regression evaluated the efficacy of combined training and the influence of acute variables of aerobic and strength exercise within a combined training program on BP reduction in adults with hypertension. **Methods**: Randomized clinical trials in adults with hypertension of interventions involving CT versus a non-exercise control group (CG) were included. Searches of MEDLINE via PubMed, Cochrane Central, EMBASE, Scopus, and LILACS databases were searched between June and December 2021 to find the studies. The methodological quality of the studies was assessed using the TESTEX checklist. A random effects meta-analysis was performed using the mean difference (MD) in BP change from baseline comparing CT versus CG as the effective measure. A simple meta-regression analysis was performed to assess the relationship between the CT variables (follow-up, weekly frequency, intensity, weekly volume, and frequency) and BP reduction. **Results**: Thirty-seven studies with 41 interventions (1942 participants) were analyzed. The pooled MDs results with 95% confidence interval (95% CI) on systolic (SBP) and diastolic (DBP) BP indicated a significant decrease in CT compared with CG, but containing significant heterogeneity (SBP, -6.4 mmHg; 95% CI, -9.1 to -3.6; DBP, -3.7 mmHg; 95% CI, -4.9 to -2.4). Meta-regression analysis revealed that an increase in exercise intensity and weekly training volume is associated with a greater magnitude of reduction in SBP. In DBP, only the increase in intensity showed such an association. **Conclusion**: CT is an effective intervention to reduce SBP/DBP and the manipulation of different acute training variables influences the magnitude of BP reduction in adults with hypertension.

Keywords: Exercise; Circuit-Based Exercise; Blood pressure; Cardiovascular diseases; Heart disease risk factors

INTRODUCTION

Hypertension is the main risk factor for cardiovascular diseases and mortality[1], with increased prevalence due to aging[2] and physical inactivity[3]. Regular physical exercise has been suggested as the first line of non-pharmacological therapy for hypertension[4,5]. Current guidelines for the treatment of hypertension have suggested aerobic training as the most efficacy exercise intervention for BP reduction, with reductions between 6-10 mmHg[6,7]. Resistance training performed alone also reduces BP among adults with hypertension but at lower magnitudes (i.e., 2-3 mmHg)[8,9]. In addition to the benefit on blood pressure, aerobic training is considered the best exercise strategy to improve cardiorespiratory fitness and other cardiometabolic risk factors (i.e., obesity, dyslipidemia, and glycemic profile)[10,11], while resistance training is the cornerstone intervention muscle strength, muscle mass gain, and bone density[12]. Taken together, the combination of aerobic and resistance training, known as combined training, seems to be the ideal physical exercise modality for simultaneously improving these health-related outcomes[13].

The meta-analysis that has evaluated the effects of combined training on blood pressure has found controversial results, with reductions in systolic and diastolic BP between 1 and 6 mmHg[7,11,14,15] or no reduction[16,17]. The variation in BP response after combined training may be related to the use of different acute training variables during each type of exercise (i.e., aerobic and resistance), such as time of follow-up (weeks), weekly frequency (days), exercise intensity (%VO_{2max} and %1RM for aerobic and resistance training, respectively), and weekly volume (min.·week)[18]. Previous meta-analyses investigated associations between the acute training variables of aerobic training and resistance training alone on blood pressure behavior, in which potential dose-response relationships between acute variables and BP reduction were observed, with higher training doses promoting greater reductions[19,20]. However, there is insufficient evidence to determine how much the relationship between the magnitude of BP reduction and exercise varies as a function of follow-up, weekly frequency, exercise intensity, and weekly volume.

No previous meta-analysis has verified the effects of combined training in adults with hypertension alone and also no exploration of statistical heterogeneity considering acute variables of combined training as a potential modifier in effect size was performed. Our systematic review aims to update the evidence on the effects of combined training and, in particular, to study the dose-response relationship of follow-up, frequency, intensity, and the weekly volume of combined training interventions on BP reduction in adults with hypertension.

2. METHODS

We followed the instructions outlined in the Cochrane Handbook for Systematic Reviews to conduct our systematic review[21]. In addition, the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA)[22], and implemented PRISMA in Exercise, Rehabilitation, Sport medicine and SporTs science (PERSiST)[23] for reporting systematic reviews were also followed. This study is registered on the International Prospective Register of Systematic Reviews: PROSPERO (CRD42021284886).

Eligibility Criteria

Types of studies

Only randomized controlled trials comparing a combined training intervention (i.e., aerobic + resistance) with a non-exercise control treatment were eligible for this study.

Participants

We included studies with adults ≥ 18 years (men and women) with hypertension (SBP ≥ 130 mmHg or DBP ≥ 80 mmHg or using any antihypertensive medication)[4]. Studies with participants who had metabolic or cardiovascular risk factors in combination with hypertension were also included. We excluded studies with populations with cardiovascular or other diseases (i.e., cancer, HIV/AIDS, lung and cognitive disorders).

Combined training interventions

The combined training interventions included the combination of any aerobic exercise on land (i.e., cycling, walking, or running) with any dynamic resistance/strength training performed near each other (i.e., in a single session or on separate days), with a minimum duration of 4 weeks. Combined training was considered in which the participants performed the training with supervision by an exercise training specialist. Unsupervised combined training programs and with co-interventions (diet or lifestyle counseling and titration of medication) were not included.

Non-exercising control interventions

As a comparator intervention, a group of the participants who did not perform any type of regular exercise training was included. Studies in which the control group was involved in any exercise or physical activity intervention (including stretching) were excluded.

Outcomes assessment

The outcomes of interest were measurements of changes in systolic and/or diastolic BP after combined training interventions that could be assessed by different BP measurement methods (i.e., auscultatory, oscillometric or ambulatory monitoring)

Search strategy

We systematically searched in PubMed, Cochrane Central, Embase, Scopus, and LILACS databases, between June and December 2021. In the search strategy, we used the terms "Combined training" and "Randomized clinical trials, complementing with the addition of keywords (synonyms) and MeSH/ DeCS terms through boolean operators (AND/OR). The complete search strategy that was used in all databases is detailed in the supplementary table S1.

Previous systematic reviews of related topics were also searched for relevant studies[9,14] and references of identified potentially relevant studies were manually searched for inclusion of additional studies. In addition, to search the gray literature (unpublished studies) we used Google Scholar[24] to identify possible studies eligible for inclusion in the review. There was no language or year of study limitation in our search, however we found only studies published in English or Portuguese that met the eligibility criteria. All searches were conducted by the same author (V.M.S.), the search results were collated using EndNote software (Thomson Reuters, New York), and duplicates were removed.

Selection and Data collection process

The screening was carried out independently, following the exclusion of duplicate articles by two reviewers blind (V.M.S. and L.B.D). Initially, these authors screened titles and abstracts to identify potentially relevant articles according to the eligibility criteria described above. Any study selected for the next step of the evaluation was analysis in full text and considered if, after the randomization, reported pre-post intervention BP changes after a combined training intervention versus a control group. Disagreements regarding the eligibility of the studies were resolved by consensus and, eventually, by a third reviewer (R.F). The study selection process followed the PRISMA flowchart in figure 1[23].

The authors (V.M.S. and L.B.D.) independently performed data extraction using a standardized form in Microsoft Excel (2020). Data regarding the characterization of the sample (number of participants included in the analysis, age of the participants, athletic category, baseline BP values, gender of the sample, and cardiovascular risks factors) were extracted; protocol adherence (session attendance [%]), sample loss rate (participants dropout [%]), acute variables of the combined training interventions (weekly duration [min.·week^{-1}], volume, frequency, follow-up, intensity and type) and method of BP assessment used in each study were also collected. Data were extracted in their original units of mean, and measures of dispersion (standard deviation, standard error, confidence interval) or the mean difference before and after the training period for the systolic and diastolic BP results of interventions (i.e., combined training and control groups). If there was not enough information, the authors of these studies (n=4)[25-28] were contacted via e-mail. Three studies[25,26,28] did not respond to the email. So, we used the online Web Plot Digitizer software (https://apps.automeris.io/wpd/) to extract BP data for further analysis in our review. In addition, we performed the classification and standardization of the combined training intensity (aerobic + resistance) for further analysis at Low = 1; Moderate = 2; Vigorous = 3[19]. Being low when performed between 37-45%VO_{2max} and 30-49%1RM; moderate between 46-63%VO_{2max} and 50-69%1RM; vigorous ≥64%VO_{2max} and ≥70%1RM. In studies that did not report the intensity of aerobic exercise in %VO_{2max}, the intensity was converted to %VO_{2max} using the classification of exercise intensity correspondence table[19].

Methodological quality

The methodological quality of the included studies was assessed using the "Tool for the assesment of Study qualiTy and reporting in EXercise" (TESTEX) checklist[29], two reviewers (V.M.S. and L.B.D.) evaluated each study and they worked independently. The checklist has two sections that refer to study quality (items 1–5) and study reporting (items 6–12). Each item on the TESTEX checklist is answered with a "yes" if the criteria are satisfied or with a "no" if the criteria are not satisfied (only the answer "yes" is associated with a point). Items 6 and 8 have three and two questions, respectively. The answer "yes" to each of these sub-questions is also associated with a point. Therefore, the maximum number of possible points on the checklist is 15. Based on the summary scores, we classified studies from 0 to 5 points as a low quality study, from 16 to 10 points as a medium quality study, and from 11 to 15 points as a high quality study.

