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EFEITOS DO TREINAMENTO ISOMÉTRICO COM *HANDGRIP* NA PRESSÃO ARTERIAL AMBULATORIAL DE ADULTOS: UMA REVISÃO SISTEMÁTICA COM METANÁLISE

RECIFE
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Dissertação apresentada ao Programa de Pós-Graduação em Educação Física da Universidade Federal de Pernambuco, como requisito para obtenção do título de Mestre em Educação Física. Área de concentração: Biodinâmica do movimento humano.

Orientador: Prof. Dr. Breno Quintella Farah

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RESUMO

Estudos de metanálise vêm demonstrando que o treinamento isométrico com *handgrip* é uma alternativa eficaz para redução da pressão arterial clínica em hipertensos. Contudo, até o presente momento, nenhum estudo de metanálise foi realizado analisando os efeitos do TIH na medida ambulatorial da pressão arterial, que é considerado melhor discriminador de risco cardiovascular em hipertensos. Portanto, o objetivo dessa dissertação foi analisar os efeitos do treinamento isométrico com *handgrip* nas variáveis cardiovasculares em hipertensos e normotensos. Para tanto, foi realizado uma revisão sistemática com meta-análise de estudos que investigaram os efeitos do TIH na pressão arterial ambulatorial nas bases de dados Medline e Web of Science, bem como foi utilizado estudos presentes na literatura cinza. Foi realizada metanálise de efeitos aleatórios das diferenças de médias (MD) com intervalo de confiança de 95% (IC95%). Seis estudos foram incluídos na revisão, totalizando 157 participantes (82 TIH e 75 controles). A metanálise não identificou efeito significante do TIH sobre a pressão arterial sistólica de 24 horas (MD: -2,5 mmHg, IC95%: -5,44 a 0,45, p=0,10), de sono (MD: -1,88 mmHg, IC95%: -4,86 a 1,10, p=0,22), de vigília (MD: -1,85 mmHg, IC95%: -4,81 a 1,10, p=0,22), pressão arterial diastólica de 24 horas (MD: -1,91mmHg, IC95%: -4,06 a 0,24, p=0,08) e de sono (MD: -1,90 mmHg, IC95%: -4,60 a 0,81, p=0,17), enquanto que houve redução da pressão arterial diastólica de vigília (MD: -2,53 mmHg, IC95%: -4,87 a -0,18, p= 0,03) no grupo o treinamento isométrico com *handgrip*. Assim, pode-se concluir que o treinamento isométrico com *handgrip* reduziu a pressão arterial diastólica de vigília. Por outro lado, este tipo de treinamento não reduziu a pressão arterial diastólica e sistólica de 24 horas, de sono, assim como a pressão arterial sistólica de vigília em adultos.

Palavras-chave: exercício físico; pressão arterial; treinamento de força; hipertensão.

ABSTRACT

Meta-analysis studies have shown that isometric training with handgrip (IHT) is an effective alternative to reduce clinical blood pressure in hypertensive patients. However, to date, no meta-analysis study has been carried out analyzing the effects of HIT on ambulatory blood pressure, which is considered a better discriminator of cardiovascular risk in hypertensive patients. Therefore, the objective of this dissertation was to analyze the effects of isometric training with handgrip on cardiovascular variables in hypertensive and normotensive individuals. Therefore, a systematic review with meta-analysis of studies investigating the effects of HIT on ambulatory blood pressure in the Medline and Web of Science databases was performed, as well as studies present in the gray literature. A meta-analysis of random effects of mean difference and/or standardized mean difference with a 95% confidence interval was performed. Six studies were included in the review, totaling 157 participants (82 IHT, 75 control). The meta-analysis did not identify any significant effect of HIT on 24-hour systolic blood pressure (MD: -2.5 mmHg, 95% CI -5.44 to 0.45, p=0.10), asleep (DM -1.88 mmHg , 95% CI -4.86 to 1.10, p=0.22), and awake (MD: -1.85 mmHg, 95% CI -4.81 to 1.10, p=0.22) and pressure 24-hour diastolic blood pressure (MD: -1.91 mmHg, 95% CI -4.06 to 0.24, p=0.08) and asleep (MD -1.90 mmHg, 95% CI -4.60 to 0, 81, p=0.17). There was an effect on awake diastolic blood pressure (MD: -2.53 mmHg, 95% CI -4.87 to -0.18, p=0.03). Thus, although consolidated in the literature for clinical blood pressure, isometric training with handgrip had an effect only on awake diastolic blood pressure.

Keywords: exercise; arterial pressure; resistance training; hypertension.

SUMÁRIO

1 INTRODUÇÃO

A hipertensão arterial sistêmica (HAS) é uma doença crônica não transmissível, de origem multifatorial, caracterizada pela elevação sustentada da pressão exercida pelo sangue na parede das artérias, sendo o principal fator de risco para doenças cardíacas e cerebrovasculares, como: doença arterial coronariana e isquemia cerebral (WHELTON et al., 2018). Essas doenças foram responsáveis por 17,8 milhões de mortes no mundo em 2017 (KAPTOGE et al., 2019), o que remete à importância de manter níveis pressóricos controlados.

Estima-se que cerca de 1,13 bilhões de pessoas tenham HAS e que desses, 80% não tenham controle dos níveis pressóricos, apresentando medidas acima de 140 mmHg e/ou 90 mmHg para pressão arterial sistólica e diastólica, respectivamente (RILEY et al., 2018). Além da elevada taxa de mortalidade, as doenças cardiovasculares apresentam forte impacto econômico. Por exemplo, os custos médicos diretos com a HAS é de 370 bilhões por ano (FRIEDEN; JAFFE, 2018). Nos Estados Unidos, o absenteísmo relacionado à HAS chega a ser de 12 dias por ano, gerando uma perda de produtividade equivalente a 473 milhões de dólares (VUONG; WEI; BEVERLY, 2015).

Especificamente no Brasil, o sistema de Vigilância de Fatores de Risco para Doenças Crônicas Não-Transmissíveis demonstrou que, em 2018, 24,7% da população brasileira apresentavam HAS (VIGITEL, 2019) e que 50% dos hipertensos têm consciência de sua condição, e destes, metade não estavam sob tratamento e a outra metade, embora estivessem em tratamento, apresentavam, pressão arterial sistólica e diastólica com níveis acima de 120 mmHg e 80 mmHg, respectivamente (MACHADO; PIRES; LOBÃO, 2012).

Esses números são maiores quando analisa-se a população idosa, por exemplo, Sousa et al., (2019) demonstraram que a prevalência de idosos hipertensos foi de 74,9%, dos quais 72,6% estavam sob tratamento, contudo, 50,8% alcançavam as metas estabelecidas de controle pressórico. Esses dados são importantes do ponto de vista da saúde pública, especificamente, se considerar o impacto na morbimortalidade da população brasileira, bem como, o custo econômico com a HAS e as doenças cardiovasculares, que foi de 56,2 milhões de reais em 2015 (STEVENS et al., 2018).

Em relação ao nível adequado da pressão arterial, há divergências entre as diretrizes da comunidade científica no mundo quanto ao ponto de corte a ser aplicado

para o diagnóstico da HAS que pode ser obtida pela pressão arterial clínica, monitorização da pressão arterial ambulatorial (MAPA) e a medida da pressão arterial residencial. Os critérios para classificação da HAS de acordo com a medida da pressão arterial e a diretriz são apresentados no quadro 1.

Quadro 1. Pontos de corte utilizados pelas Diretrizes de Hipertensão para diagnóstico da hipertensão arterial sistêmica de acordo com a medida utilizada.

Tipo de medida	**PAS em mmHg**				**PAD em mmHg**		
	SBC	**AHA**	**ESC**		**SBC**	**AHA**	**ESC**
Clínica (consultório)	≥ 140	≥ 130	≥ 140	e/ou	≥ 90	≥ 90	≥ 90
MAPA – Vigília	≥ 135	≥ 130	≥ 135	e/ou	≥85	≥85	≥85
MAPA – Sono	≥ 120	≥ 110	≥ 120	e/ou	≥ 70	≥ 70	≥ 70
MAPA – 24 Horas	≥ 130	≥ 125	≥ 130	e/ou	≥ 80	≥ 80	≥ 80
MRPA	≥ 130	≥ 130	≥ 135	e/ou	≥ 80	≥ 80	≥ 85

Fonte: Autor, 2021.

PAS: Pressão arterial sistólica; PAD: Pressão arterial diastólica; mmHg: milímetro de mercúrio; MRPA: Medida residencial de pressão arterial; SBC: Sociedade Brasileira de Cardiologia; AHA: *American Heart Association*; ESC: *European Society of Cardiology.*

Diferentemente do diagnóstico, não há divergência quanto aos fatores de risco para o desenvolvimento da HAS. De fato, os fatores podem ser divididos em não modificáveis (idade, sexo e genética) e modificáveis, que estão diretamente associados ao estilo de vida, como: ingestão de alimentos ultraprocessados, sódio e álcool, sedentarismo, fumo, obesidade e inatividade física (MALAQUIAS et al., 2016). A literatura vem demonstrando que a modificação no estilo de vida para adoção de hábitos de vida mais saudáveis é recomendado como parte do tratamento e prevenção da HAS (ARNETT et al., 2019; BAKRIS; ALI; PARATI, 2019; MALAQUIAS et al., 2016). No entanto, para o tratamento da HAS, torna-se necessário a associação entre modificação no estilo de vida e o uso de medicamentos anti-hipertensivos (SINHA; AGARWAL, 2019), os quais promovem maiores reduções da pressão arterial (NACI et al., 2019).