Data synthesis and statistical analysis

Effect sizes were calculated based on the change score (mean difference, MD) with a 95% confidence interval (95% CI) between baseline and follow-up measures to demonstrate the clinical impact of combined training. Random effects models were used because great heterogeneity was expected due to the different methodological variations of the studies. Primarily, an pooled analysis of combined training versus the control group on the effects on systolic and diastolic BP was conducted. P values ≤0.05 were considered statistically significant. Heterogeneity was assessed using the Cochran Q (chi2) test, with P ≤0.05 indicating statistically significant heterogeneity between treatment effects. The extent of heterogeneity was quantified using the inconsistency index (I^2), and values >50% were considered to represent substantial heterogeneity[21].

Subgroup analyses were performed to investigate possible factors that promoted statistical heterogeneity in our analysis. We assumed that different baseline BP values, BP assessment methods, and assessment of systolic and diastolic BP as the primary or secondary outcomes may have influenced heterogeneity. Meta-regression analysis was performed to investigate potential moderators in estimating effect: baseline BP values follow-up duration (weeks), weekly frequency (number of sessions per week), intensity (aerobic + resistance), weekly volume ($min \cdot week^{-1}$), attendance, mean age, and TEXTEX score. A minimum of 10 studies per moderator was required to perform meta-regression[21].

Publication bias was assessed by visually examining the asymmetry of the funnel plot of the analysis variable (systolic and diastolic BP). The Egger test was used to verify the funnel asymmetry, being considered significant when P ≤ 0.05. In case of publication bias, the trim and fill method would be performed to identify and correct the asymmetry of the funnel plot and produce a new effect estimate. Statistical analysis and the forest plots were performed in OpenMeta Analyst Software version 10.10[30].

RESULTS

A total of 4606 records were retrieved from database searches, of which 2764 records were duplicates. A further 1784 records were eliminated after the screening of titles and abstracts. Seventeen potentially relevant articles were identified from the screening of systematic review and gray literature reference lists.

After screening the full text of 99 articles (82 via databases and 17 other methods), 37 randomized clinical trials were included in this review. Four trials included multiple arms of combined training, therefore 41 interventions for systolic BP and 38 interventions for diastolic BP were included. Participants were randomized individually in all clinical trials. The flowchart of study selection is shown in figure 1.

Study characteristics

A detailed summary of the characteristics of the 37 studies (41 interventions) included is described in supplementary material table S2. Most of the included studies were European (32%) or Brazilian (30%). In total, 37 trials including 1942 participants (1028 combined training and 914 control group without exercise) aged 60 years (range 39-85 years) were analysis. Fifteen trials (40%) included populations with chronic diseases and cardiovascular risk factors (i.e., type 2 diabetes, obesity, metabolic syndrome) in combination with hypertension. On average, participants had baseline systolic BP values of 138 mmHg (range 124-160 mmHg), and diastolic BP of 82 mmHg (range 70-95 mmHg).

The combined training programs lasted 22 weeks (range 4-52 weeks) and were performed 3 days a week (range 1-5 days). The participants achieved adherence of 86% to the training sessions (range 70-100%), and the dropout rate was 7% (range 0-24%).

Of the 37 studies, 20 studies (54%) fully reported details of the combined training program. The individual details of the combined training program are presented in supplementary material table S2. The intensity of aerobic exercise during the combined training was 65% VO_{2max} (range 40-85% VO_{2max}), each aerobic exercise session lasted 30 minutes (range 17-45 minutes), and were performed on treadmills, bicycles or ellipticals. During the resistance training, an intensity corresponding to 65% (range 50-80%) of the one maximum repetition test (1RM), 8-20 repetitions per set, 1-4 sets per exercise, and a total of 5-15 exercises per session were adopted. The weekly volume of the combined training was 170 $min \cdot week^{-1}$ (range 60-270 $min \cdot week^{-1}$). All studies reported the order of execution of aerobic and resistance exercises during combined training. Twenty-six interventions initiated with aerobic exercises followed by resistance exercises, and 10 started with resistance exercises followed by aerobic exercises and during 5 combined training interventions, the aerobic and resistance exercises were performed on separate days.

In the control interventions, participants were usually instructed to continue with their habitual activity (n=16 studies). Seven studies provided lifestyle advice and discussion about physical activity levels, but no structured/supervised exercise to the control group. In another 3 studies, participants had to visit the research laboratory 2-3 days a week to attend lectures with lifestyle themed sessions. Eleven studies did not report details about the control group.

Combined training effect on blood pressure

The systolic (n=41 interventions) and diastolic (n=38 interventions) BP results after combined training are presented in figures 2 and 3. When compared to the control, combined training reduced systolic BP (MD: -6.4 mmHg, 95% CI: 9.1 to -3.7, $P < 0.001$) and diastolic BP (MD: -3.7 mmHg, 95% CI: 5.0 to -2.4, $P < 0.001$). There was significant heterogeneity between studies in systolic BP ($I^2 = 84\%$, P for heterogeneity <0.001) and diastolic BP ($I^2 = 68\%$, P for heterogeneity <0.001) after combined training. Figure 2 and 3 shows the forest plots for systolic and diastolic BP.

Quality assessment (Risk of bias) and publication bias

Supplementary Material Figure S1 presents the results of the quality assessment. The average score on the checklist was 8 points (range 4-14 points). Based on the qualitative classification, 8 studies presented high methodological quality, 24 studies medium, and 5 low methodological qualities. Egger's regression test showed no publication bias for combined training in the analysis of systolic ($P = 0.96$) and diastolic ($P = 0.63$) BP (see Figure S2 and S3 in Supplementary material).

Subgroup analysis

Table 2 displays the results of the subgroup analysis, we found that the baseline BP and the method used to evaluate BP can influence the magnitude of BP reduction after combined training. A higher BP value at baseline is associated with greater BP reduction after combined training. In relation to the BP measurement, for systolic BP, only the studies that assessed BP through the oscillometric method showed BP reductions after combined training. For diastolic BP, the oscillometric and the auscultatory methods reduced BP after exercise. No significant BP reductions after combined training were observed when BP was assessed through the ambulatory BP monitoring method ($P= 0.17$). Finally, when analysing studies that assessed systolic and diastolic BP as primary or secondary outcome, we observed greater magnitudes of reduction in systolic and diastolic BP when studied the primary outcome.

Meta-regression

According to the results of the meta-regression analysis baseline BP, weekly volume, and the intensity of the combined training intervention were associated with the magnitude of BP reduction after the exercise interventions. For systolic BP, baseline BP between 135-165 mmHg seems to promote greater reductions after combined training. Similarly, combined training interventions performed for 150-270 min.week^{-1} with moderate to vigorous intensities seem to promote greater reductions in systolic BP. For diastolic BP, baseline BP between 75-95 mmHg and moderate or vigorous intensities seem to promote greater reductions after a combined training intervention. Mean age, attendance, weekly frequency, follow-up duration, and TEXTEX score were not associated with any additional BP improvement after combined training (Table 3).

DISCUSSION

The purpose of our study was to evaluate the efficacy of combined training and deepen the dose-response relationship of the acute training variables in the reduction of BP in adults with hypertension. We found a reduction in systolic and diastolic BP of -6.4 mmHg and -3.7 mmHg, respectively, favouring the combined training versus a control group without exercise. Furthermore, our findings showed that baseline BP values, weekly volume, and intensity were possible moderators in the BP reduction response. The findings found in the present review are clinically important, mainly due to the role of BP as a predictor of cardiovascular disease and mortality[31,32]. The magnitudes of reduction we found through interventions with combined training (-6.4/-3.7 mmHg) are shown to reduce stroke and heart failure by 13%, coronary artery disease by 8%, and cardiovascular death by 5%[33]. Previous reviews have also found a beneficial effect of combined training on BP reduction, however smaller magnitudes of reduction were observed (-3/-4 mmHg)[14,15]. The explanation why we observed a greater magnitude of BP reduction in the present study is possibly due to the update of new evidence on the subject and, mainly, to our eligibility criteria for inclusion of studies in the review (only adults with hypertension in all age groups and interventions with combined training without co-intervention).

The analysis indicated considerable heterogeneity[21] in relation to changes in the overall analysis of the combined training versus the control group (I^2 = 84% for systolic BP, I^2 = 68% for diastolic BP). We performed meta-regression analyses to investigate possible moderators influencing heterogeneity. Results showed an association between baseline values, weekly volume, and intensity for greater systolic BP reduction, and for diastolic BP baseline values and weekly volume were associated with greater reductions. These analysis are based on 25-41 interventions, which is greater than the minimum number of 20 observations recommended for meta-regression analysis[34]. The results suggest that adults with hypertension elevated resting BP values may benefit even more from combined training interventions, this is possibly because the magnitude of the BP reduction after exercise is directly related to the preintervention BP of the participants[35]. Furthermore, it seems that combined training when performed for longer periods, with higher intensities, may result in greater reductions in BP, with the total overload of training (volume + intensity) being of great importance for the reduction of BP, both for aerobic exercises[7,36], and resistance exercises[8,37]. With combined training, we have the simultaneous performance of these modalities of physical exercise, where we must be careful to apply the minimum dose when we combine aerobic and resistance exercises to achieve reductions in BP. Through meta-regression we could observe a minimum dose to be applied with the combined training, we observed that studies carried out with larger weekly volumes at moderate-vigorous intensities showed reductions in BP of greater magnitude, and when carried out at smaller volumes at low intensities, smaller magnitudes were observed. It appears that intensity and volume of combined training are determinants of BP reduction in a dose-response pattern, possibly because when exercise is performed at higher volumes and intensities, a greater acute peak of BP reduction occurs in the training session, so that the acute reduction in

BP after exercise may predict the extent of BP lowering after chronic training interventions[38,39]. The mechanisms that explain a greater reduction in BP through increases in volume and intensity of combined training have not yet been completely clarified, it is possible that different isolated or combined physiological routes contributed to such a phenomenon. Evidence suggests that greater improvements in endothelial function, increased insulin sensitivity and neural parameters, such as reduced sympathetic activation, explain the mechanisms behind the benefits when exercise training is performed at higher exercise volumes and intensities[40,41]. However, further studies on the chronic effects of different intensities and volumes of aerobic and resistance exercises in adults with hypertension should be explored.

When organized into subgroups, we found greater effect modifications in the magnitude of the reduction of systolic and diastolic BP in studies that used oscillometric/auscultatory methods to measure BP, while in studies that used 24h ambulatory monitoring no reductions were observed ($P = 0.13$ for systolic; $P = 0.17$ for diastolic). It is well known that the use of ambulatory monitoring over a 24h period is the gold standard for measuring BP, and may promote more accurate measurements due to the multiple readings taken throughout the day, and may be more useful in not overestimating actual BP and identifying possible masked, white coat hypertension[42]. In addition, oscillometric and auscultatory methods for BP measurement may produce uncertainties in the measurements due to the different protocols used that increase their variability[43]. In the studies included in this review, the measurement protocols with oscillometric and auscultatory methods differed between the trials, the differences in measurement techniques between the trials include the device used, the use and duration of a resting period, the number of measurements taken and the number of measurement occasions, protocol differences that may have influenced the BP results. A possible explanation for not finding a reduction in subgroup analysis by ambulatory monitoring is that of the 4 interventions included in the analysis, 2 interventions had adults with controlled hypertension <130/80 mmHg[44] where no reductions in BP were observed with combined training, whereas 2 other interventions observed reductions with ambulatory monitoring[26,45].

The findings of this systematic review need to be considered in the context of some limitations. We found statistically significant heterogeneity for the main outcomes of systolic and diastolic BP. However, we were able to explain this heterogeneity by meta-regression analysis, where methodological variations and differences between studies were explained by the moderators of combined training volume and intensity and baseline BP values of participants in the studies. Furthermore, although the meta-regression analysis did not indicate influence of study quality on effect estimates, most studies were of medium-high quality and randomized clinical trials, however, few studies adequately reported the process of randomization, allocation concealment or blinding of outcome assessment, which may have affected the estimates of outcomes with combined training. Another limitation that can be pointed out and may have influenced the results, is that most studies used oscillometric and auscultatory methods for BP measurement, instead of a gold standard method such as 24h ambulatory monitoring that would allow greater reliability in pre- and post-intervention BP measurements.It is recommended to future researchers that further studies are needed using ambulatory monitoring for BP assessment. It is worth noting that the present findings by subgroup analysis and meta-regression should be interpreted with caution, false negative and false positive significance tests increase in likelihood as more sensitivity analyses are performed[21]. Furthermore, subgroup analyses and meta-regressions are observational in nature and are not based on random comparisons. We encourage more studies with combined training to be conducted, in particular, using ambulatory monitoring to assess BP, and especially to directly investigate the effects of different acute training variables.

The strengths of our systematic review are also evident. This is the first review that evaluated the effects of combined training versus a control group without exercise to include only adults with hypertension, who did not perform any other co-intervention with professional monitoring during exercise sessions. We produced new updates about the effects of combined training on the reduction of BP, where through meta-regression analysis, we were able to demonstrate a possible influence of the acute training variables of physical exercise, especially on the volume and intensity in the reduction of BP, which was the main objective of our study. Another strong point to be highlighted is that we correctly implemented the practices recommended in systematic reviews, which included independent procedures in practically all phases and taking specific care to avoid the duplication of results generated by common samples in different studies. Similarly, we found no publication bias in our analysis, which reinforces the extensive search we conducted in the databases including positive and negative studies on the topic.

CONCLUSION

Our findings suggest that the combined training is an effective intervention in reducing systolic and diastolic BP in adults with hypertension. In addition, we evidenced a potential dose-response relationship between the magnitude of BP reduction with higher volumes and the intensity of the combined training. Even though more evidence is necessary, the combined training appears as an effective supporting intervention for BP reduction, especially in those with higher resting BP values.

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Conflict of interest

None declared.

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Figure legends

Figure 1. PRISMA flow diagram

Figure 2. Random-effects meta-analysis of the effects of combined training versus control group in the reduction of systolic blood pressure.

Figure 3. Random-effects meta-analysis of the effects of combined training versus control group in the reduction of diastolic blood pressure.

Tables

Table 1. Subgroup analysis for net change in blood pressure

Subgroup	Number of interventions	Number of participants CT	CON	Mean difference [95% CI]	P values	Heterogeneity
Systolic Blood Pressure						
Baseline BP values						
>140 mmHg	20	617	576	−8.74 [-12.37 to -5.11]	**< 0.01**	I² = 84%, P < 0.01
130–139 mmHg	14	249	202	−3.93 [-9.19 to 1.33]	0.14	I² = 83%, P < 0.01
120–129 mmHg	6	138	121	−3.13 [-7.41 to 1.14]	0.15	I² = 9%, P = 0.35
BP assessment methods						
Oscillometric	16	462	394	−7.80 [-12.93 to -2.64]	**0.03**	I² = 86%, P < 0.01
Auscultatory	8	224	208	−1.90 [-7.70 to 3.86]	0.51	I² = 70%, P < 0.01
ABPM	4	69	38	−8.34 [-19.35 to 2.65]	0.13	I² = 78%, P = 0.03
Primary outcome	15	431	380	−9.55 [-15.20 to -3.90]	**<0.01**	I² = 89%, P < 0.01
Secondary outcome	26	603	534	−4.52 [-7.62 to -1.42]	**0.04**	I² = 79%, P < 0.01
Diastolic Blood Pressure						
>90 mmHg	5	104	71	−11.15 [-14.24 to -8.07]	**<0.01**	I² = 28%, P = 0.02
80–89 mmHg	19	488	424	−2.94 [-4.66 to -1.21]	**<0.01**	I² = 69%, P < 0.01
<80 mmHg	13	338	330	−2.02 [-3.22 to -0.82]	**<0.01**	I² = 0%, P = 0.98
BP assessment methods						
Oscillometric	16	459	396	−3.51 [-5.80 to -1.22]	**0.03**	I² = 73%, P < 0.01
Auscultatory	8	228	207	−4.19 [-6.78 to -1.60]	**0.02**	I² = 48%, P = 0.06
ABPM	4	69	38	−3.07 [-7.51 to 1.35]	0.17	I² = 0%, P = 0.87
Primary outcome	15	431	380	−5.33 [-7.73 to -2.92]	**<0.01**	I² = 71%, P < 0.01
Secondary outcome	23	529	460	−2.66 [-4.26 to -1.06]	**<0.01**	I² = 69%, P < 0.01