Dentre os diferentes componentes do estilo de vida, há evidências que a prática regular do exercício físico é eficaz no controle pressórico de indivíduos hipertensos (NACI et al., 2019; PESCATELLO et al., 2019). Os exercícios aeróbicos e os de força dinâmico já têm seus benefícios consolidados na literatura, bem como os protocolos recomendados. No quadro 2, são apresentadas as recomendações do exercício aeróbico e treinamento de força dinâmico, bem como o impacto esperado na pressão arterial sistólica e diastólica, segundo as recomendações do *American College of Sports Medicine* (PESCATELLO et al., 2019).

Quadro 2. Intervenções não farmacológicas para o tratamento e prevenção da hipertensão arterial segundo a *American College of Sports Medicine* (PESCATELLO et al., 2019):

Intervenção não farmacológica	**Orientação**	**Impacto esperado (mmHg)**	
		PAS	**PAD**
Exercício Aeróbio	• 90-150 min/semana • 40-80% da frequência cardíaca de reserva	-8,3	-5,2
Exercício Resistido	• 90-150 min/semana • 60%-80% de 1RM • 8-10 exercícios, 2-4 séries, 8-12 repetições	-5,7	-5,2

Fonte: Autor, 2021.

RM: repetição máxima; mmHg: milímetro de mercúrio; PAS: pressão arterial sistólica; PAD: pressão arterial diastólica.

Entretanto, mesmo já bem definido os efeitos positivos da prática do exercício físico na pressão arterial, bem como as suas recomendações mínimas, a aderência ao exercício ainda é um desafio (SABBAHI et al., 2016). De fato, 15% dos hipertensos alcançam as recomendações da prática de atividade física, o que pode estar associado a intensidade mínima requerida (moderada a vigorosa) e ao tempo necessário para a prática (acima de 90 minutos semanais). Portanto, torna-se necessário identificar exercícios físicos eficazes e com protocolo rápido e simples, possibilitando maior aderência ao exercício.

Nesse sentido, o treinamento isométrico com handgrip (TIH), surge como possibilidade, devido ao seu baixo custo, otimização do tempo em sessões de treinamento (33 minutos por semana), uma vez que o protocolo mais utilizado é composto por três sessões semanais de 4 séries de 2 minutos à 30% da contração voluntária máxima (CVM) e 1 minuto de intervalo entre cada série, totalizando 11 minutos por sessão (MILLAR et al., 2014).

Curiosamente, o exercício isométrico era desaconselhado pelas diretrizes internacionais, devido à elevação da pressão arterial, especialmente durante e logo após a sua realização. De fato, no exercício isométrico há contração sustentada dos músculos, não havendo alteração do seu comprimento. Portanto, à medida que a intensidade e a duração da contração aumentam, a pressão arterial se eleva, devido ao aumento da resistência vascular periférica provocada por uma obstrução mecânica do fluxo sanguíneo muscular (SILVA et al., 2018; VANHEES et al., 2012).

No entanto, sabe-se que o aumento da resistência vascular periférica durante o exercício isométrico é proporcional a massa muscular envolvida. Nesse sentido, o exercício isométrico com *handgrip* parece não promover elevações pressóricas consideráveis (GOESSLER; BUYS; CORNELISSEN, 2016), nem durante a execução do exercício e nem durante os intervalos das sessões (OLHER et al., 2013). De fato, Araujo et al., (2011) observaram aumento de 16 mmHg na pressão arterial sistólica, 7 mmHg na pressão arterial diastólica e 3 bpm na frequência cardíaca, valores clinicamente seguros para hipertensos com pressão arterial controlada.

Além disso, respostas hipotensoras oriundas dos esforços isométricos já eram apresentadas no início de 1970 por Kiveloff e Huber (1971), uma vez que reduções de até 42 mmHg para pressão arterial sistólica e 24 mmHg para a diastólica foram possíveis seguindo um protocolo de 6 segundos de contração isométrica, três vezes ao dia, ao longo de 5 a 8 semanas. Anos depois, Buck e Donner (1985) apresentam um estudo apontando que indivíduos cujas atividades ocupacionais eram caracterizadas por esforços isométricos apresentavam menor chances de desenvolver hipertensão do que seus pares. Em 1992, Wiley et al. (1992) desenvolveram o primeiro ensaio clínico para testar a hipótese de que o TIH seria eficiente em reduzir a pressão arterial de repouso. Através de dois protocolos de intensidade e forma distintas (4 séries de 2 minutos, a 30% da CVM, unilateral, com 3 minutos de intervalo e outro com 4 séries de 45 segundos a 50% da CVM, bilateral com intervalos de 1 minuto) observaram que ambos foram capazes de

reduzir a pressão arterial dos voluntários envolvidos, abrindo precedente para novos estudos sobre o treinamento isométrico como terapia não medicamentosa.

Na última década, estudos de meta-análise vêm demonstrando que o treinamento isométrico, em especial o com *handgrip*, é eficaz na redução da pressão arterial sistólica e diastólica de hipertensos e normotensos (Quadro 3). No entanto, algumas diretrizes recomendam com ressalva ou não recomendam o uso do TIH. De fato, o American Heart Association (classe de recomendação IIb; nível de evidência C), a Hypertension Canada e o Exercise and Sports Science Australia (ARNETT et al., 2019; SHARMAN et al., 2019; NERENBERG et al., 2018) recomendam o treinamento, enquanto o American College of Sports Medicine (PESCATELLO et al., 2019) e a European Society of Cardiology (WILLIAMS et al., 2018) não recomendam. A Diretriz Brasileira de Hipertensão introduziu o uso do TIH para controle da HAS na atualização das diretrizes de 2020(BARROSO et al., 2020).

Quadro 3. Síntese dos estudos de meta-análise da última década que analisaram os efeitos do exercício isométrico na pressão arterial clínica

Autor (ano)	**Total de estudos**	**Estudos com handgrip**	**PAS (mmHg)**	**PAD (mmHg)**
Almeida et al. (2021)	5	5	↓8,1	↓2,7
Smart et al. (2019)	12	8	↓6,2	↓2,8
López-Valenciano et al. (2019)	16	9	↓5,2	↓1,6
Jin et al. (2017)	7	7	↓8,3	↓3,9
Inder et al. (2015)	11	6	↓5,2	↓3.9
Carlson et al. (2014)	9	6	↓6,8	↓4,0
Cornelissen et al. (2011)	28	3	↓13,5	↓7,8
Owen et al. (2010)	5	3	↓10,4	↓6,7
Kelley; Kelley (2010)	3	3	↓13,4	↓7,8

Fonte: Autor, 2021.

PAS: Pressão arterial sistólica; PAD: Pressão arterial diastólica; mmHg: milímetro de mercúrio;

Parte dessa restrição nas recomendações, deve-se a necessidade de mais estudos. Fator que chama atenção é quantidade pequena de estudos que analisaram os efeitos do TIH na MAPA. De fato, até o presente momento, não há estudos de metanálise que testaram os efeitos do TIH na MAPA de hipertensos e normotensos, o que representa uma lacuna importante, dado que a MAPA apresenta melhor prognóstico cardiovascular do que a medida clínica, e é melhor preditor para mortalidade cardiovascular (HUANG et al., 2011). Huang et al., (2011) em estudo com 1014 voluntários saudáveis, verificaram que a medida da pressão arterial de 24 horas apresentou relação significante com mortalidade cardiovascular, diferentemente da pressão arterial central e periférica. Além do mais, a MAPA é amplamente utilizada na prática clínica para o diagnóstico e do controle da HAS (NIIRANEN et al., 2014; PIPER et al., 2015).

Em relação aos estudos aos ensaios clínicos, pelo atual conhecimento, é sabido que quatro estudos analisaram os efeitos do treinamento isométrico com *handgrip* na MAPA (STILLER-MOLDOVAN et al., 2012; FARAH et al., 2018; GOESSLER et al., 2018; SEIDEL et al., 2020). Destes, Goesller et al., (2018) realizou com adultos saudáveis, treinando todos os dias por 8 semanas, Stiller-Moldovan et al. (2012), Farah et al. (2018) e Seidel et al. (2020) realizaram com hipertensos, os dois primeiros com uma menor frequência (3 vezes por semana) durante 8 e 12 semanas, respectivamente e Seidel et al. (2020) durante 12 semanas com 5 sessões semanais. Em todos eles não foram identificados efeitos positivos do treinamento isométrico com *handgrip* na MAPA.

Curiosamente, ao analisar os bancos do *clinical trials* verifica-se que alguns estudos estão sendo conduzidos (PALMEIRA et al., 2020; ANDRADE et al., 2020; GERAGE et al., 2020), com o objetivo de avaliar as respostas do TIH na MAPA em hipertensos. Assim, a utilização desses estudos em andamento vem a colaborar com a metanálise, somando informações aos já presentes na literatura.

2 OBJETIVOS

2.1 Objetivos gerais

Analisar os efeitos crônicos do treinamento isométrico com *handgrip* nas variáveis cardiovasculares em hipertensos e normotensos.

2.2 Objetivos Específicos

Analisar os efeitos do treinamento isométrico com *handgrip* na pressão arterial de 24 horas, sono, vigília e 24 horas de hipertensos e normotensos.

3 MÉTODOS

3.1 Delineamento do estudo e busca na literatura

A revisão sistemática com metanálise foi conduzida de acordo com as recomendações do PRISMA e registrada na base de dados internacional da PROSPERO (CRD42020197305) em julho 2020.

Foi realizada uma busca sistemática nas bases de dados da PubMed e Web of Science, da sua origem até junho de 2021 usando os termos e boleanos apresentados no quadro 4:

Quadro 4. Descrição da busca realizada nas bases de dados.