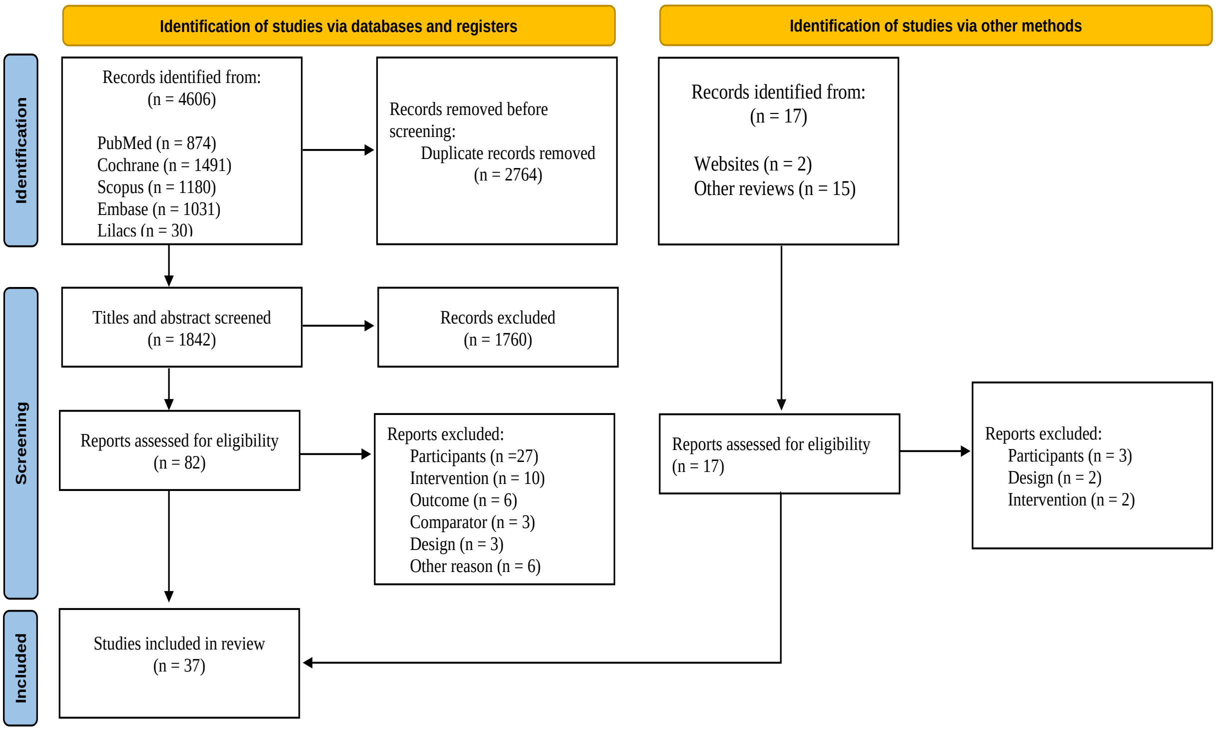
ABPM: ambulatory blood pressure monitoring; BP: blood pressure CT: combined training; CG: control group; P values statistically significant (P < 0.05).

Table 2. Meta-regression analysis for relationships between net change in blood pressure and moderators

Moderator	Number of interventions estimates	Coefficient	P value
Systolic Blood Pressure	**41**		
Baseline Systolic (per 1mmHg)	40	−0.56 (−0.81 to −0.31)	**< 0.01**
Age (per 1 year)	40	−0.03 (−0.37 to 0.30)	0.84
Attendance (per 1%)	26	−0.01 (−0.19 to 0.23)	0.10
Frequency (per 1 day/week)	41	−1.53 (−5.96 to 2.89)	0.49
Weekly volume (per 1 min/week)	33	−0.06 (−0.13 to −0.03)	**0.03**
Follow-up (per 1 week)	41	0.16 (−0.03 to 0.36)	0.10
Intensity (1=low, 2= moderate, 3= vigorous)	28	−5.70 (−11.36 to −0.05)	**0.04**
TESTEX score (per 1 point)	41	0.71 (−0.45 to 1.87)	0.23
Diastolic Blood Pressure	**38**		
Baseline Diastolic (per 1mmHg)	38	−0.33 (−0.52 to −0.13)	**< 0.01**
Age (per 1 year)	37	−0.06 (−0.17 to 0.16)	0.94
Attendance (per 1%)	26	−0.19 (−0.50 to 0.10)	0.20
Frequency (per 1 day/week)	38	−1.02 (−3.48 to 1.42)	0.41
Weekly volume (per 1 min/week)	30	−0.03 (−0.06 to 0.03)	0.70
Follow-up (per 1 week)	38	0.05 (−0.04 to 0.15)	0.27
Intensity (1=low, 2= moderate, 3= vigorous)	25	−3.14 (−6.07 to −0.22)	**0.03**
TESTEX score (per 1 point)	38	0.34 (−0.19 to 0.88)	0.20

Values: mean (95% Confidence Interval); Coefficient: describe how the blood pressure variable (the combined training effect) changes with a unit increase in the moderators (the potential effect modifier); P values statistically significant ($P < 0.05$).

Figures



Identification of studies via databases and registers
Identification of studies via other methods
Identification
Screening
Included
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Cochrane (n = 1491)
Scopus (n = 1180)
Embase (n = 1031)
Lilacs (n = 30)
Records removed before screening:
Duplicate records removed
(n = 2764)
Records identified from:
(n = 17)
Websites (n = 2)
Other reviews (n = 15)
Titles and abstract screened
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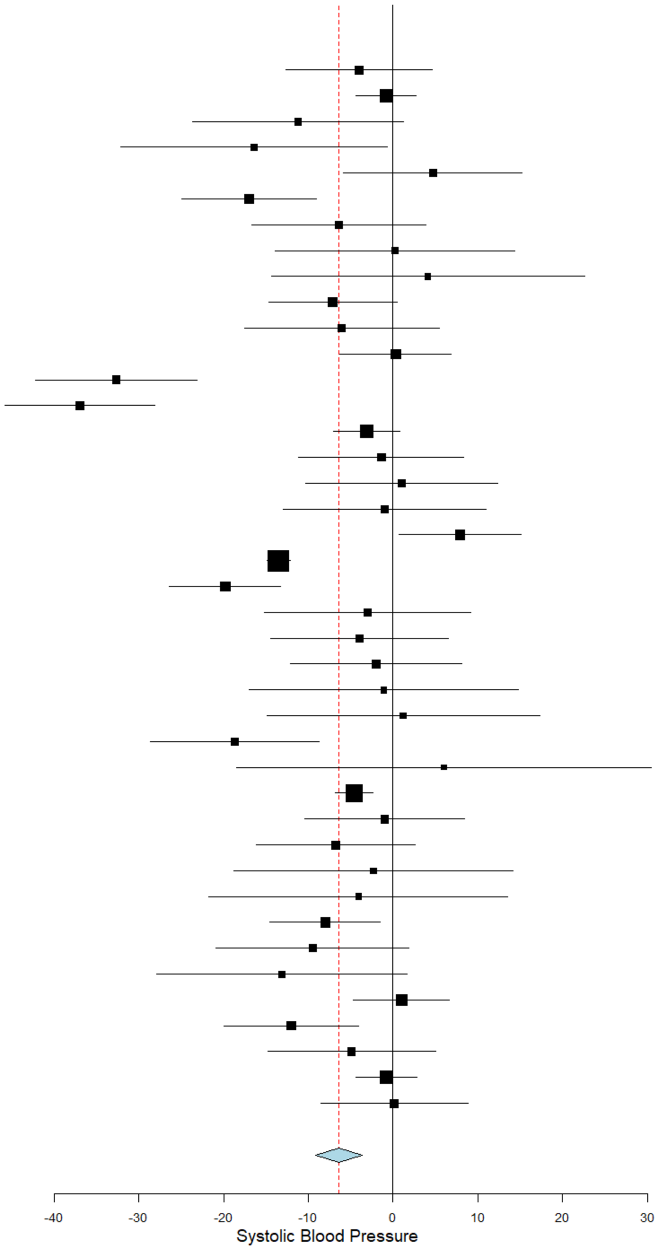
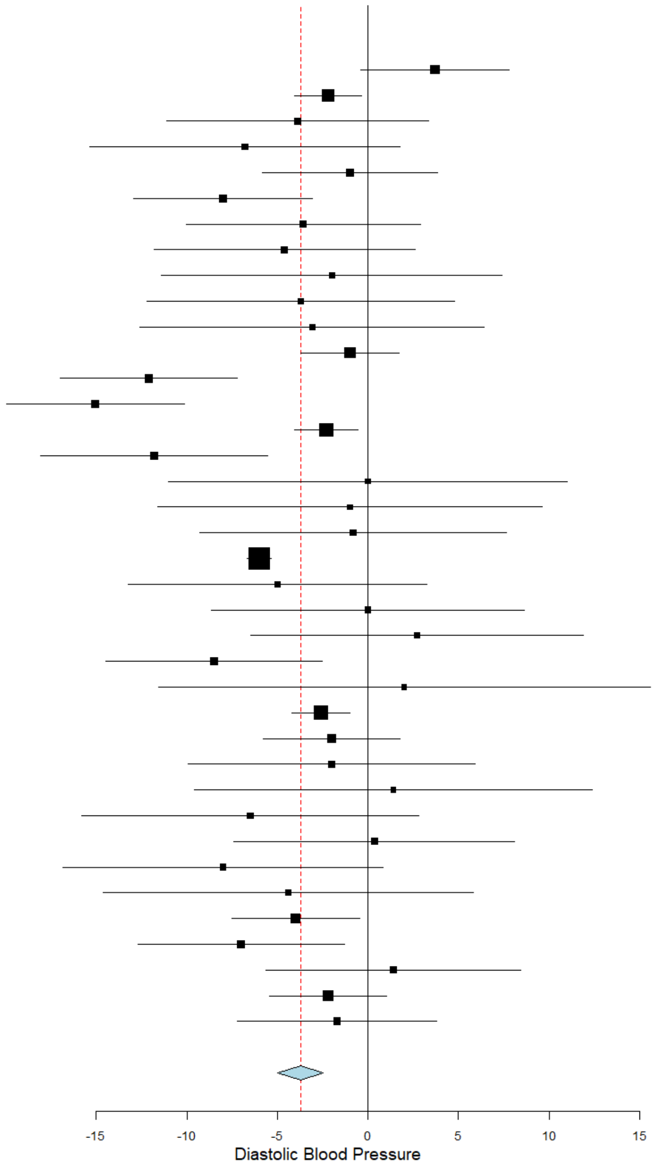
Reports assessed for eligibility
(n = 82)
Reports excluded:
Participants (n =27)
Intervention (n = 10)
Outcome (n = 6)
Comparator (n = 3)
Design (n = 3)
Other reason (n = 6)
Reports assessed for eligibility
(n = 17)
Reports excluded:
Participants (n = 3)
Design (n = 2)
Intervention (n = 2)
Studies included in review
(n = 37)