#1	"isometric contraction"[MeSH Terms] OR "resistance training"[MeSH Terms] OR "isometric training"[Title/Abstract] OR "isometric resistance training"[Title/Abstract] OR "hand grip"[Title/Abstract] OR "grip strength"[Title/Abstract] OR "handgrip"[Title/Abstract] OR "dynamometer"[Title/Abstract] OR "isometric handgrip"[Title/Abstract] OR "handgrip exercise"[Title/Abstract] OR "isometric grip"[Title/Abstract] OR "static grip"[Title/Abstract] OR "forearm grip"[Title/Abstract] OR "isometric exercise training"[Title/Abstract] OR "resistance training"[Title/Abstract]
#2	"blood pressure"[MeSH Terms] OR "blood pressure determination"[MeSH Terms] OR "arterial pressure"[MeSH Terms] OR "normotension"[Title/Abstract] OR "arterial blood pressure"[Title/Abstract] OR "blood pressure monitoring, ambulatory"[MeSH Terms] OR "ambulatory blood pressure"[Title/Abstract] OR "blood pressure"[Title/Abstract]
#3	"aging"[MeSH Terms] OR "aged"[MeSH Terms] OR "adult"[MeSH Terms] OR "normotensive"[Title/Abstract] OR "hypertensive"[Title/Abstract]
#4	"systematic review"[Publication Type] OR "guideline"[Publication Type] OR "meta-analysis"[Publication Type] OR "review"[Publication Type]
#5	#1 AND #2 AND #3 AND #4 NOT

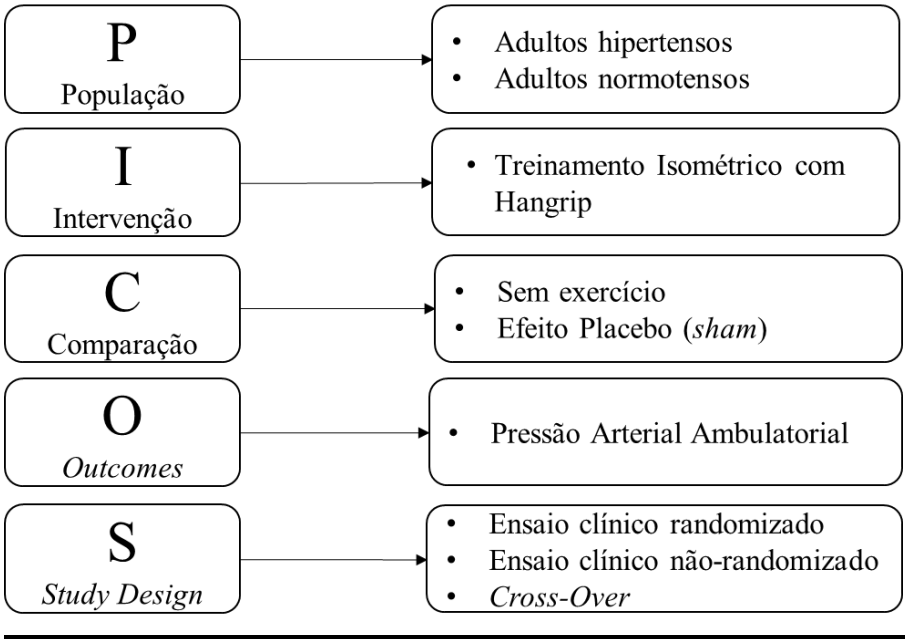
Fonte: Autor, 2021.

As referências dos estudos identificados foram consideradas para identificar possíveis novos estudos. Assim como também, realizamos uma busca no Clinical Trials para verificar estudos finalizados ainda não publicados (https://clinicaltrials.gov/), e uma busca manual nas referências utilizadas (literatura cinza).

3.2 Elegibilidade e seleção dos estudos

O critério de elegibilidade foi estabelecido de acordo com a estratégia PICOS, conforme apresentado na Figura 1.

Figura 1 - Descrição da estratégia PICOS para conduzir a revisão sistemática com meta-análise sobre os efeitos do treinamento isométrico com *handgrip* na pressão arterial ambulatorial em adultos.



Fonte: Autor, 2021.

3.3 Coleta dos dados

A extração de dados de todos os estudos elegíveis foi realizada separadamente e em duplicata por dois revisores independentes (MSO e PHM) e checados por um terceiro avaliador (BQF). Os dados extraídos foram: características do estudo (delineamento, tamanho da amostra, estado de saúde, sexo, idade e estado de treinamento, MAPA), protocolo de intervenção (tipo, intensidade, frequência semanal, duração, número de séries e recuperação intervalo); mudanças na pressão arterial ambulatorial. A qualidade dos estudos foi avaliada pela escala Tool for the Study of Study Quality and Reporting in

Exercise (TESTEX). Essa escala varia de 0 a 15, e pontuações mais altas representam maior qualidade metodológica.

3.4 Análise dos dados

Os resultados contínuos foram extraídos da baseline e pós-intervenção de cada um dos estudos individuais. Os autores foram contatados quando havia falta de informações. Se relatado, a diferença média dentro do grupo e desvio padrão ou intervalo de confiança de 95% (IC) também foram extraídos. Se não relatado, a diferença média foi calculada como a média pós-intervenção - média da baseline

A diferença média combinada e o IC de 95% foram calculados usando um método de variância inversa com um modelo de efeitos aleatórios, devido ao pequeno número de estudos, os pequenos grupos e as diferenças nas populações de estudo. Obtivemos a meta-análise para cada resultado, separadamente, usando o software Revman v5 (The Nordic Cochrane Center, Copenhagen, Dinamarca). Funnel (Egger) plot foi realizado para analisar o risco de viés de publicação. Além disso, sub-análises foram realizadas considerando todos os estudos e apenas aqueles publicados.

4 RESULTADOS

4.1 Artigo 1 - Effects of isometric handgrip training on ambulatory blood pressure in normotensive and hypertensive subjects: a systematic review and meta-analysis

ABSTRACT

Background: Although the effects of isometric handgrip training (IHT) on office blood pressure is well established, the effects of this training on ambulatory blood pressure (ABP) still unclear**.** Therefore, the aim of this systematic review and meta-analysis was to analyze the effects of IHT on ABP in normotensive and hypertensive subjects. **Methods:** We conducted a systematic review and meta-analysis of studies with at least 4 weeks duration that investigated the effects of IHT on ABP in normotensive and/or hypertensive subjects. For this, Medline and Web of Science were searched for relevant studies published until July 2020 as well as the gray literature. For each main outcome measure, mean difference (MD) and 95% confidence interval (95% CI) were calculated using an inverse variance method with a random effects model. **Results:** Six trials were included in the systematic review and meta-analysis, totaling 157 participants: 82 IHT, 75 control. The meta-analysis did not identify any significant effect of IHT on 24-hour systolic blood pressure (MD: -2.5 mmHg, 95% CI -5.44 to0.45, p=0.10), asleep (MD: -1.88 mmHg, 95% CI -4.86 to 1.10, p=0.22), and awake (MD: -1.85 mmHg, 95% CI -4.81 to 1.10, p=0.22) and 24-hour diastolic blood pressure (MD: -1.91 mmHg, 95% CI -4.06 to 0.24, p=0.08) and asleep (MD: -1.90 mmHg, 95% CI -4.60 to 0, 81, p=0.17). There was an effect on waking diastolic blood pressure (MD: -2.53 mmHg, 95% CI -4.87 to -0.18, p=0.03). **Conclusion:** In conclusion, current literature indicates that IHT shows reductions on awake diastolic blood pressure, but there were not effects on systolic blood pressure, asleep and 24h diastolic blood pressure.

Keywords: blood pressure, exercise, hypertension

INTRODUCTION

Hypertension is the most prevalent chronic disease in the world, affecting approximately 1.39 billion people, being the first cause of death around the world (1) which were responsible for 17.8 million deaths worldwide in 2017 (2). Physical exercise has been indicated as an adjunct component in the management of blood pressure levels (3). Previous studies have shown that isometric handgrip training (IHT) reduce office systolic blood pressure (SBP) by 5 to 8 mmHg and office diastolic blood pressure (DBP) by approximately 2 to 4 mmHg in both normotensive and hypertensive individuals (4,5). The American Heart Association categorizes IHT as a nonpharmacological intervention for blood pressure-lowering (6), similarly to Exercise and Sports Science Australia (7)and Hypertension Canada (8).

Contrary to the well-established long-term effects of IHT on office blood pressure, the effects of this training mode on ambulatory blood pressure (ABP) is not yet clear. In general, there are few studies with low number of participants and high heterogeneity in the sample and exercise's protocol and just found effects on clinical measurement. For example, Stiller-Moldovan et al. (9) conducted 8-weeks of supervised IHT (three times a week) with 20 hypertensives (11 IHT and 9 Control), whereas Goesller et al.(10) carried out a similar protocol training, but in a home-based setting, in 38 health individuals (22 IHT and 16 control). Farah et al. (11) conducted both training modes (supervised and home-based) for 12 weeks (three times a week) in 30 medicated hypertensive patients (10 per group) and Seidel et al. (12), conducted supervised training protocol for 12 weeks (five times a week) with 24 hypertensive individuals.

Given that the ABP is a better predictor for fatal and non-fatal cardiovascular events than office blood pressure (13,14) it is important to fill this gap. Thus, this systematic review and meta-analysis aim to analyze the effects of IHT on ABP in normotensive and hypertensive subjects.

METHODS

Protocol and registration

This review was conducted according to the Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA) recommendations (15). It was registered in the international database of prospectively registered systematic reviews.

Literature search

We conducted a systematic literature search in PubMed and Web of Science databases from its inception up to June 2021 using the following terms: ‘isometric handgrip training’ and ‘ambulatory blood pressure’. The complete search strategy used for both databases are shown in supplementary document. The reference lists from published original and review articles were searched manually to identify other possible eligible studies. In addition, we performed a search in Clinical Trials database for finished studies without publication (https://clinicaltrials.gov/).

Eligibility criteria

The eligibility criteria were established according to the PICOS (Population, Intervention, Comparator, Outcomes and Setting) question:

Population. This review included studies with adults (18 years or older), both sexes without restrictions regarding of physical activity level and blood pressure classification (normotensive and hypertensive).

Intervention. Only IHT intervention lasting a minimum of four weeks were considered. Each intervention group was considered separately in the meta-analysis, which means that the studies that have investigated the effect of two different types of IHT interventions on ambulatory blood pressure were analyzed individually.

Comparator. Control group was defined as no exercise who carried out their usual daily activities or an attention placebo (Sham group).

Outcomes. The primary outcome of this review was ambulatory blood pressure, which was measured continued blood pressure along of 24 hours pre and post intervention period.

Settings. Randomized controlled trial, nonrandomized controlled trial and crossover studies were considered. No sample size limitation was applied.

Study selection

One reviewer (MSO) conducted the literature search and the results from all databases were downloaded into bibliographic software (EndNote X9; Thompson Reuters, New York, USA). After eliminating duplicates, two independent reviewers (MSO and PHM) screened all records retrieved by the search strategy by title and abstract. The same reviewers then retrieved the full-text of potentially eligible studies and reviewed them in duplicate according to the inclusion criteria. Disagreements between the reviewers were resolved by a third reviewer (BQF).

Data extraction

Data extraction of all eligible study was undertaken separately and in duplicate by two independent reviewers. The extracted data were: i) study characteristics (i.e. design, sample size, health status, sex, age, and training status, ABP), ii) intervention protocol (i.e. type, intensity, weekly frequency, duration, number of sets and recovery interval); iii) outcome measures (instrument, position, duration); iv) changes in ambulatory blood pressure and; v) indices of study quality which was assessed by the Tool for the Assessment of Study Quality and reporting in Exercise (TESTEX) (16) This scale ranges from 0 to 15, and higher scores represent higher methodological quality.

Data analysis

Continuous outcomes were extracted from baseline and post intervention data provided within the individual studies. Authors were contacted for missing information. If reported, the within group mean difference (MD) and SD or 95% confidence interval (CI) were also extracted. If not reported, the within group MD was calculated as post-intervention mean – baseline mean. Missing change score SDs were calculated from pre -and post-SD values, using the following formula: $SD_{change} = \sqrt{[(SD_{pre})^2 + (SD_{post})^2 - 2*corr(pre, post)*SD_{pre}*SD_{post}]}$ (17), for which we used a calculated correlation coefficient (corr) for each outcome, using the pre- and post-SD and the SD of the change of the study of Farah et al., (9) (supervised group) in the following formula: $corr = (SD_{pre}^2 + SD_{post}^2 - SD_{change}^2)/(2 * SD_{pre} * SD_{post})$.

Pooled MD and 95%CI were calculated using an inverse variance method with a random effects model, due the small number of studies, the small study groups and the differences in study populations. We obtained the meta-analysis for each outcome, separately using Revman software v5 (The Nordic Cochrane Centre, Copenhagen,

Denmark). In addition, we performed analysis considering all studies and only those published. Heterogeneity was investigated using Higgins I^2 with scores ranging from 0% to 100% (18). Funnel (Egger) plots were provided to assess the risk of publication bias.

RESULTS

A total of 5,082 studies were identified through the databases, of which 1,142 were excluded by duplicates. Of these, 3,882 were excluded after screening by title and abstract (Figure 1). One study was excluded for not being able to contact the author. After the full reading of the remaining studies, three were selected, (9-11) and Farah et al. (11) study was divided into A and B trials (A – supervised training, B – home-based training). In addition, two more studies were included through the search of the gray literature (19, 20). Thus, seven trials were included in the systematic review and meta-analysis, totaling 157 participants: 82 IHT and 75 control group.

The characteristics of the studies have shown in Table 1. All of the six studies included in this meta-analysis, had hypertensive patients in the sample. Four studies included both sexes (9,11, 19, 20) and one included only men (10). Aged was 30 to 80 years old.

All studies followed the same protocol: four sets of 2 min of isometric contraction, 30% of maximum voluntary contraction, 1 min of interval between sets and alternating arms, but the frequency and duration of training were different. Frequency varied between 3 (9, 11) and 7 (10) days per week, whereas the duration of the training intervention ranged from 8 weeks (9, 10) to 12 weeks (11, 19, 20). In addition, some studies have used supervised training (9, 19, 20) and others applied home-based training (10,11). The methodological quality of the trials ranged from 10 to 12, with a median of 11 out of 15

maximum points in the TESTEX scale. The most prevalent limitations regarding studies reporting were related to the use of intention-to-treat analysis and activity monitoring in the control group, with no studies reporting both. Two studies (9,10) no met the blinding of assessors criteria (28%).

For the outcome of ABP, studies evaluated 24h blood pressure, awake and sleep SBP and DBP. Meta-analysis revealed no significant effect of IHT on SBP (MD: -2.5, 95% IC -5.44-0.45, p=0.10) and DBP (MD: -1.91, 95% IC -4.06- 0.24, p=0.08) over 24 hours. Low heterogeneity was observed for SBP (I^2 = 8%) and DBP (I^2 = 18%) (Figure 2). Figure 3 shown the effect of IHT on blood pressure awake period. The IHT did not show a significant effect in the awake SBP (MD: -1.85, 95% IC -4,81-1.10, p=0,22), but in awake DBP (MD: -2.53, 95% IC -4.87-0.18, p= 0.03) . No heterogeneity was observed for SBP (I^2 = 0%) and high heterogeneity for DBP awake (I^2 = 56%). There was no significant effect of IHT on asleep SBP (MD: -1.88, 95% IC -4.86-1.10, p=0.22) and DBP (MD: -1.90, 95% IC -4.60-0.81, p=0.17) with no heterogeneity for both (I^2 = 0%) (Figure 4).

Sub-analyses considering only published studies showed no effect for SBP (24h - MD: -1.5, 95% IC -6.08-3.07, p=0,67; asleep - MD: -2.40, 95% IC -6.20-1.39, p=0.65; awake - MD: -1.80, 95% IC -5.90-2.29, p=0.47) and DBP (24h - MD: -0.47, 95% IC -3.56- 2.62, p=0.73; asleep - MD: -1.46, 95% IC -4.84-1.93, p=0.78; awake - MD: -0.95, 95% IC -3.23-1.34, p= 0.54) (Electronic Supplementary 2 to 4). Funnel (Egger) plots indicated a low risk of publication bias (Electronic Supplementary Figure 5)

DISCUSSION

The main findings of this meta-analysis were that IHT reduces awake DBP, whereas no effects on SBP (24h, asleep and awake periods) or asleep and 24h DBP were

observed. Previously, Stiller-Moldovan et al. (9) observed no effect on ABP in their study after 8 weeks of IHT, which may be due to the fact that the sample was composed by medicated hypertensive patients with adequate blood pressure control (127/76 mmHg). The same was observed in studies of Goesller et al. (10) with healthy (120/75 mmHg) and Farah et al. (11) with hypertensives (Supervised group: 121/79 mmHg; Home-based: 117/72 mmHg). In fact, it is widely known that patients with higher blood pressure are more responsive to training.

Interestingly, among the studies that have not been published, Palmeira's study showed similar responses to other studies without significant reduction on ABP and also the patients had blood pressure controlled by medication (119/80 mmHg). On the other hand, Andrade et al. included hypertensive patients with obstructive sleep apnea and uncontrolled blood pressure (138/79 mmHg) and observed reductions of -9.9, -8.4 and -9.2 mmHg for SPB, and -8.7, -7.8 and -7.6mmHg for DBP in the 24 hours, in the awake period and in the asleep period, respectively. Therefore, these results reinforce that more severe patients can benefit more from isometric training.

Our study identified a reduction of approximately 2 mmHg on awake DBP and a tendency to reduction 24 h and asleep with similar magnitude. These results were not expected in DBP, as studies are more consistent in observing a reduction in SBP (4, 5). We believe that this result is because Andrade' study performed with hypertensive patients with obstructive sleep apnea and higher baseline blood pressure value. In fact, by withdrawing this study from the analysis, there is also no effect on awake DBP. Therefore, this aspect suggests the need for further studies to increase the power of the analysis.

The mechanisms by which DBP reduced after IHT is not established, but may be due to improvement in endothelial function (21), although unlikely given that the effect of IHT is local rather than systemic (22). In addition, other mechanisms can be considered

as decrease in systemic vascular resistance, improvement in peripheral sympathetic activity, and activation of the renin-angiotensin system (23).

The methodological quality of the trials ranged from 10 to 12, with a median of 11 out of 15 maximum points in the TESTEX scale. This score indicates a moderate-good study design and reporting information. The lack of monitoring the activity of control group and the intention to treat analysis was the main bias of the studies. In addition, only Farah's study has reported adverse effects (joint pain) and one woman from home-based intervention presented dyspnea and tachycardia along the intervention (week 6 and 8, respectively), but with no losses by dropping out the study. Palmeira showed dropout about 50%; similarly, in the study of Farah et al. (11) there was a dropout of 40%, whereas Goesller et al. (10) indicated a dropout of 25%, these dropouts of the studies could influence the statistical power of the analysis.