Studies	Estimate (95% C.I.)		
Balducci 2004	-4.00	(-12.65,	4.65)
Barone 2009	-0.80	(-4.34,	2.74)
Barroso 2008	-11.20	(-23.63,	1.23)
Bassi 2016	-16.40	(-32.09,	-0.71)
Bouchonville 2013	4.70	(-5.82,	15.22)
Bundchen 2010	-17.00	(-24.98,	-9.02)
Da Silva 2010	-6.42	(-16.67,	3.83)
Da Silva (b) 2010	0.19	(-13.96,	14.34)
de Oliveira 2012	4.10	(-14.36,	22.56)
de Oliveira (b) 2019	-7.11	(-14.66,	0.44)
Dianatinasab 2020	-6.07	(-17.55,	5.41)
Dobrosielski 2012	0.30	(-6.29,	6.89)
Dos santos 2014	-32.65	(-42.14,	-23.16)
Dos santos (b) 2014	-36.95	(-45.81,	-28.09)
Eriksson 2006	-3.10	(-7.03,	0.83)
Filho 2013	-1.40	(-11.14,	8.34)
Guimarães 2010	1.00	(-10.30,	12.30)
Guimarães (b) 2010	-1.00	(-12.92,	10.92)
Jorge 2011	7.91	(0.69,	15.13)
Kadoglou 2013	-13.50	(-14.87,	-12.13)
Lima 2017	-19.80	(-26.36,	-13.24)
Loimaala 2003	-3.00	(-15.14,	9.14)
Loimaala (b) 2007	-4.00	(-14.49,	6.49)
Loimaala (c) 2009	-2.00	(-12.13,	8.13)
Magalhães 2019	-1.10	(-17.02,	14.82)
Magalhães (b) 2019	1.20	(-14.87,	17.27)
Masroor 2018	-18.70	(-28.66,	-8.74)
McGavock 2004	6.00	(-18.42,	30.42)
Miura 2015	-4.60	(-6.77,	-2.43)
Nielsen 2019	-1.00	(-10.38,	8.38)
Ohkubo 2001	-6.80	(-16.16,	2.56)
Okada 2010	-2.30	(-18.76,	14.16)
Okumiya 1996	-4.10	(-21.74,	13.54)
Pepera 2021	-8.00	(-14.50,	-1.50)
Puggard 2000	-9.50	(-20.90,	1.90)
Ruangthai 2019	-13.10	(-27.86,	1.66)
Schroeder 2019	1.00	(-4.66,	6.66)
Son 2016	-12.00	(-19.91,	-4.09)
Stensvold 2010	-4.90	(-14.78,	4.98)
Stewart 2005	-0.80	(-4.39,	2.79)
Timmons 2018	0.14	(-8.52,	8.80)
Overall (I^2=84.73 % , P< 0.01)	**-6.39**	**(-9.11,**	**-3.68)**



Studies	Estimate (95% C.I.)
Balducci 2004	3.70 (-0.38, 7.78)
Barone 2009	-2.20 (-4.06, -0.34)
Barroso 2008	-3.90 (-11.13, 3.33)
Bassi 2016	-6.80 (-15.38, 1.78)
Bouchonville 2013	-1.00 (-5.83, 3.83)
Bundchen 2010	-8.00 (-12.94, -3.06)
Da Silva (a) 2020	-3.58 (-10.05, 2.89)
Da Silva (b) 2020	-4.62 (-11.83, 2.59)
de Oliveira 2012	-2.00 (-11.40, 7.40)
de Oliveira (b) 2020	-3.70 (-12.19, 4.79)
Dianatinasab 2020	-3.09 (-12.58, 6.40)
Dobrosielskl 2012	-1.00 (-3.72, 1.72)
Dos santos 2014	-12.10 (-17.00, -7.20)
Dos santos (b) 2014	-15.05 (-19.96, -10.14)
Eriksson 2006	-2.30 (-4.05, -0.55)
Filho 2013	-11.80 (-18.09, -5.51)
Guimaraes 2010	0.00 (-10.99, 10.99)
Guimaraes (b) 2010	-1.00 (-11.63, 9.63)
Jorge 2012	-0.83 (-9.29, 7.63)
Kadoglou 2013	-6.00 (-6.66, -5.34)
Lima 2017	-5.00 (-13.26, 3.26)
Magalhaes 2019	0.00 (-8.63, 8.63)
Magalhaes (b) 2019	2.70 (-6.47, 11.87)
Masroor 2018	-8.50 (-14.46, -2.54)
McGavock 2004	2.00 (-11.58, 15.58)
Miura 2015	-2.60 (-4.22, -0.98)
Nielsen 2019	-2.00 (-5.78, 1.78)
Ohkubo 2001	-2.00 (-9.92, 5.92)
Okada 2010	1.40 (-9.60, 12.40)
Okumiya 1996	-6.50 (-15.80, 2.80)
Pepera 2021	0.35 (-7.41, 8.11)
Puggard 2000	-8.00 (-16.85, 0.85)
Ruangthai 2019	-4.40 (-14.61, 5.81)
Schroeder 2019	-4.00 (-7.54, -0.46)
Son 2017	-7.00 (-12.70, -1.30)
Stensvold 2010	1.40 (-5.63, 8.43)
Stewart 2005	-2.20 (-5.43, 1.03)
Timmons 2018	-1.71 (-7.22, 3.80)
Overall (I^2=67.95 % , P< 0.01)	**-3.72 (-4.99, -2.45)**



Material Suplementar do Artigo

Supplementary Material Table S1. Literature search strategy used for all databases

PubMed

#1 (Circuit-Based Exercise[mh] OR “Concurrent training” OR “Combined training” OR “simultaneous training” OR “aerobic exercise with resistance training” OR “multicomponent training” OR “multicomponent exercise” OR “circuit training” OR “circuit resistance training” OR “combined exercise training” OR “multi-modal exercise training” OR “concurrent exercise” OR “combined exercise” OR “Combined exercise training”)

#2 ("randomized controlled trial” OR “controlled clinical trial” OR “randomized controlled trials”[mh] OR “random allocation”[mh] OR “clinical trial” OR clinical trials[mh])

EMBASE

('circuit-based exercise'/exp OR 'circuit-based exercise' OR 'concurrent training'/exp OR 'concurrent training' OR 'combined training' OR 'simultaneous training' OR 'aerobic exercise with resistance training' OR 'multicomponent training'/exp OR 'multicomponent training' OR 'multicomponent exercise' OR 'circuit training'/exp OR 'circuit training' OR 'circuit resistance training'/exp OR 'circuit resistance training' OR 'multi-modal exercise training' OR 'concurrent exercise' OR 'combined exercise' OR 'combined exercise training') AND ('randomized controlled trial'/exp OR 'randomized controlled trial' OR 'controlled clinical trial'/exp OR 'controlled clinical trial' OR 'randomized controlled trials'/exp OR 'randomized controlled trials' OR 'random allocation'/exp OR 'random allocation' OR 'clinical trial'/exp OR 'clinical trial' OR 'clinical trials'/exp OR 'clinical trials')

Scopus

TITLE-ABS-KEY ((“Circuit-Based Exercise” OR “Concurrent training” OR “Combined training” OR “simultaneous training” OR “aerobic exercise with resistance training” OR “multicomponent training” OR “multicomponent exercise” OR “circuit training” OR “circuit resistance training” OR “combined exercise training” OR “multi-modal exercise training” OR “concurrent exercise” OR “combined exercise” OR “Combined exercise training”)) AND (("randomized controlled trial” OR “controlled clinical trial” OR “randomized controlled trials” OR “random allocation” OR “clinical trial” OR “clinical trials”)) AND (LIMIT-TO (DOCTYPE, "ar"))

LILACS

(("Circuit-Based Exercise" OR “concurrent training” OR “combined training” OR “simultaneous training” OR “aerobic exercise with resistance training” OR “multi-component training” OR “multicomponent exercise” OR “circuit training” OR “circuit resistance training” OR “combined exercise training” OR “multi-modal exercise training” OR “concurrent exercise” OR “combined exercise” OR “combined exercise training”)) AND (db:("LILACS") AND type_of_study:("clinical_trials"))