The American Heart Association categorizes IHT as a nonpharmacological intervention for blood pressure-lowering in hypertensives (6). In fact, this mode of training seems to be promising for blood pressure control in the treatment of hypertension. However, although the reduction on office blood pressure occurs after IHT, our findings demonstrate the need for further studies to attest the effectiveness of this type of training on ABP, a better predictor for fatal and non-fatal cardiovascular events than office blood pressure (13,14). We encourage new studies to use the ambulatory measurement of blood pressure as outcome, due the important relevance of this measure.

Some limitations need to be considered in this systematic review and meta-analysis. First, we have few studies relating the effects of IHT on ABP until now and the number of subjects is small limiting sub-analyzes of the training variables was not possible. The seven trials included to analyzes are from three published studies (with Farah et al., separated in two trials) and more three unpublished studies (Gerage et al with

preliminary data, Andrade et al. are data from one PhD thesis and Palmeira et al is under review). Moreover, one study (12), do not provide the data for our analysis. The included studies did not follow some important methodological procedures, such as regular follow-up of the control subjects, assessment of compliance to the training, attention to changes in other lifestyle factors, lack of medication control, lack of blinded or automated measurements, and no study conducted an intent-to- treat analysis. Finally, study quality analysis was not possible to be performed in unpublished studies.

In conclusion, current literature indicates that IHT shows reductions on awake diastolic blood pressure, but there were no effects on systolic blood pressure, asleep and 24h diastolic blood pressure.

COMPLIANCE WITH ETHICAL STANDARDS

Conflict of interest: The authors declare that they have no conflict of interest.

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TABLES

Table 1: Characteristics of the studies included in the meta-analysis.

Author (Year)	Sample	Groups (n)	Training	Frequency	Duration	Outcomes	Testex
Stille-Moldovan, et. al. (2012)	Hypertensive medicated; ≥ 60 years old	IHT (11) CG (9)	Supervised training; Alternated arms: 4x2min.;1 min. rest interval at 30% MVC	3 x/ weeks	8 weeks	24h mean: SBP and DBP Daytime: SBP and DBP Night-time: SBP and DBP	11
Farah, et. al. (2018) - A	Hypertensive medicated 38–79 years old, 70% female	SUP (10) CG (10)	Supervised training; Alternated arms: 4 × 2 min; 1 min at 30% MVC	3 x/ weeks	12 weeks	24h: SBP, DBP and MBP Awake: SBP, DBP and MBP Asleep: SBP, DBP and MBP	12
Farah, et. al. (2018) - B	Hypertensive medicated; 38–79 years old, 70% female	HB (10) CG (10)	Home-based training; Alternated arms: 4 × 2 min; 1 min rest interval at 30% MVC	3 x/ weeks	12 weeks	24h: SBP, DBP and MBP Awake: SBP, DBP and MBP Asleep: SBP, DBP and MBP	12
Goessler, et. al. (2018)	Healthy Middle aged 33 years old; 48.3% female	IHG (18) CG (14)	Home-based training; Alternated arms: 4x2min.; 1 min. rest interval at 30% MVC	7 x/ weeks	8 weeks	Awake: SBP and DBP Asleep: SBP and DBP	11
Seidel et al., (2021)	Hypertensive medicated, 41% female, 60,7±9	IHT (24) CG (23)	Home-based training; Alternated arms: 4x2min; 1 min. rest interval at 30% MVC	5x/weeks	12 weeks	24h: SBP and DBP Awake: SBP and DBP Asleep: SBP and DBP	10
Andrade et. al. (Unpublished)	Hypertensive non-medicated; 57.1% female; 57 ± 9 years old	IHT (7) CG (7)	Supervised training; Alternated arms: 4 x2min.; 1 min. rest interval at 30% MVC	3 x/weeks	12 weeks	24h: SBP and DBP Awake: SBP and DBP Asleep: SBP and DBP	NA
Gerage et al. (Unpublished)	Hypertensive medicated; 87.1% female; 55±14 years old	IHT (11) CG (9)	Supervised training; Alternated arms: 4 × 2 min; 1 min at 30% MVC	3 x/weeks	12 weeks	24h: SBP and DBP Awake: SBP and DBP Asleep: SBP and DBP	NA
Palmeira et. al. (Unpublished)	Hypertensive medicated 30–79 years old, 70% female	IHT (15) CG (16)	Supervised training; Alternated arms: 4x2min.;1 min. rest interval at 30% MVC	3 x/ weeks	12 weeks	24h: SBP and DBP Awake: SBP and DBP Asleep: SBP and DBP	NA

CG, control group; HB, Home-based training; IHT, isometric handgrip training; MVC, maximal voluntary -contraction; SUP, supervised training; BP, SBP, Systolic blood pressure; DBP, Diastolic blood pressure; MBP, Mean blood pressure. NA – not applicable.

FIGURES

Figure 1. Flow diagram of the search process.

Figure 2. Results of the meta-analysis and forest plots for 24 hours systolic (top) and diastolic (bottom) blood pressure in normotensive and hypertensive subjects. SD standard deviation; CI confidence interval. Farah 2018 (a)—"Supervised versus Control" and Farah 2018 (b) "Home-based versus Control". Gray literature – Andrade et al, Gerage et al and Palmeira et al.

Figure 3. Results of the meta-analysis and forest plots for awake systolic (top) and diastolic (bottom) blood pressure in normotensive and hypertensive subjects. SD standard deviation; CI confidence interval. Farah 2018 (a)—"Supervised versus Control" and Farah 2018 (b) "Home-based versus Control". Gray literature – Andrade et al, Gerage et al and Palmeira et al.

Figure 4. Results of the meta-analysis and forest plots for asleep systolic (top) and diastolic (bottom) blood pressure in normotensive and hypertensive subjects. SD standard deviation; CI confidence interval. Farah 2018 (a)—"Supervised versus Control" and Farah 2018 (b) "Home-based versus Control". Gray literature – Andrade et al, Gerage et al and Palmeira et al.

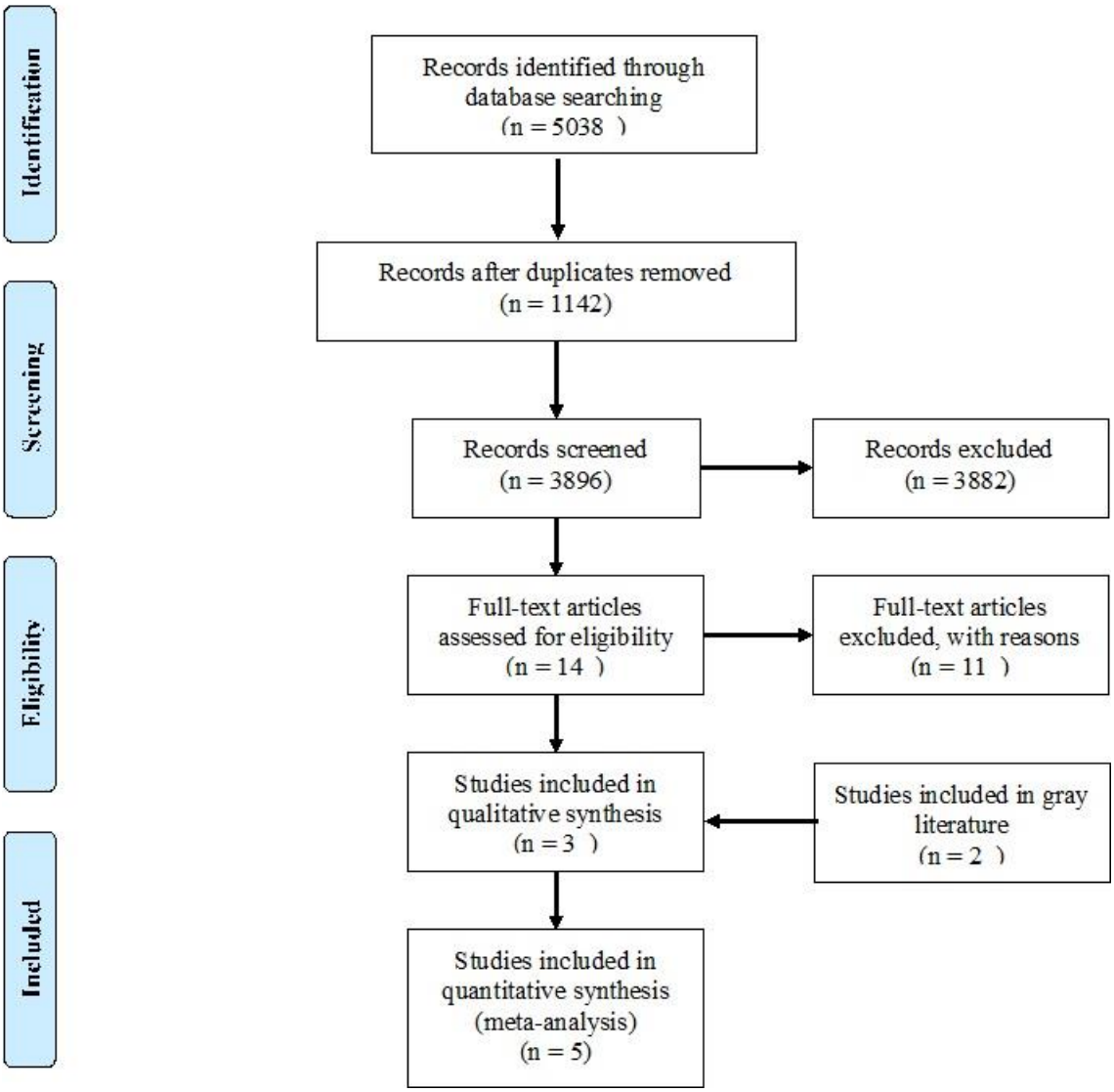

Identification
Screening
Eligibility
Included
Records identified through database searching (n = 5038)
Records after duplicates removed (n = 1142)
Records screened (n = 3896)
Records excluded (n = 3882)
Full-text articles assessed for eligibility (n = 14)
Full-text articles excluded, with reasons (n = 11)
Studies included in qualitative synthesis (n = 3)
Studies included in gray literature (n = 2)
Studies included in quantitative synthesis (meta-analysis) (n = 5)

Figure 1.