Table S2. Study and intervention characteristics

Study	Country	Participants (Sample Size and Mean Age)	Follow-up	Training Frequency	Duration per week	Intensity	Volume	BP measurement method
Balducci et al. 2004	Italy	CT: n=62 (≈61y) CG: n=58 (≈61y)	48 weeks	3x per week	180 minutes	AER: 60% $HR_{reserve}$ RT: 60% RM	AER: 30 minutes RT: 3 sets | 12 [illegible]	Oscillometric
Barone et al. 2009	USA	CT: n=51 (≈65y) CG: n=53 (≈65y)	26 weeks	3x per week	270 minutes	AER: 60% HR_{max} RT: 50% RM	AER: 45 minutes RT: 2 sets | 12 reps. | 7 exerc.	Oscillometric
Barroso et al. 2008	Brazil	CT: n=22 (≈66y) CG: n=13 (≈71y)	24 weeks	3x per week	180 minutes	AER: 75% HR_{max} RT: 60% RM	AER: 30 minutes RT: 3 sets | 10 reps.	ABPM
Bassi et al. 2016	Brazil	CT: n=21 (≈50y) CG: n=20 (≈52y)	12 weeks	3x per week	180 minutes	AER: 65% $VO2_{peak}$ RT: 70% RM	AER: 30 minutes RT: 3 sets | 12 reps. |8 exerc.	Not reported
Bouchonville et al. 2013	USA	CT: n=26 (≈70y) CG: n=27 (≈69y)	52 weeks	3x per week	180 minutes	AER: 65% HR_{peak} RT: 65% RM	AER: 30 minutes RT: 2 sets | 12 reps.	Auscultatory
Bündchen et al. 2010	Brazil	CT: n=57 (≈58y) CG: n=60 (≈60y)	12 weeks	3x per week	270 minutes	AER: 60% $VO2_{peak}$ RT: 50% RM	AER: 45minutes RT: 3 sets | 15 reps.	Auscultatory
Da silva et al. 2020	Portugal	CT: n=13 (≈71y) CG: n=6 (≈67y)	12 weeks	3x per week	150 minutes	AER: 60-70% HRmax RT: 2-5 CR10 BORG	AER: 25 minutes RT: 2 sets | 8-15 reps. | 5 exerc.	Auscultatory
Da silva et al. 2020 (b)	Portugal	CT: n=13 (≈63y) CG: n=7 (≈67y)	12 weeks	3x per week	150 minutes	AER: 80-90% HRmax RT: 2-5 CR10 BORG	AER: 18 minutes RT: 2 sets | 8-15 reps. | 5 exerc.	Auscultatory

Table S2. Continued

Study	Country	Participants (Sample Size and Mean Age)	Follow-up	Training Frequency	Duration per week	Intensity	Volume	BP measurement method
de Oliveira et al. 2012	Brazil	CT: n=10 (≈58y) CG: n=12 (≈53y)	12 weeks	3x per week	180 minutes	AER: Lactate threshold RT: 8-12RM's	AER: 25 minutes RT: 2 sets | 15	Auscultatory
de Oliveira et al. 2020	Brazil	CT: n=13 (≈63y) CG: n=10 (≈63y)	8 weeks	3x per week	150 minutes	AER: 70% $HR_{reserve}$ RT: 6 OMNI-RES	AER: 25 minutes RT: 2 sets | 15 reps. | 6 exerc.	Oscillometric
Dianatinasab et al. 2020	Iran	CT: n=13 (≈53y) CG: n=15 (≈53y)	8 weeks	3x per week	180 minutes	AER: 75% HR_{max} RT: 80% RM	AER: 20 minutes RT: 1 set | 10 reps. | 10 exerc.	Not reported
Dobrosielski et al. 2012	USA	CT: n=51 (≈57y) CG: n=63 (≈56y)	26 weeks	3x per week	Not reported	AER: 60-90% HR_{max} RT: 50% RM	AER: 45 minutes RT: 2 sets | 10-15 reps. | 7	Oscillometric
dos Santos et al. 2014	Brazil	CT: n=20 (≈64y) CG: n=10 (≈63y)	16 weeks	3x per week	240 minutes	AER: 75% $HR_{reserve}$ RT: ≈110% RM	AER: 20 minutes RT: 3 sets | 10 reps. | 7 exerc.	Oscillometric
dos Santos et al. 2014 (b)	Brazil	CT: n=20 (≈63y) CG: n=10 (≈63y)	12 weeks	3x per week	270 minutes	AER: 75% $HR_{reserve}$ RT: 80% RM	AER: 20 minutes RT: 3 sets | 10 reps. | 7 exerc.	Oscillometric
Eriksson et al. 2006	Sweden	CT: n=60 (≈55y) CG: n=63 (≈53y)	48 weeks	3x per week	180 minutes	AER: 70% HR_{max} RT: Not reported	AER: 30 minutes RT: 2 sets | 12 reps. | 12 exerc.	Auscultatory
Filho et al. 2013	Brazil	CT: n=33 (≈69y) CG: n=21 (≈67y)	16 weeks	3x per week	180 minutes	AER: 3-5 OMNI-RES RT: Not reported	AER: 25 minutes RT: 2 sets | 12 reps.	Auscultatory

Table S2. Continued

Study	Country	Participants (Sample Size and Mean Age)	Follow-up	Training Frequency	Duration per week	Intensity	Volume	BP measurement method
Guimarães et al. 2010	Brazil	CT: n=16 (≈50y) CG: n=6 (≈47y)	16 weeks	3x per week	180 minutes	AER: 60% $HR_{reserve}$ RT: Not reported	AER: 40 minutes RT: Not reported	ABPM
Guimarães et al. 2010	Brazil	CT: n=16 (≈45y) CG: n=5 (≈47y)	16 weeks	3x per week	180 minutes	AER: 60% $HR_{reserve}$ RT: Not reported	AER: 40 minutes RT: Not reported	ABPM
Jorge et al. 2011	Brazil	CT: n=12 (≈58y) CG: n=12 (≈53y)	12 weeks	3x per week	180 minutes	AER: Lactate threshold RT: Not reported	AER: Not reported RT: 7 exerc. .	Auscultatory
Kadoglou et al. 2013	Brazil	CT: n=22 (≈58y) CG: n=24 (≈58y)	24 weeks	4x per week	180 minutes	AER: 67% HR_{max} RT: 70% RM	AER: 22 minutes RT: 3 sets | 10 reps. | 8 exerc.	Not reported
Lima et al. 2017	Brazil	CT: n=15 (≈68y) CG: n=14 (≈70y)	10 weeks	3x per week	Not reported	AER: Not reported RT: Not reported	AER: 30 minutes RT: 2 sets | 8 exerc.	ABPM
Loimaala et al. 2003	Finland	CT: n=25 (≈54y) CG: n=14 (≈70y)	48 weeks	4x per week	120 minutes	AER: 70% $VO2_{max}$ RT: 75%RM	AER: 30 minutes RT: 3 sets | 10-12 reps. | 8	Not reported
Loimaala et al. 2007	Finland	CT: n=24 (≈53y) CG: n=24	48 weeks	4x per week	120 minutes	AER: 70% $VO2_{max}$ RT: 75%RM	AER: 30 minutes RT: 3 sets | 10-	Not reported
Loimaala et al. 2009	Finland	CT: n=24 (≈54y) CG: n=24 (≈54y)	50 weeks	4x per week	120 minutes	AER: 70% $VO2_{max}$ RT: 75%RM	AER: 30 minutes RT: 3 sets | 10-12 reps. | 8 exerc.	Not reported

Table S2. Continued

Study	Country	Participants (Sample Size and Mean Age)	Follow-up	Training Frequency	Duration per week	Intensity	Volume	BP measurement method
Magalhães et al. 2019	Portugal	CT: n=25 (≈57y) CG: n=14 (≈59y)	48 weeks	3x per week	Not reported	AER: 80% $VO2_{reserve}$ RT: Not reported	AER: 34 minutes RT: 1 sets | 12 reps. | 8 exerc.	Oscillometric
Magalhães et al. 2019 (b)	Portugal	CT: n=28 (≈60y) CG: n=13 (≈59y)	48 weeks	3x per week	Not reported	AER: 60% $VO2_{reserve}$ RT: Not reported	AER: 42 minutes RT: 1 sets | 12 reps. | 8 exerc.	Oscillometric
Masroor et al. 2018	India	CT: n=15 (≈40y) CG: n=13 (≈41y)	4 weeks	5x per week	Not reported	AER: 65% HR_{max} RT: 65% RM	AER: 20 minutes RT: 3 sets | 10 reps. | 15 exerc.	Oscillometric
McGavock et al. 2004	Canada	CT: n=11 (≈58y) CG: n=7 (≈59y)	10 weeks	3x per week	Not reported	AER: 70% $HR_{reserve}$ RT: 57% RM	AER: 45 minutes RT: 3 sets | 10 reps. | 7 exerc.	Not reported
Miura et al. 2015	Japan	CT: n=45 (≈73y) CG: n=47 (≈70y)	12 weeks	2x per week	180 minutes	AER: 75% $HR_{reserve}$ RT: 15-20 RM's	AER: 20 minutes RT: 3-5 sets | 15-20 reps. | 6-8	Not reported
Nielsen et al. 2019	Denmark	CT: n=30 (≈71y) CG: n=15 (≈70y)	15 weeks	2x per week	120 minutes	AER: 75% $HR_{reserve}$ RT: 10 RM's	AER: 10-? minutes RT: Not reported	Oscillometric
Ohkubo et al. 2001	Japan	CT: n=32 (≈67y) CG: n=33 (≈67y)	25 weeks	2x per week	Not reported	AER: 50% $HR_{reserve}$ RT: 20 RM's	AER: 17 minutes RT: 1 set | 20 reps. | 5 exerc.	Not reported
Okada et al. 2010	Japan	CT: n=21 (≈62y) CG: n=17 (≈65y)	12 weeks	3x per week	225 minutes	Not reported	AER: 40 minutes RT: Not reported	Not reported