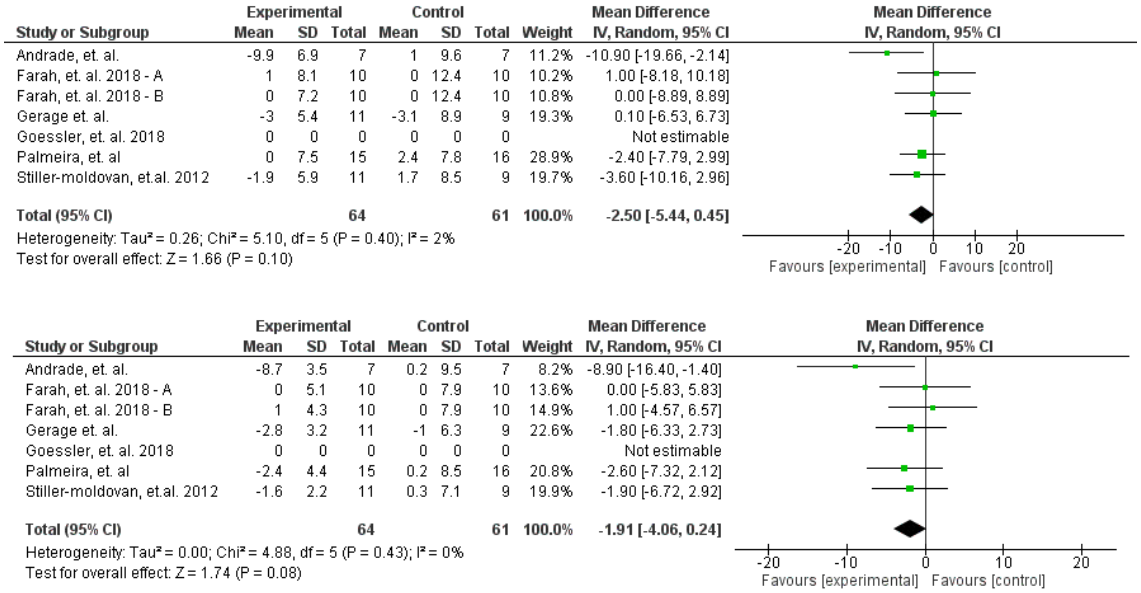
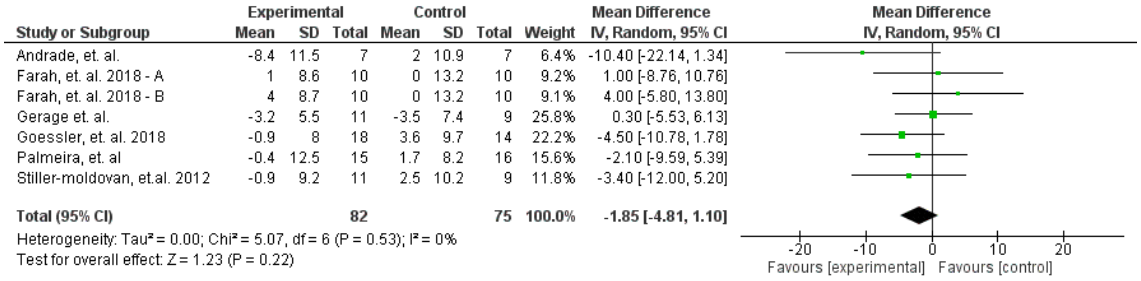

Experimental
Control
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
Andrade, et. al. -9.9 6.9 7 1 9.6 7 11.2% -10.90 [-19.66, -2.14]
Farah, et. al. 2018 - A 1 8.1 10 0 12.4 10 10.2% 1.00 [-8.18, 10.18]
Farah, et. al. 2018 - B 0 7.2 10 0 12.4 10 10.8% 0.00 [-8.89, 8.89]
Gerage et. al. -3 5.4 11 -3.1 8.9 9 19.3% 0.10 [-6.53, 6.73]
Goessler, et. al. 2018 0 0 0 0 0 0 Not estimable
Palmeira, et. al 0 7.5 15 2.4 7.8 16 28.9% -2.40 [-7.79, 2.99]
Stiller-moldovan, et.al. 2012 -1.9 5.9 11 1.7 8.5 9 19.7% -3.60 [-10.16, 2.96]
Total (95% CI) 64 61 100.0% -2.50 [-5.44, 0.45]
Heterogeneity: Tau² = 0.26; Chi² = 5.10, df = 5 (P = 0.40); I² = 2%
Test for overall effect: Z = 1.66 (P = 0.10)
-20 -10 0 10 20
Favours [experimental] Favours [control]
Experimental
Control
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
Andrade, et. al. -8.7 3.5 7 0.2 9.5 7 8.2% -8.90 [-16.40, -1.40]
Farah, et. al. 2018 - A 0 5.1 10 0 7.9 10 13.6% 0.00 [-5.83, 5.83]
Farah, et. al. 2018 - B 1 4.3 10 0 7.9 10 14.9% 1.00 [-4.57, 6.57]
Gerage et. al. -2.8 3.2 11 -1 6.3 9 22.6% -1.80 [-6.33, 2.73]
Goessler, et. al. 2018 0 0 0 0 0 0 Not estimable
Palmeira, et. al -2.4 4.4 15 0.2 8.5 16 20.8% -2.60 [-7.32, 2.12]
Stiller-moldovan, et.al. 2012 -1.6 2.2 11 0.3 7.1 9 19.9% -1.90 [-6.72, 2.92]
Total (95% CI) 64 61 100.0% -1.91 [-4.06, 0.24]
Heterogeneity: Tau² = 0.00; Chi² = 4.88, df = 5 (P = 0.43); I² = 0%
Test for overall effect: Z = 1.74 (P = 0.08)
-20 -10 0 10 20
Favours [experimental] Favours [control]

Figure 2


Experimental
Control
Mean Difference
Mean Difference
Study or Subgroup
Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
Andrade, et. al. -8.4 11.5 7 2 10.9 7 6.4% -10.40 [-22.14, 1.34]
Farah, et. al. 2018 - A 1 8.6 10 0 13.2 10 9.2% 1.00 [-8.76, 10.76]
Farah, et. al. 2018 - B 4 8.7 10 0 13.2 10 9.1% 4.00 [-5.80, 13.80]
Gerage et. al. -3.2 5.5 11 -3.5 7.4 9 25.8% 0.30 [-5.53, 6.13]
Goessler, et. al. 2018 -0.9 8 18 3.6 9.7 14 22.2% -4.50 [-10.78, 1.78]
Palmeira, et. al -0.4 12.5 15 1.7 8.2 16 15.6% -2.10 [-9.59, 5.39]
Stiller-moldovan, et.al. 2012 -0.9 9.2 11 2.5 10.2 9 11.8% -3.40 [-12.00, 5.20]
Total (95% CI) 82 75 100.0% -1.85 [-4.81, 1.10]
Heterogeneity: Tau² = 0.00; Chi² = 5.07, df = 6 (P = 0.53); I² = 0%
Test for overall effect: Z = 1.23 (P = 0.22)
-20 -10 0 10 20
Favours [experimental] Favours [control]

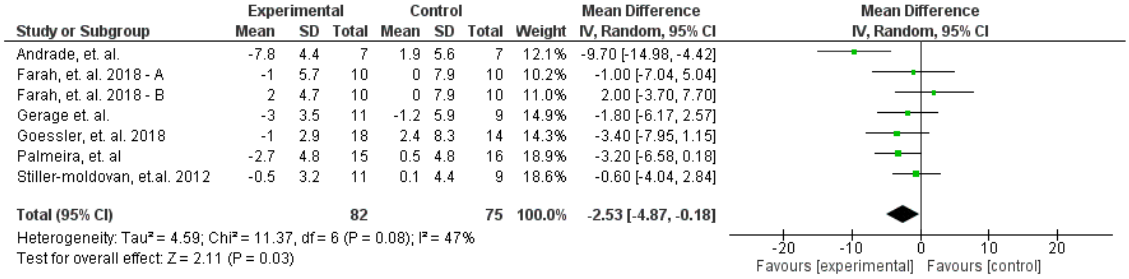

Experimental
Control
Mean Difference
Mean Difference
Study or Subgroup
Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
Andrade, et. al. -7.8 4.4 7 1.9 5.6 7 12.1% -9.70 [-14.98, -4.42]
Farah, et. al. 2018 - A -1 5.7 10 0 7.9 10 10.2% -1.00 [-7.04, 5.04]
Farah, et. al. 2018 - B 2 4.7 10 0 7.9 10 11.0% 2.00 [-3.70, 7.70]
Gerage et. al. -3 3.5 11 -1.2 5.9 9 14.9% -1.80 [-6.17, 2.57]
Goessler, et. al. 2018 -1 2.9 18 2.4 8.3 14 14.3% -3.40 [-7.95, 1.15]
Palmeira, et. al -2.7 4.8 15 0.5 4.8 16 18.9% -3.20 [-6.58, 0.18]
Stiller-moldovan, et.al. 2012 -0.5 3.2 11 0.1 4.4 9 18.6% -0.60 [-4.04, 2.84]
Total (95% CI) 82 75 100.0% -2.53 [-4.87, -0.18]
Heterogeneity: Tau² = 4.59; Chi² = 11.37, df = 6 (P = 0.08); I² = 47%
Test for overall effect: Z = 2.11 (P = 0.03)
-20 -10 0 10 20
Favours [experimental] Favours [control]

Figure 3

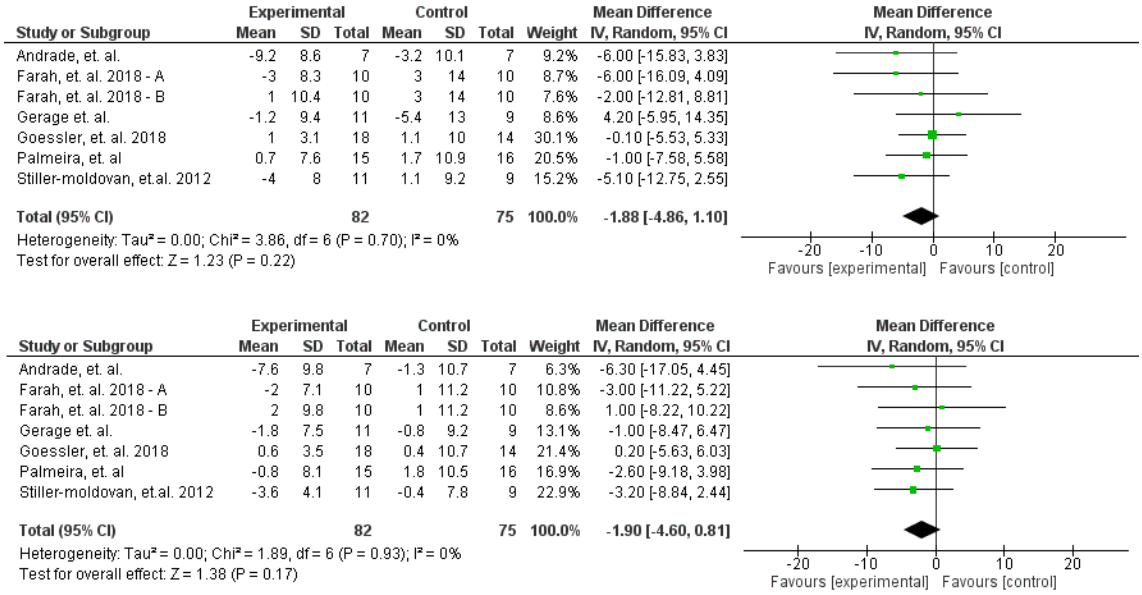

Experimental
Control
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
Andrade, et. al. -9.2 8.6 7 -3.2 10.1 7 9.2% -6.00 [-15.83, 3.83]
Farah, et. al. 2018 - A -3 8.3 10 3 14 10 8.7% -6.00 [-16.09, 4.09]
Farah, et. al. 2018 - B 1 10.4 10 3 14 10 7.6% -2.00 [-12.81, 8.81]
Gerage et. al. -1.2 9.4 11 -5.4 13 9 8.6% 4.20 [-5.95, 14.35]
Goessler, et. al. 2018 1 3.1 18 1.1 10 14 30.1% -0.10 [-5.53, 5.33]
Palmeira, et. al 0.7 7.6 15 1.7 10.9 16 20.5% -1.00 [-7.58, 5.58]
Stiller-moldovan, et.al. 2012 -4 8 11 1.1 9.2 9 15.2% -5.10 [-12.75, 2.55]
Total (95% CI) 82 75 100.0% -1.88 [-4.86, 1.10]
Heterogeneity: Tau² = 0.00; Chi² = 3.86, df = 6 (P = 0.70); I² = 0%
Test for overall effect: Z = 1.23 (P = 0.22)
-20 -10 0 10 20
Favours [experimental] Favours [control]
Experimental
Control
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
Andrade, et. al. -7.6 9.8 7 -1.3 10.7 7 6.3% -6.30 [-17.05, 4.45]
Farah, et. al. 2018 - A -2 7.1 10 1 11.2 10 10.8% -3.00 [-11.22, 5.22]
Farah, et. al. 2018 - B 2 9.8 10 1 11.2 10 8.6% 1.00 [-8.22, 10.22]
Gerage et. al. -1.8 7.5 11 -0.8 9.2 9 13.1% -1.00 [-8.47, 6.47]
Goessler, et. al. 2018 0.6 3.5 18 0.4 10.7 14 21.4% 0.20 [-5.63, 6.03]
Palmeira, et. al -0.8 8.1 15 1.8 10.5 16 16.9% -2.60 [-9.18, 3.98]
Stiller-moldovan, et.al. 2012 -3.6 4.1 11 -0.4 7.8 9 22.9% -3.20 [-8.84, 2.44]
Total (95% CI) 82 75 100.0% -1.90 [-4.60, 0.81]
Heterogeneity: Tau² = 0.00; Chi² = 1.89, df = 6 (P = 0.93); I² = 0%
Test for overall effect: Z = 1.38 (P = 0.17)
-20 -10 0 10 20
Favours [experimental] Favours [control]

Figure 4

ELECTRONIC SUPPLEMENTARY

Electronic Supplementary 1. Prisma Checklist

PRISMA 2020 Main Checklist

Topic	No.	Item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 3, Line 11
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 3, Line 23
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 4, Line 18
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 4, Line 9
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Eletronic Supplementary 1
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 5 Line 11

Topic	No.	Item	Location where item is reported
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 5 Line 21
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 6, Line 6
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 6, Line 10
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 6, Line 23
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 6, Line 17
I	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item 5)).	Page 6, Line 23
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 6, Line 23
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Table 1

Topic	No.	Item	Location where item is reported
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 6, Line 18
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Page 6, Line 22
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Page 6, Line 19
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 6, line 23
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page 6, Line 16
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 7, Line 2
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Page 7, Line 3
Study characteristics	17	Cite each included study and present its characteristics.	Page 7, Line 11
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Page 8, Line 16
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Page 8, Line 2
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Electronic Supplementary 5

Topic	No.	Item	Location where item is reported
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Electronic Supplementary 2, 3, 4
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	No
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	No
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	No
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Electronic Supplementary 2, 3, 4
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 9,10
	23b	Discuss any limitations of the evidence included in the review.	Page 11, Line 17
	23c	Discuss any limitations of the review processes used.	Page 11, Line 23
	23d	Discuss implications of the results for practice, policy, and future research.	Page 11, Line 15
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	No
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Electronic Supplementary 1
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	No

Topic	No.	Item	Location where item is reported
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 12, Line 12
Competing interests	26	Declare any competing interests of review authors.	Page 12 Line 9
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	No

PRISMA Abstract Checklist

Topic	No.	Item	Reported?
TITLE			
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	No
Synthesis of results	6	Specify the methods used to present and synthesize results.	Yes
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Yes
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	No
Interpretation	10	Provide a general interpretation of the results and important implications.	No
OTHER			
Funding	11	Specify the primary source of funding for the review.	No
Registration	12	Provide the register name and registration number.	No

Electronic supplementary 2 . Search strategy

1 ((((((((((((("isometric contraction"[MeSH Terms] OR "resistance training"[MeSH Terms]) OR "isometric training"[Title/Abstract]) OR "isometric resistance training"[Title/Abstract]) OR "hand grip"[Title/Abstract]) OR "grip strength"[Title/Abstract]) OR "handgrip"[Title/Abstract]) OR "dynamometer"[Title/Abstract]) OR "isometric handgrip"[Title/Abstract]) OR "handgrip exercise"[Title/Abstract]) OR "isometric grip"[Title/Abstract]) OR "static grip"[Title/Abstract]) OR "forearm grip"[Title/Abstract]) OR "isometric exercise training"[Title/Abstract]) OR "resistance training"[Title/Abstract])

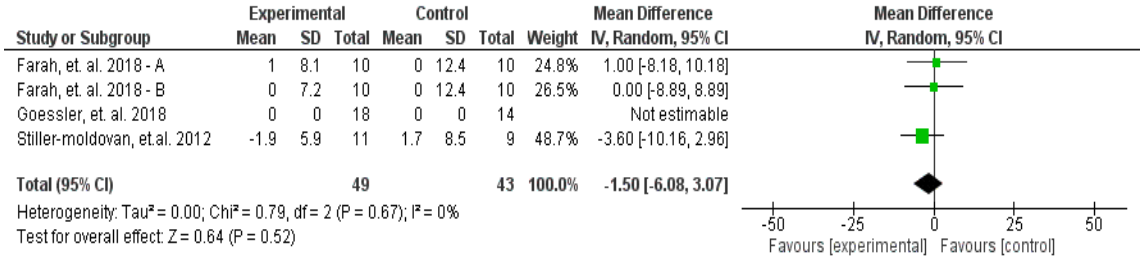
#2 (((((((("blood pressure"[MeSH Terms] OR "blood pressure determination"[MeSH Terms]) OR "arterial pressure"[MeSH Terms]) OR "normotension"[Title/Abstract]) OR "arterial blood pressure"[Title/Abstract]) OR "blood pressure monitoring, ambulatory"[MeSH Terms]) OR "ambulatory blood pressure"[Title/Abstract]) OR "blood pressure"[Title/Abstract])

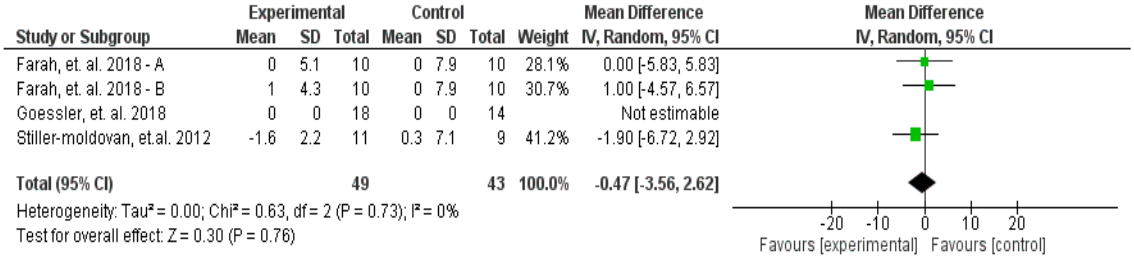
#3 ((((("aging"[MeSH Terms] OR "aged"[MeSH Terms]) OR "adult"[MeSH Terms]) OR "normotensive"[Title/Abstract]) OR "hypertensive"[Title/Abstract])))