Table S2. Continued

Study	Country	Participants (Sample Size and Mean Age)	Follow-up	Training Frequency	Duration per week	Intensity	Volume	BP measurement method
Okumiya et al. 1996	Japan	CT: n=21 (≈79y) CG: n=21 (≈79y)	24 weeks	2x per week	120 minutes	Not reported	Not reported .	Oscillometric
Pepera et al. 2021	Greece	CT: n=20 (≈80y) CG: n=20 (≈79y)	8 weeks	2x per week	90 minutes	Not reported	AER: 45 minutes RT: Not reported	Oscillometric
Puggaard et al. 2000	Denmark	CT: n=16 (≈85y) CG: n=17 (≈85y)	32 weeks	1x per week	60 minutes	AER: 69% HR_{max} RT: Not reported	Not reported	Not reported
Ruangthai et al. 2019	Thailand	CT: n=16 (≈67y) CG: n=12 (≈67y)	12 weeks	3x per week	180 minutes	AER: 60% HR_{max} RT: 65% RM	AER: 20 minutes RT: 2 sets | 10 reps. | 14 exerc.	Oscillometric
Schroeder et al. 2019	USA	CT: n=18 (≈58y) CG: n=17 (≈58y)	8 weeks	3x per week	180 minutes	AER: 55% $HR_{reserve}$ RT: 15 RM's	AER: 30 minutes RT: 2 sets | 12 reps. | 8 exerc.	Oscillometric
Son et al. 2016	USA	CT: n=10 (≈76y) CG: n=10 (≈75y)	12 weeks	3x per week	210 minutes	AER: 40-70% $HR_{reserve}$ RT: Not reported	AER: 30 minutes RT: 10 exerc.	Not reported
Stensvold et al. 2010	Norway	CT: n=10 (≈53y) CG: n=11 (≈47y)	12 weeks	3x per week	130 minutes	AER: 80% HR_{peak} RT: 80% RM	AER: 43 minutes RT: 3 sets | 10 reps. | 3 exerc.	Not reported
Stewart et al. 2005	USA	CT: n=51 (≈63y) CG: n=53 (≈64y)	26 weeks	3x per week	Not reported	AER: 60-90% HR_{max} RT: 50% RM	AER: 45 minutes RT: 2 sets | 10-15 reps. | 7 exerc.	Oscillometric

Table S2. Continued

Study	Country	Participants (Sample Size and Mean Age)	Follow-up	Training Frequency	Duration per week	Intensity	Volume	BP measurement method
Timmons et al. 2018	Ireland	CT: n=21 (≈66y) CG: n=12 (≈63y)	10 weeks	3x per week	120 minutes	AER: 80% $HR_{reserve}$ RT: 60% RM	AER: 20 minutes RT: 4 sets | 15 reps. | 6 exerc.	Oscillometric

1RM: one repetition maximum; RM´s: repetition maximum; $VO2_{max}$: maximal oxygen consuption; HR: heart rate; CT: combined training; CG: control group; AER: aerobic training; RT: resistance training; BP: blood pressure

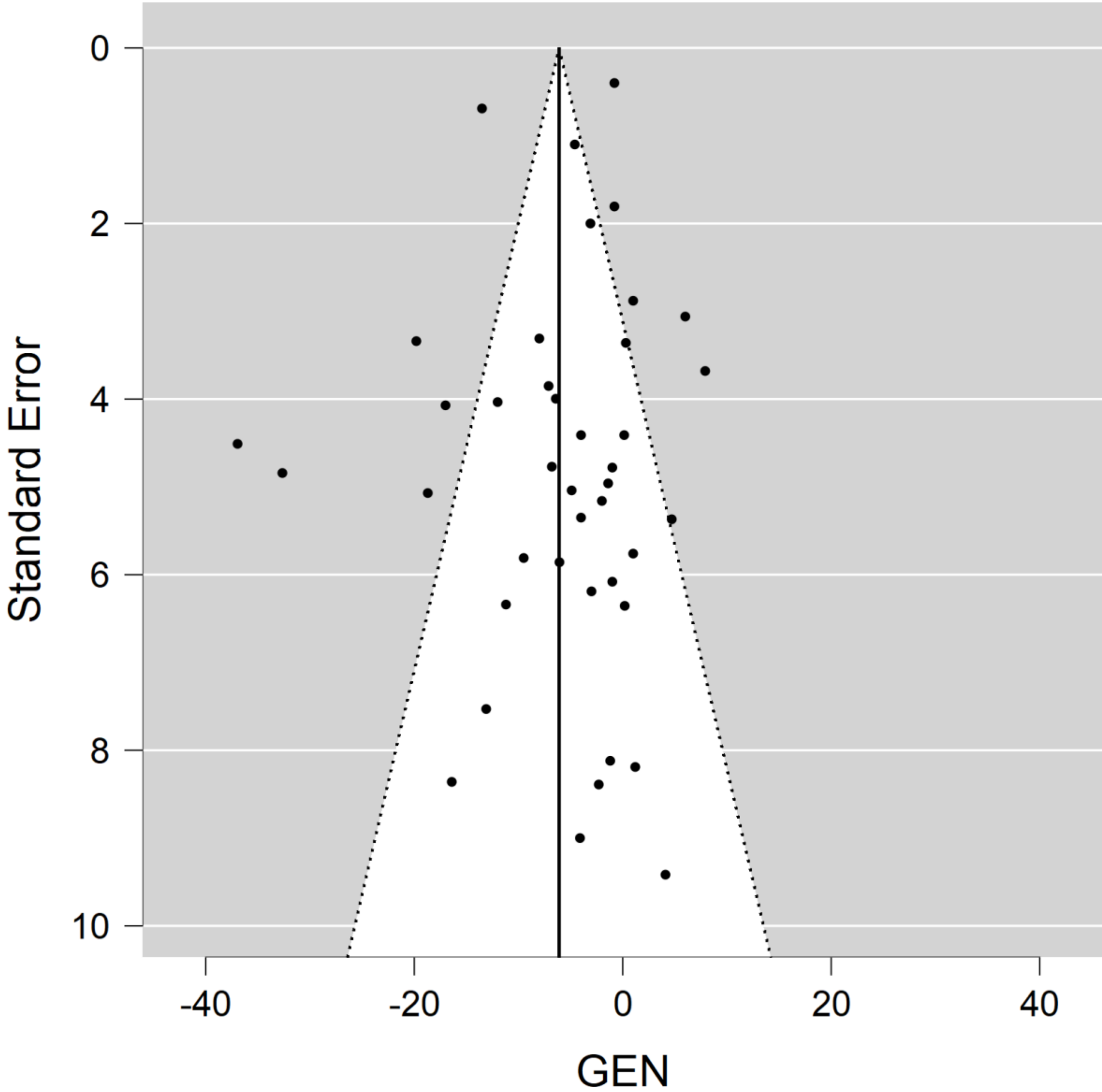
Reference	Year	Study Quality					Score (0-5)	Study Reporting										Score (0-10)	Total Score (0-15)
		1	2	3	4	5		6a	6b	6c	7	8a	8b	9	10	11	12		
Balducci	2004	-	-	-	+	-	1	+	+	+	-	+	+	+	-	-	+	6	8
Barone	2008	+	-	-	+	-	2	+	-	+	-	+	+	+	-	-	+	6	8
Barroso	2008	+	-	-	+	-	2	-	-	-	-	+	+	+	-	-	+	4	6
Bassi	2016	+	+	+	+	-	4	+	+	+	-	+	+	+	-	+	+	8	12
Bouchonville	2013	+	+	+	+	+	5	+	+	+	+	+	+	+	-	-	+	8	13
Bündchen	2010	-	-	-	+	-	1	-	-	-	-	+	+	+	-	-	-	3	4
Da silva	2020	+	-	-	-	-	1	+	-	-	+	+	+	+	+	-	+	7	8
de Oliveira	2012	-	-	-	+	-	1	+	-	-	+	+	+	+	+	-	+	7	8
de Oliveira	2020	+	+	+	+	-	4	+	-	-	-	+	+	+	-	-	+	5	9
Dianatinasab	2020	+	+	-	+	+	4	+	-	-	-	+	+	+	+	-	+	6	10
Dobrosielski	2012	+	-	-	+	-	2	-	-	+	-	+	+	+	-	-	-	4	6
dos Santos	2014	+	-	-	+	-	2	-	+	+	-	+	+	+	-	-	+	6	8
Eriksson	2006	+	+	+	+	-	4	-	-	-	-	+	+	+	-	-	-	3	7
Filho	2013	-	-	-	+	-	1	-	-	-	-	+	+	+	-	-	-	4	5
Guimarães	2010	+	+	-	+	+	4	-	-	+	-	+	+	+	-	-	+	5	9
Jorge	2011	+	-	-	+	-	2	-	-	+	-	+	+	+	+	-	-	5	7
Kadoglou	2013	+	+	-	+	-	3	-	+	+	-	+	+	+	+	-	+	7	9
Lima	2017	+	-	-	+	-	2	-	-	-	-	+	+	+	-	-	-	3	5
Loimaala	2003	-	-	-	+	-	1	+	-	-	-	+	+	+	-	-	-	4	5
Loimaala	2007	+	-	-	+	-	2	-	-	-	-	+	+	+	-	-	-	3	5
Loimaala	2009	-	-	-	+	-	1	+	-	+	-	+	+	+	-	-	-	5	9
Magalhães	2019	+	+	+	+	+	5	+	+	+	+	+	+	+	-	-	+	8	13
Masroor	2018	+	+	+	+	+	5	+	-	-	+	+	+	+	-	-	+	6	11
McGavock	2004	+	-	-	+	-	2	+	-	+	-	+	+	+	-	-	+	6	8
Miura	2015	+	-	-	+	-	2	+	-	-	-	+	+	+	-	-	-	4	6
Nielsen	2019	+	+	+	+	+	5	+	+	+	+	+	+	+	+	-	+	9	14
Ohkubo	2001	+	+	-	+	-	3	+	+	+	+	+	+	+	-	-	+	8	11
Okada	2010	+	+	-	+	-	3	-	-	-	+	+	+	+	-	-	-	4	7
Okumiya	1996	-	-	-	+	+	2	+	-	+	-	+	+	+	-	-	+	6	8
Pepera	2021	+	+	-	+	-	3	+	-	-	+	+	+	+	-	-	+	6	9
Puggaard	2000	+	-	-	+	-	2	+	-	+	-	+	+	+	-	-	-	5	7
Ruangthai	2019	+	-	-	+	-	2	+	-	+	-	+	+	+	-	-	+	6	8
Schroeder	2019	+	+	+	+	+	5	+	+	+	+	+	+	+	-	-	+	8	13
Son	2016	-	+	+	+	-	3	-	-	-	-	+	+	+	-	-	+	4	7
Stensvold	2010	+	+	+	+	-	4	-	-	-	-	+	+	+	-	-	+	4	8
Stewart	2005	+	-	-	+	-	2	+	-	+	-	+	+	+	-	-	+	6	8
Timmons	2018	+	+	+	+	+	5	+	-	+	-	+	+	+	-	-	+	6	11