#4 ((("systematic review"[Publication Type] OR "guideline"[Publication Type]) OR "meta-analysis"[Publication Type]) OR "review"[Publication Type])

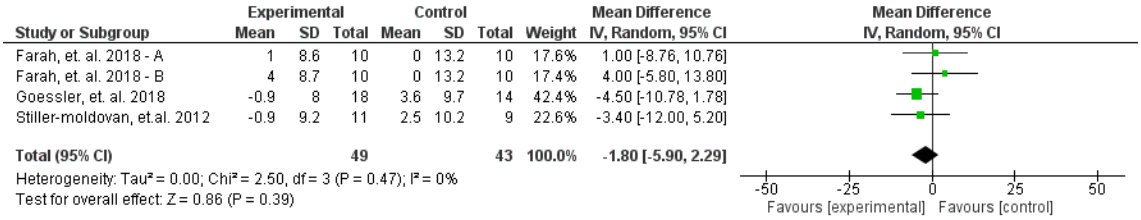
#1 AND #2 AND #3AND #4 NOT

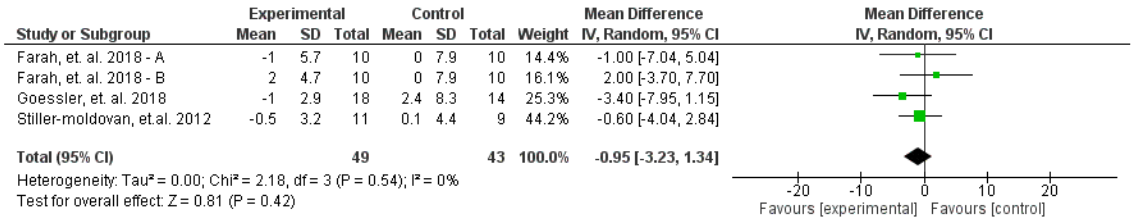
Electronic supplementary 3. Results of the meta-analysis and forest plots for 24 hours systolic (top) and diastolic (bottom) blood pressure in normotensive and hypertensive subjects in published studies. SD standard deviation; CI confidence interval. Farah 2018 (a)— "Supervised versus Control" and Farah 2018 (b) "Home-based versus Control".



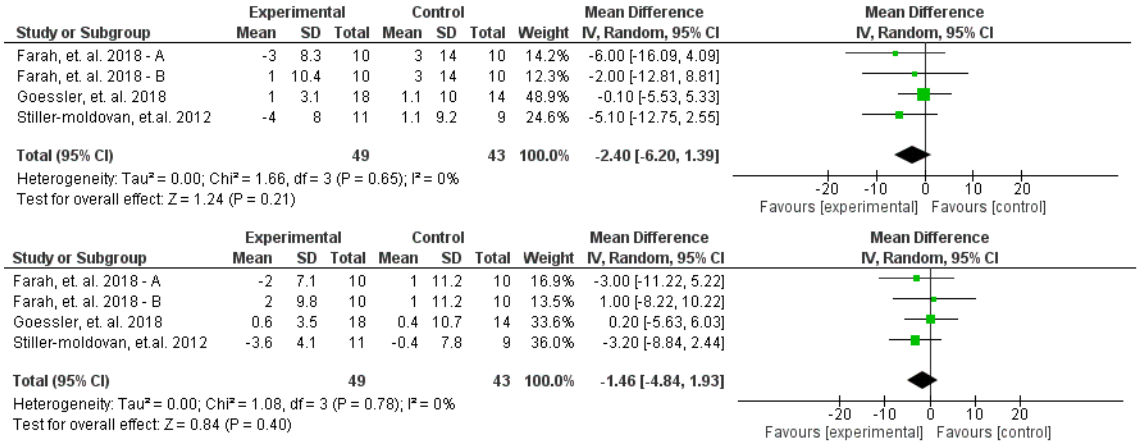


Electronic supplementary 4. Results of the meta-analysis and forest plots for awake systolic (top) and diastolic (bottom) blood pressure in normotensive and hypertensive subjects in published studies. SD standard deviation; CI confidence interval. Farah 2018 (a)—"Supervised versus Control" and Farah 2018 (b) "Home-based versus Control".

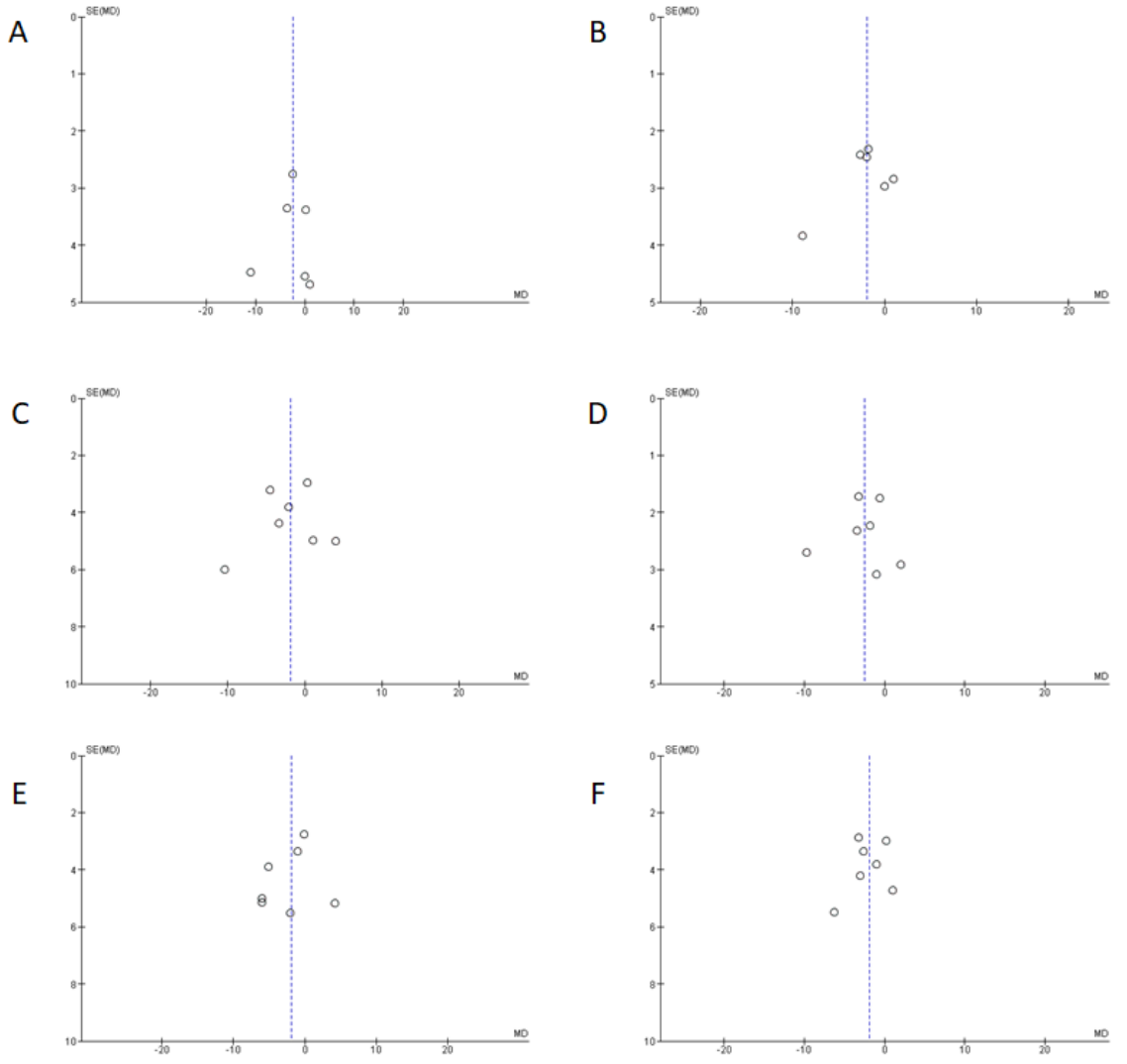




Electronic supplementary 5. Results of the meta-analysis and forest plots for asleep systolic (top) and diastolic (bottom) blood pressure in normotensive and hypertensive subjects in published studies. SD standard deviation; CI confidence interval. Farah 2018 (a)—"Supervised versus Control" and Farah 2018 (b) "Home-based versus Control".



Electronic Supplementary 6. Funnel plot for evaluation of publication bias of all studies. A - 24 hours systolic blood pressure, B - 24 hours diastolic blood pressure, C - awake systolic blood pressure, D – awake diastolic blood pressure; E – asleep systolic blood pressure and F – asleep diastolic blood pressure.



4 CONSIDERAÇÕES FINAIS

Embora presente em várias diretrizes como possível ferramenta adjuvante no controle e prevenção da hipertensão arterial, o TIH, sobre a medida ambulatorial da pressão arterial não se mostrou efetivo segundo nossa revisão sistemática com metanálise, contudo há ainda poucos estudos sobre essa variável específica, o que provavelmente limitou o poder da análise. Novos estudos são necessários avaliando as respostas do TIH nessa variável importante e comumente utilizada na prática clínica.

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