Supplementary Material Figure S1. The methodological quality of studies included in the meta-analysis.

Study quality: 1 = Eligibility criteria specified; 2 = Randomization specified; 3 = Allocation concealment; 4 = Groups similar at baseline; 5 = Blinding of assessor (for at least one key outcome)

Study reporting: 6 = Outcome measures assessed in 85% of participants (6a = 1 point if completion rate is [85%; 6b = 1 point if adverse events are reported; 6c = 1 point if exercise attendance is reported); 7 = Intention-to-treat analysis; 8 = Between-group statistical comparisons reported (8a = 1 point if between-group statistical comparisons are reported for the primary outcome measure of interest; 8b = 1 point if between-group statistical comparisons are reported for at least one secondary outcome measure); 9 = Point measures and measures of variability for all reported outcome measures; 10 = Activity monitoring in control groups; 11 = Relative exercise intensity remained constant; 12 = Exercise volume and energy expenditure

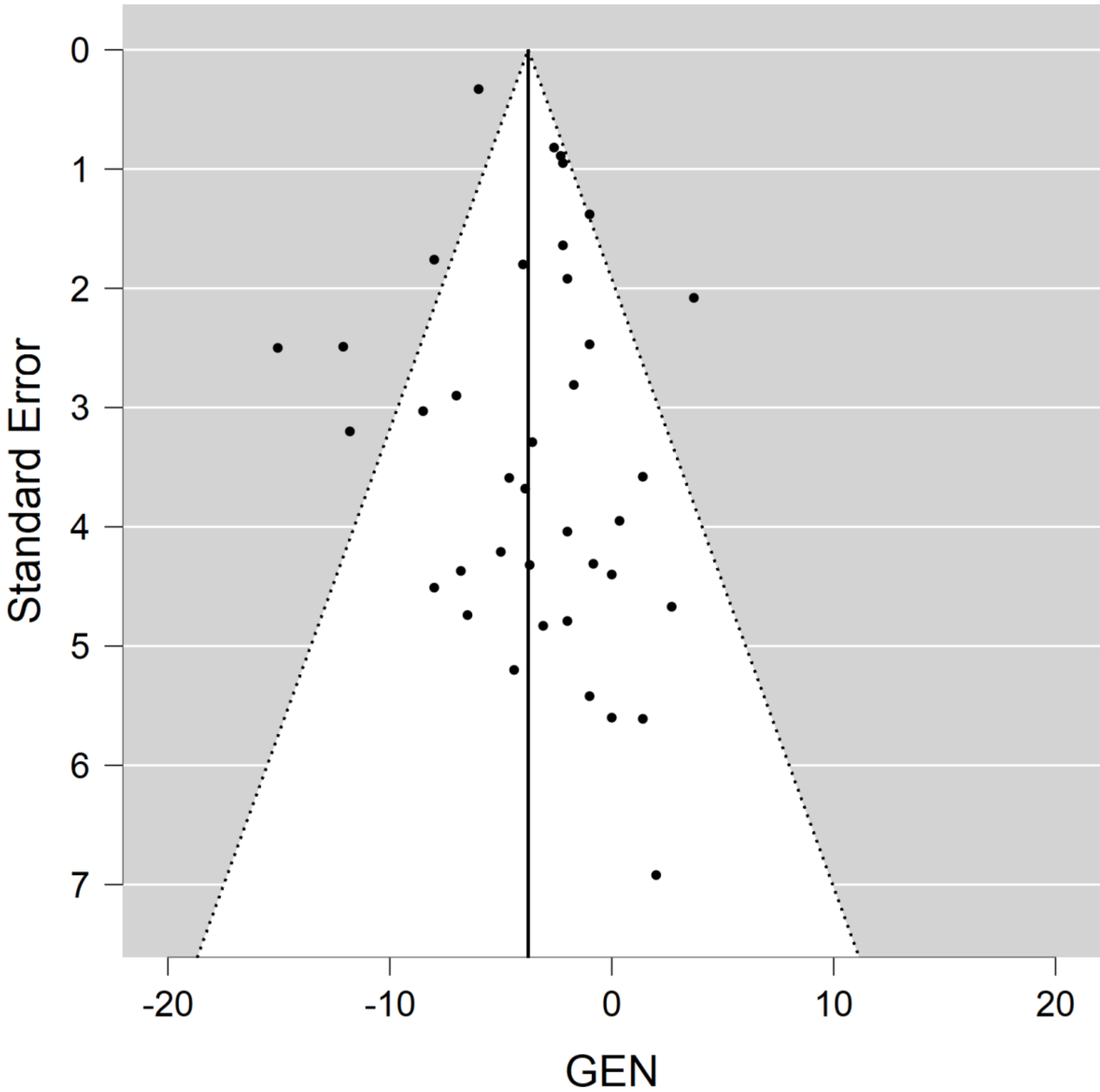
+ meet the criteria; - do not meet the criteria



Supplementary Material Figure S2. Funnel plot of the effect of combined training versus control group for systolic blood pressure. The solid line represents the pooled effect estimate expressed as the mean difference (MD) for each analysis. Dashed lines present pseudo-95% confidence intervals and the circles represent effect estimates for each included study.

Regression test for Funnel plot asymmetry ("Egger's test")

	z	**p**
sei	-0.039	0.969



Supplementary Material Figure S3. Funnel plot of the effect of combined training versus control group for diastolic blood pressure. The solid line represents the pooled effect estimate expressed as the mean difference (MD) for each analysis. Dashed lines present pseudo-95% confidence intervals and the circles represent effect estimates for each included study.

Regression test for Funnel plot asymmetry ("Egger's test")

	z	**p**
sei	0.479	0.632

7 CONSIDERAÇÕES FINAIS

A HAS possui elevada prevalência, sendo responsável por milhões de mortes prematuras. Mudanças no estilo de vida constituem estratégias recomendadas na prevenção e tratamento da hipertensão, e a prática de exercício físico regular através do treinamento combinado vem sendo utilizada como principal orientação das diretrizes para tratamento e prevenção da HAS.

Os resultados desta dissertação confirmam a eficácia do treinamento combinado na redução crônica da pressão arterial em indivíduos adultos com HAS. Além do mais, foi possível identificar moderadores como a intensidade e volume dos exercícios aeróbios e resistidos, que parecem influenciar a magnitude de redução da pressão arterial em indivíduos adultos com HAS.